Activator-Inhibitor Model for Seashell Pattern Formation

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Abstract

Seashells exhibit diversified types of pigmentation patterns on their surfaces. While pattern formation is a ubiquitous phenomena in many different systems, seashells are a rare type of system that can record the formation and time evolution of the spatial pattern through calcium deposition [1]. This essay mainly reviews the activator-inhibitor model for seashell pattern formation, where spatial variation arises from diffusion [2]. We derive the instability condition for a uniform state, which initiates the pattern formation, through linear stability analysis. Based on this model, computer simulations are performed and the results match well with observation in nature, which are shown in several examples [3]. Furthermore, we review the application of the activator-inhibitor model to many other systems. Though extensive literature can be found on this topic, many features of seashell patterns and their molecular basis remain unexplained while some others are still in debate [1][4].

1 Introduction

Many invertebrates, such as snails and clams, have mollusc shells as their exoskeletons to support their body structure and protect their soft inner parts. Varieties of shapes and surface patterns from seashells are observed. Some of them are similar to patterns formed in other physical and biological systems. While there are many patterned features of seashells, we will focus on the pigmentation patterns on the shell surface. During the growing process of the animal, the shell pattern is formed gradually through deposition of some calcium substance containing certain pigments on the front edge. In most cases, we can approximate the growing front by a one-dimensional dynamical system, where the underlying molecular interactions are expressed through the choice of pigments [1]. Therefore, the evolutionary history of this one-dimensional system is recorded as a two-dimensional pattern along the growing direction, neglecting the curvature of the shell. Many scientists have been working on the formation mechanism of these patterns and seeking their similarities to other dynamical systems, such as Turing patterns widely observed in nature and even in inorganic systems [5]. Hence, in this paper, the subject of our interest is a one-dimensional reaction-diffusion system containing two species and its time evolution.

1.1 Seashell patterns as a dynamical system

By treating the seashell growing front as a coupled reaction-diffusion system, we assume that the dominant processes are production, diffusion and spontaneous decay of species and the interaction merely between species, instead of being driven by external forces. One reason for this assumption is the lack of selective pressure on the seashell patterns. Some clams live underground and their patterns are thus not visible, while some others have patterns on the inner side of their shells. The patterns on some individuals among the same species, even those living under similar conditions, vary drastically [1]. In addition, experiments find that the shell pattern can change significantly in reaction to varying environmental conditions, without endangering the species. This further confirms the animals' survival does not have a strong dependence on the shell patterns, and reveals the lack of a strong regulation on patterns at a genetic or physiological level [1]. The arguments above allow us to make an effective model of seashell patterns as a dynamical system of species related to the expression of different pigments, without knowing the details of the underlying biochamical mechanisms [1].

1.2 Patterns emerging from a uniform state

For a diffusive system without interactions, a spatially uniform state is stable. On the other hand, if a nonlinear dynamical system has a stable steady point, it also has a

uniform state at the steady point. However, in certain reaction-diffusion systems, the diffusion process and the reactions between species create a linear instability for the uniform state, which can be analyzed by linear stability analysis [5]. Ordered states, some of which exhibit periodic patterns, emerge from the breaking of translational symmetry by this linear instability.

1.3 Activator-inhibitor model

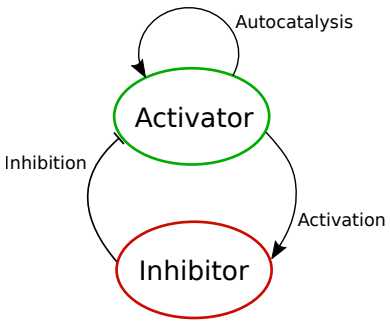

Figure 1: Basic mechanism of activator-inhibitor systems

In this essay, we will mainly review the work on the activator-inhibitor model for seashell pattern formation. This model describes a reaction-diffusion system of two species: a localized activator promoting the production of both species, and a rapidly diffusing inhibitor decelerating the growth of the activator [5], illustrated by figure 1. Because of the self-enhancement, the local density of the activator tends to increase futher when elevated by a small local perturbation. This will also promote the production of the inhibitor, which diffuses away quickly, while the activator can accumulate if its motility is much less. Intuitively, a local maximum of activator density will form, surrounded by an evenly increasing density of the inhibitor within a characteristic length of its diffusion. The inhibition prevents another local maximum of the activator from forming within the close neighbourhood of the first maximum; but when it is far enough, another local maximum can form following the same mechanism. Therefore, a spatially periodic pattern can form [1]. Other types of patterns, such as temporal patterns generated by oscillations of population can be explained by our more familiar predator-prey model. The quantitative analysis and variations of the activator-inhibitor model are shown in the next section.

2 Methods and results

In this section, we explain the mathematical contruction of the activator-inhibitor model, and show how such a system allows patterns to emerge.

2.1 Mathematical model of activator-inhibitor system

The activator-inhibitor model describes a reaction-diffusion system with two species that allows spatial patterns to form. The activator calalyzes the production of itself and the inhibitor, but only in a short distance. The inhibitor suppresses the production of the activator and influences in a longer range through a much faster diffusion

than that of the activator [1]. The two species are represented by two coupled fields that specify the density of species at each point. Here, we write the activator and inhibitor fields as $a(x,t)$ and $h(x,t)$, respectively, so the evolution of the system will be two coupled PDEs. Depending on the specific system, several mathematical forms of the activator-inhibitor model have been proposed since Turing first constructed the prototypical model for chemical system in 1952 [5]. Here, we introduce the Gierer-Meinhardt model to model seashell patterns, proposed by Alfred Gierer and Hans Meinhardt in 1972 and developed since then [2]:

$$\begin{aligned} \frac{\partial a}{\partial t} &= \rho_a \frac{a^2}{h} - \mu_a a + D_a \frac{\partial^2 a}{\partial x^2} + \delta_a \\ \frac{\partial h}{\partial t} &= \rho_h a^2 - \mu_h h + D_h \frac{\partial^2 h}{\partial x^2} + \delta_h \end{aligned} \tag{1}$$

In the first equation of 1, $\rho_a a^2/h$ is the growth term of the activator, where ρ_a is the growth rate, a^2 accounts for the self-catalytic effect giving the higher power than exponential growth, and $1/h$ represents the inhibition. The term $-\mu_a a$ is a natural decay of population and the third term is the diffusion of the activator. The last term δ_a is a small constant external source of the activator, which initiates the generation of new activator peaks at empty space. The second equation for the inhibitor has similar interpretation, but the growth process is only catalyzed by the local activator without inhibition. This model also requires the difference of diffusivity, $D_h >> D_a$, and fast adaption of the inhibitor to change of activator density, which is sometimes realized by imposing $\mu_h > \mu_a$. Note that the diffusion here is an approximation of other motile behaviours of agents in many situations.

The activator-substrate model is a variation of the activator-inhibitor model described by equation 1. In this case, growth of the activator consumes a substrate represented by a field $s(x,t)$, and therefore is limited by the amount of substrate available locally, instead of a direct antagonistic influence from the inhibitor. The substrate cannot reproduce by itself, but relies on a external source to create and inject it into the system. Mathematically, this mechanism is formulated by the following PDEs [2]:

$$\begin{aligned} \frac{\partial a}{\partial t} &= \rho s a^2 - \mu_a a + D_a \frac{\partial^2 a}{\partial x^2} + \delta_a \\ \frac{\partial s}{\partial t} &= -\rho s a^2 - \nu s + D_s \frac{\partial^2 s}{\partial x^2} + \delta \end{aligned} \tag{2}$$

where we again require the substrate to diffuse faster than the activator, $D_s >> D_a$. The last term $\delta = \delta(x)$ is usually a spatial distribution of a steady external source, instead of a spatially uniform constant.

The models above assume an arbitrary capacity of the system for all species, which is an ideal case, so another modification is imposing a saturation condition on the activator. This is accomplished by substituting a^2 in the growth term with $\frac{a^2}{1+\kappa a^2} + \rho_0$ [2]. One physical example of the saturation limit is the number of enzymes available

in cells for the catalytic effect from the activator [1].
The original Gierer-Meinhardt model was proposed for general biological pattern formation, main ideas introduced above. For patterns on some seashells, empirical observation of patterns suggests that some global regulation on the total amount of the activator might act on the system through some hormone-like substance $c(x,t)$ [3]. Including the saturation effect, these systems can be described by:

$$\begin{aligned}\frac{\partial a}{\partial t} &= \frac{\rho_a}{h+h_0}\left(\frac{a^2}{1+\kappa a^2}+\delta_a\right)-\mu_a a+D_a\frac{\partial^2 a}{\partial x^2}\\ \frac{\partial h}{\partial t} &= \rho_h\frac{a^2}{1+\kappa a^2}-\frac{\mu_h h}{c}+D_h\frac{\partial^2 h}{\partial x^2}+\delta_h\\ \frac{\partial c}{\partial t} &= \frac{\rho_c}{L}\int_0^L a dx-\mu_c c\end{aligned} \tag{3}$$

where h_0 is a base inhibition effect, and the global control of the activator is indirectly imposed through the decay term of the inhibitor.

2.2 Linear stability analysis

A spatial pattern can form only when all uniform steady states are unstable. Here, we first introduce linear stability analysis, show possible instability in a general diffusion-reaction system [6] and at last apply it to the activator-inhibitor model of our interest. Suppose we have a one-dimensional dynamical system described by a field $u(x,t)$, whose time evolution locally follows the ODE,

$$\frac{\partial u}{\partial t}=f(u). \tag{4}$$

If there is no interaction between neighbouring sites through diffusion, then for a given position point x, the evolution of $u(x,t)$ depends only on the initial condition $u(x,0)$. The system might reach a steady point along the evolutionary trajectory if there exists u_0 such that $\frac{\partial u}{\partial t}|_{u=u_0}=f(u_0)=0$. However, a steady point is only stable to small perturbation if $f'(u_0)<0$. This is equivalent to linearizing the system around the steady point u_0,

$$\frac{\partial u}{\partial t}=f'(u_0)(u-u_0)+\mathcal{O}((u-u_0)^2), \tag{5}$$

and by solving the linear ODE we can see that the solution blows up as time increases if $f'(u_0)>0$, and stablizes at u_0 if $f'(u_0)<0$.
Genenalizing to a coupled system with n species, we have $\mathbf{u}=(u^0,u^1,...,u^n)$ and

$$\frac{\partial \mathbf{u}}{\partial t}=\mathbf{F}(\mathbf{u})\approx\mathbf{J}(\mathbf{u}-\mathbf{u}_0),\quad \mathbf{u}\to\mathbf{u}_0, \tag{6}$$

where the Jacobian $\mathbf{J} \equiv \frac{\partial \mathbf{F}}{\partial \mathbf{u}}|_{\mathbf{u}=\mathbf{u}_0}$ and $\mathbf{F}(\mathbf{u}_0) = \mathbf{0}$. The condition for $\mathbf{u}_0$ to be a stable state is that all the eigenvalues of $\mathbf{J}$ are negative. In a system with two-species like the activator-inhibitor model, by solving the eigenvalue problem directly, this can also be interpreted as the conditions

$$tr(\mathbf{J}) < 0, \quad det(\mathbf{J}) > 0. \tag{7}$$

If a system has a single steady point $\mathbf{u}_0$ satisfying the statbility condition above, every point of the system will eventually stabilize to this point and thus form a stable uniform state.

Now let's introduce a diffusion process and analyze a two-species system as an example. For a chemical reaction, the diffusion term has a straightforward origin, but in many other contexts, it is an approximation of the motility of the species or other long-range interactions.

Suppose we have two species $u(x,t)$ and $v(x,t)$ following

$$\begin{aligned} \partial_t u &= D_1 \partial_x^2 u + f(u,v) \\ \partial_t v &= D_2 \partial_x^2 v + g(u,v) \end{aligned} \tag{8}$$

and suppose there exists a stable steady point (u_0, v_0) if there is no diffusion, i.e.,

$$\mathbf{J} \equiv \begin{bmatrix} a & b \\ c & d \end{bmatrix} = \begin{bmatrix} \partial_u f & \partial_v f \\ \partial_u g & \partial_v g \end{bmatrix}_{(u_0,v_0)} \tag{9}$$

satisfies conditions 7.

In order to show that the diffusion terms can possibly knock the system out of the uniform stable state, we linearize the Laplacian around $\mathbf{u}_0$, which is equivalent to solving

$$\partial_x^2 \mathbf{w} + \lambda \mathbf{w} = 0 \tag{10}$$

where $\mathbf{w} = (u - u_0, v - v_0)$, and $\mathbf{D} = \begin{bmatrix} D_1 & 0 \\ 0 & D_2 \end{bmatrix}$. By separation of variables, we can obtain $\lambda > 0$ from the time-dependent factor. Hence we can solve $\lambda = k^2$, where $k = \frac{n\pi}{L}$, L being the system size. This gives

$$\partial_t \mathbf{w} = (-k^2 \mathbf{D} + \mathbf{J})\mathbf{w} \tag{11}$$

Note that $tr(-k^2\mathbf{D} + \mathbf{J}) < 0$ is automatically satisfied, so we need to set $det(-k^2\mathbf{D} + \mathbf{J}) < 0$ to break the stability condition 7,

$$det(-k^2\mathbf{D} + \mathbf{J}) = D_1 D_2 k^4 - (D_1 d + D_2 a)k^2 + ad - bc < 0 \tag{12}$$

Then a necessary condition for inequality 12 to have a solution is

$$\frac{D_1}{D_2} d^2 + \frac{D_2}{D_1} a^2 + (4bc - 2ad) > 0 \tag{13}$$

which is possible to hold when the ratio of two diffusion constants is far enough away from one. The first momentum mode to become unstable is $k = \sqrt{\frac{D_1 d + D_2 a}{2 D_1 D_2}}$ if $D_1 d + D_2 a > 0$. These k-modes are oscillators in space, and are one of the causes for the system to form spatial patterns [6].
Now we apply linear stability analysis to the basic activator-inhibitor model following equation 1 and use u for the activator and v for the inhibitor. First to find the steady uniform state, we set $f(u, v) = g(u, v) = 0$, and find $v = \frac{\rho_h u^2 + \delta_h}{\mu_h}$ and

$$\mu_a \rho_h u^3 - (\mu_h \rho_a + \delta_a \rho_h) u^2 + \mu_a \delta_h u - \delta_a \delta_h = 0 \tag{14}$$

Notice that equation 14 has at least a positive solurion because the left hand side is negative when evaluating at $u = 0$. Call the steady solution (u_0, v_0), we can find the Jacobian for the linearized term:

$$\mathbf{J} = \begin{bmatrix} a & b \\ c & d \end{bmatrix} = \begin{bmatrix} \partial_u f & \partial_v f \\ \partial_u g & \partial_v g \end{bmatrix}_{(u_0, v_0)} = \begin{bmatrix} \frac{2\rho_a u_0}{v_0} - \mu_a & -\frac{\rho_a u_0^2}{v_0^2} \\ 2\rho_h u_0 & -\mu_h \end{bmatrix} \tag{15}$$

Imposing conditions 7, we require $a + d < 0$ and $ad - cd > 0$, which is a constraint on the parameters. Next, we want to verify that introduing diffusion can create instability for this steady state. That is to say, we need to find the existence of some positive range of $\frac{D_2}{D_1}$ satisfying equation 13, which can be also written as

$$a^2 \left(\frac{D_2}{D_1}\right)^2 + (4bc - 2ad) \left(\frac{D_2}{D_1}\right) + d^2 > 0 \tag{16}$$

After careful checking of algebra, we find the positive half solution (while the solution range below the smaller root is also interesting to discuss, we skip that part in this essay)

$$\frac{D_2}{D_1} > \frac{ad - 2bc + 2\sqrt{bc(bc - ad)}}{a^2} > 0 \tag{17}$$

where $bc < 0$ according to equation 15 and $bc - ad < 0$ by the constraint on stable uniform state. Hence, we prove that diffusion can introduce instability to the steady uniform state of activator-inhibitor, when the inhibitor diffuses much faster than the activator.

2.3 Simulation and comparison to observation

In the last section, we have shown that diffusion can be the origin of the emergence of patterns in the activator-inhibitor model. However, because of the complexity of dynamical systems, it is hard to solve the analytical form of $\mathbf{u}(x, t)$, and thus we cannot read the pattern out of a closed expression in general. Computer simulation is a powerful tool to study the evolution of dynamical systems. Simulations of PDEs

and visualization of results reveal that models proposed in section 2.1 can reproduce various types of seashell patterns in nature, as figure 2, 3, 4 and 5 show below.

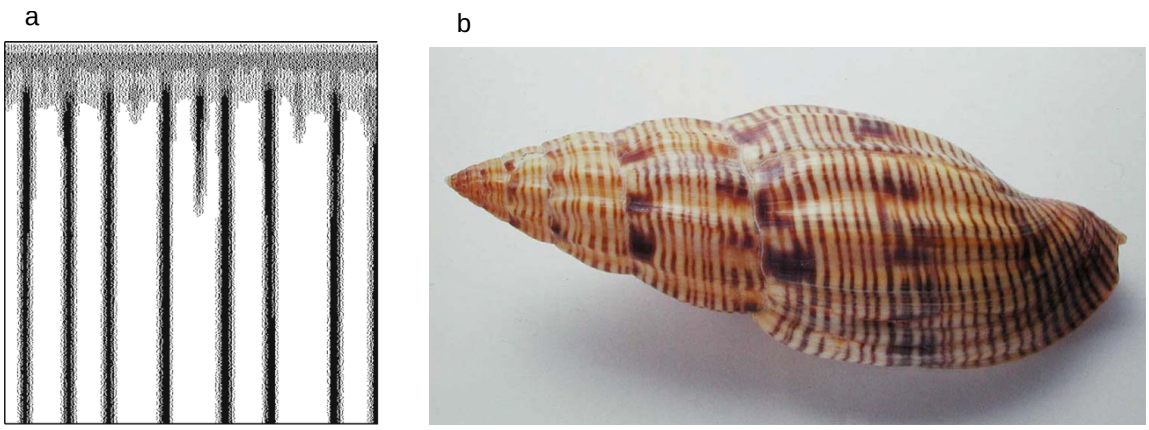

Figure 2: Emergence of a periodic pattern for (a) simulation equation 1 and (b) photo of *Lyria planicostata taiwanica*[1].

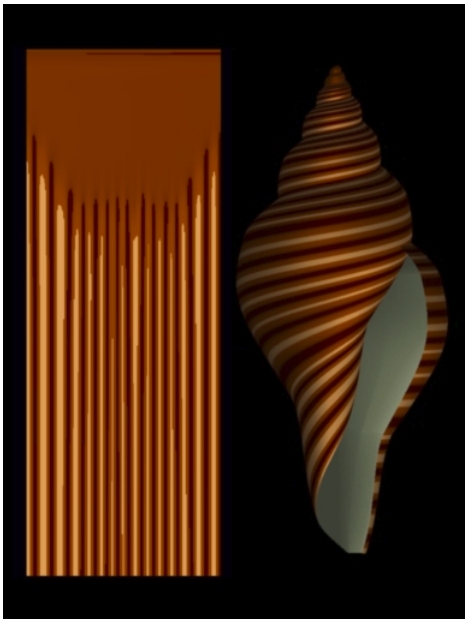

Figure 3: Emergence of a stable pattern from uniform initial state [3]. Simulation of equation 2, including the saturation effects. Parameters are $\rho_a = 0.01 \pm 2.5\%$, $\rho_0 = 0.001$, $\kappa = 0.0$, $\mu_a = 0.01$, $\delta_a = 0.0$, $\mu_a = 0.01$, $D_a = 0.002$, $\delta = 0.015$, $\mu_s = 0.0$, $D_s = 0.4$.

Figure 4: Activator-substrate system with a spatially periodic substrate source [3]. Left: photo of *Volutoconus bednalli*. Right: simulation of equation 3 with parameters $\rho_a = 0.1 \pm 2.5\%$, $\rho_0 = 0.0025$, $\kappa = 0.5$, $\mu_a = 0.1$, $\delta_a = 0.0$, $D_a = 0.01$, $\delta(x)periodic$, $\delta_{max} = 0.11$, $\mu_s = 0.002$, $D_s = 0.05$.

Figure 5: "Colliding wave" pattern generated by hormone inluenced activator-inhibitor model [3]. Left: photo of *Oliva porphyvia*. Right: simulation of equation 3 with parameters $\rho_a = 0.1 \pm 2.5\%$, $h_0 = 0.1$, $\kappa = 0.25$, $\delta_a = 0.0001$, $\mu_a = 0.1$, $D_a = 0.015$, $\delta_h = 0.0002$, $\mu_h = 0.014$, $D_h = 0.0$, $\rho_c = 0.1$, $\mu_c = 0.1$.

3 Discussion

3.1 Other models for seashell pattern formation

The models introduced in section 2.1, which originated from the Gierer-Meinhardt model, have the direct inhibitive effect proportional to the population of the inhibitor, which shows up in the denominator of the activator's growth term. While these models are capable of reproducing seashell patterns observed in nature (see section 2.3), some other mechanisms cannot be ruled out because of the lack of molecular explanation so far [1].

Here we introduce another inhibition mechanism realized by destruction of the activator [1], which is also extensively studied in the literature. If the inhibitor can annihilate the activator, the antagonistic effect will appear as a decay term of the activator, with the decay rate depending on the density of the inhibitor. This predator-prey mechanism for a reaction-diffusion system was proposed by L.A. Segel and J.L. Jackson [7] as the following form:

$$\begin{aligned} \frac{\partial a}{\partial t} &= \rho_a a^2 - \mu_a a h + D_a \frac{\partial^2 a}{\partial x^2} + \delta_a \\ \frac{\partial h}{\partial t} &= \rho_h a^2 - \mu_h h + D_h \frac{\partial^2 h}{\partial x^2} + \delta_h \end{aligned} \tag{18}$$

which is a successful ecological model for pattern formation in plankton-herbivore systems.

A neuron-based model also successfully reproduces many seashell pigment patterns [4]. In addition to a diffusive process, noise can also be a factor to break the uniformity and induce patterns in a diffusion-reaction system [8]. Even though the molecular mechanism of seashell pattern formation are not yet clear, these effective models constructed from broken symmetry and empirical observation in a population scale manage to describe the macroscopic patterns. However, on the other hand, we cannot rule out any model because of the lack of both microscopic picture and experimental facts. We know even very simple cellular automata are capable of producing varies type of patterns in their time evolution plots, so how much these models actually characterize the system still need further study [9].

3.2 Seashell pattern as a complex system

In this essay, we mainly focus on a one-dimensional reaction-diffusion system with only two species, and the quantitative analysis is limited to linear order. The examples shown above are basic patterns (but already show a large variation). In some other seashells, the pigmentation patterns exhibit complex behaviour [1]. For example, the bifurcation of activator waves requires nonlinear analysis. Figure 6 shows a pattern that potentially has more than one type of pigment, and the entire pattern seems to be a superposition of multiple subpatterns [1].

Figure 6: Complex pattern on *Conus textile* [1]

Another challenge to the reaction-diffusion model might be the global behaviour, which violates our essentially Markovian assumption [1]. Examples include the memory of previous pattern when the new ones form at the next round and the reflection symmetry of patterns on the bivalved shells [1]. Moreover, in some cases, the one-dimensional assumption is not sufficient to capture behaviour of a growing front partly because of uneven growth caused by the curved geometry of seashells [1].

4 Conclusion

In this essay, we model the pigmentation patterns on seashell surfaces as a dynamical system. We introduce the one dimenional activator-inhibitor model for two species, and show that it can create a linear instability for a uniform steady state that allows patterns to emerge. Through computer simulation results, it has been found that the model and its variations, with properly chosen parameters, can reproduce pigment patterns observed in nature. Yet, despite the success of the activator-inhibitor model at the population level, the lack of understanding of the underlying molecular mechanisms along with the difficulty of conducting targeted experiments leaves many questions in this subject open for future research.

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