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Review Article

Mathematical approach to unpinning of spiral waves anchored to an obstacle with high-frequency pacing

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Spiral waves are observed in wide variety of reaction-diffusion systems. Those observed in cardiac tissues are important since they are related to serious disease that threatens human lives, such as atrial or ventricular fibrillation. We consider the unpinning of spiral waves anchored to a circular obstacle on excitable media using high-frequency pacing. Here, we consider two types of the obstacle; *i.e.*, that without any diffusive interaction with the environment, and that with diffusive interaction. We found that the threshold frequency for success in unpinning is lower for the obstacle with diffusive interaction than for the one without it. We discuss the threshold frequency based on the angular velocity of a chemical wave anchoring the obstacle.

Key words: reaction-diffusion system, Belousov-Zhabotinsky reaction, pattern formation, chemical wave

Our hearts consist of a large number of cardiomyocyte cells, and they can pump blood to the whole body by a regular contraction with synchrony. The region of contraction propagates as a wave on the cardiac tissue; the cardiomyocyte cells transmit the information to the neighbor cells as an electric signal [1,2]. Once a cardiomyocyte cell receives the electric signal from the neighbor cell, the auto-catalytic process occurs and ion flow is induced through the cell membrane. At the same time, the cell itself contracts. The ion flow induces the electric signal and propagates to the neighbor cell at the opposite side. This process is modeled as a reaction-diffusion system by considering the array of cardiomyocyte cells as continuum excitable medium. Here, the "excitable" means the property that the system is activated through an auto-catalytic process only when it receives a signal exceeding a threshold value. In this case, a cardiomyocyte cell contracts and ion flow occurs only when it is suffered by an electric signal exceeding a threshold. Reaction-diffusion systems with excitable dynamics are important because they are good models representing not only wave propagation on cardiac tissues but also wave propagation in neuronal systems [2], on retina [3], on a surface of fertilized egg [4], and so on. The systems that can be described as excitable reaction-diffusion systems are not limited within the biological systems. Chemical systems like Belousov-Zhabotinsky (BZ) reaction [5–7] and carbon monooxide oxidation catalyzed by platinum surface [7,8] are also

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◀ ***Significance*** ▶

Spiral waves are observed in wide variety of reaction-diffusion systems. Those observed in cardiac tissues are important since they are related to serious disease that threatens human lives, such as atrial or ventricular fibrillation. Thus, we consider the unpinning of spiral waves anchored to a circular obstacle on excitable media using high-frequency pacing. Here, we consider two types of the obstacle; *i.e.*, that without any diffusive interaction with the environment, and that with diffusive interaction. The threshold frequency for success in unpinning is lower for the obstacle with diffusive interaction than for the one without it.

examples of excitable reaction-diffusion systems.

When a human being suffers from disease like vascular infarction and some parts become inactive, the wave of the electrical signal cannot be transmitted regularly but the spiral wave occurs, which causes irregular contraction. A heart with such irregular contraction cannot deliver a sufficient amount of blood to the body. This situation is called a tachycardia, atrial fibrillation, and ventricular fibrillation, and may threaten our life. Therefore, it is important to remove spiral waves from the cardiac tissue for saving lives. In fact, an automated external defibrillator (AED) is used to eliminate spiral waves on a heart [1]. AED is effective for the recovery from serious pathology but the body suffers from the damages by the high electric voltage. Therefore it is important to develop the better cure for tachycardia, atrial fibrillation, and ventricular fibrillation. Since spiral wave formation is not specific for the cardiomyocyte cell system, but universal for the reaction-diffusion systems with excitable dynamics, and thus there have been many studies on the manner of elimination of spiral waves in reaction-diffusion systems [1,9–13]. These studies may contribute to develop such cure for the disease.

Spiral waves in reaction-diffusion systems are not only important from the viewpoint of medicine but also interesting as one of scientific topics in mathematics, physics and biology, because the spiral wave formation is considered to be a spontaneous pattern formation in nonlinear non-equlibrium systems. A number of analytical approaches to the formation of spiral waves have been performed, and several important theoretical frameworks have been developed to analytically understand the dynamics of spiral waves [14–18] together with experimental observation [19,20].

As for the elimination of the spiral wave, there have been also many studies. It has been clarified that spiral waves can be eliminated by applying high-frequency pacing. In such a case, chemical waves with shorter wave length are generated, and the spiral waves are pushed away by pair annihilation with the generated chemical waves with shorter wave length. In many studies on the elimination of spiral waves, the behaviors on homogenous media are considered [1,21,22]. However, in recent studies, it is known that spatial heterogeneity is important; for example damaged regions by vascular infarction play an important role in the behaviors of spiral waves.

In the present article, we first briefly introduce the mechanism of spiral waves in excitable systems and their elimination by high-frequency pacing. Then, we introduce the outline of our recent results on the unpinning of spiral waves attached to a circular inactive region called "obstacles" [12,13]. We here consider the unpinning of spiral waves around two types of obstacles; *i.e.*, that without any diffusive interaction with the environment, and that with diffusive interaction. We found that the threshold frequency for the success in unpinning is lower for the obstacle with diffusive interaction than for the one without it.

Spiral waves in reaction-diffusion systems

In this section, we introduce the fundamental knowledges on theoretical approaches to the dynamics of spiral waves in reaction-diffusion systems, which have been widely used as a mathematical model describing time evolution of a system with spatial distribution. We consider a dynamics of a chemical system that is described by the local concentrations of some chemical species. The time evolution of the system is described by two terms; a reaction and a diffusion terms as

$$\frac{\partial c_i}{\partial t} = f_i(c_1, c_2, ..., c_n) + D_i \nabla^2 c_i. \tag{1}$$

The first term of the right-hand side represents the local change determined by the local concentration and the second one the diffusion process of the chemicals which leads the system to a uniform state. Here, we consider n chemical species, where the concentration of i-th species is c_i, whose local dynamics and diffusion coefficient are represented as f_i and D_i, respectively.

As for the local change in chemical concentration, we here adopt a so-called "activator-inhibitor" system with two variables. That is to say, we consider that the system is represented by two variables corresponding to the concentrations of two relevant chemical species, which are called an activator and an inhibitor. Here, an activator tends to activate the system, *i.e.*, it increases the concentration of the inhibitor, and it also increases the concentration of activator itself through auto-catalytic reaction, while an inhibitor decreases the concentration of the activator. The time evolution of the concentrations of activator and inhibitor, A and I, is represented most simply as follows:

$$\frac{dA}{dt} = f(A, I), \tag{2}$$

$$\frac{dI}{dt} = g(A, I). \tag{3}$$

The fixed point of the systems in Eqs. (2) and (3) is defined as a set of the values of A and I that satisfies $dA/dt = dI/dt = 0$. Assuming that the system has only one fixed point $A = A_0$ and $I = I_0$, then the following condition typically holds for an activator-inhibitor system.

$$\left.\frac{\partial f}{\partial A}\right|_{A=A_0, I=I_0} > 0, \quad \left.\frac{\partial g}{\partial A}\right|_{A=A_0, I=I_0} > 0,$$
$$\left.\frac{\partial f}{\partial I}\right|_{A=A_0, I=I_0} < 0, \quad \left.\frac{\partial g}{\partial I}\right|_{A=A_0, I=I_0} < 0. \tag{4}$$

It is known that activator-inhibitor systems often exhibit excitability. Here "excitability" is defined as follows; a system with "excitability" has the following properties: (i) A system has one stable steady state. (ii) When an external stimulus is smaller than a certain threshold value, the system linearly relaxes to the stable steady state. (iii) When the

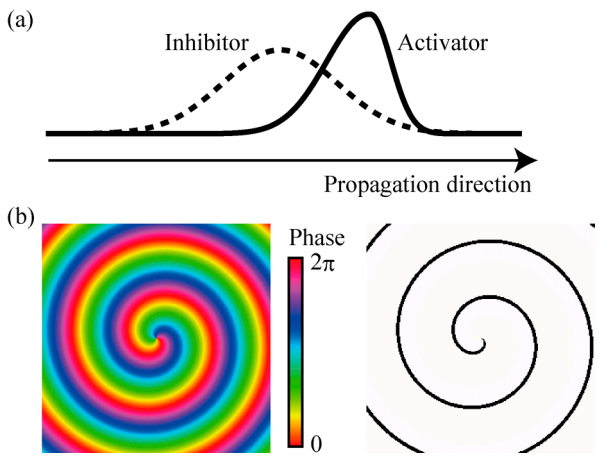

Figure 1 (a) Schematic diagram of a chemical wave propagating in a one-dimensional excitable system with activator-inhibitor dynamics. The activator-rich region precedes the inhibitor-rich region. (b) Schematic diagram of a spiral wave. Phase distribution (left) and front of a spiral wave (right) is shown. The center of the spiral wave corresponds to a phase singularity point.

external stimulus exceeds the threshold value, large response called "excitation" occurs and then relaxes to the stable steady state. Of course, an activator-inhibitor system does not always show excitability. It often shows sustained oscillation instead of excitability. There are many actual systems that show excitability and sustained oscillation, depending on the system parameters. It should be noted that a system can have more-than-one fixed points, and it is known that bistability can be observed in such a system. Mathematical discussion on the dynamics of such systems is extensively studied in the field of "dynamical systems" [2,23,24].

In a reaction-diffusion system with an excitable activator-inhibitor-type dynamics as a reaction term, a travelling wave propagating in one direction can be seen. A travelling wave consists of a region with a high concentration of activator in front of the wave followed by a region with a high concentration of the inhibitor as shown in Figure 1a. Unlike waves in linear systems such as light, sound, ripples at water surface etc., these traveling waves exhibit pair annihilation and structural stability. Pair annihilation means that two waves disappear when two traveling waves collide with each other, and structural stability means that the shape and speed of the traveling wave are determined by the parameter of the system. These properties show clear contrast to the waves in linear systems; two waves pass through without any interaction and waves with any amplitude can stand in linear systems.

Propagation of a spiral wave can be seen in a two-dimensional system with activator-inhibitor-type dynamics. When such a spiral wave is propagating, periodic change in concentration of chemical species is observed in each point. Therefore, it is possible to define the phase so that one period corresponds to 2π as shown in Figure 1b. The origin of the phase is set such that the highest concentration state of activator corresponds to the phase of an integer multiple of 2π, for example. Then, spiral waves are considered to be curves connecting the points where the phase is an integer multiple of 2π. It is noteworthy that such periodic behavior is not seen at the center of the spiral wave, and thus the phase cannot be defined there; that is to say, the center of the spiral wave is a "phase singularity point". When detecting the phase along the curve surrounding the singular point, the phase is shifted by $\pm 2\pi$ per one rotation in a general case (see Fig. 1b). The phase singularity point is characterized by the phase shift. When the two phase singularity points around which the phase is shifted by 2π and -2π, respectively, *i.e.*, with different chirality, collide with each other, then they disappear, *i.e.*, pair annihilation occurs. In contrast, the pair generation of spiral waves is also important; If a travelling wave is passing over an obstacle or a heterogeneous media, a pair of phase singularity points with opposite phase shift, *i.e.* 2π in almost all cases, are generated. Thus, the behavior of the phase singularity point is important and has been widely studied [25–27].

BZ reaction as an excitable system and myocardial cells

In this section, we introduce Belousov-Zhabotinsky (BZ) reaction as an example of an excitable reaction-diffusion system. BZ reaction [5–7] is an oscillatory chemical reaction that can be realized by mixing several chemical species. It is often observed as an oscillation in a redox potential of metal ions or metal complexes, which corresponds to the periodic change in solution color. For example, when ferroin, a complex composed of ferrous iron and phenanthroline, is used as a metal complex, it shows periodic change between blue and red, which corresponds to oxidized and reduced states of the metal complex, respectively. This BZ reaction shows sustained oscillation or excitability depending on the initial concentration of chemicals. In the sustained oscillation, the period is in the order of seconds to several tens of seconds. In the excitable state, the solution is relaxed to be in a reduced state without any fluctuation or stimulation, and when it is given a stimulus such as contact with a silver wire and a voltage application with an electrode, it becomes excited, that is to say, the system quickly changes to the oxidized state and then relaxes to the reduced state again. So far, its reaction mechanism has been clarified; the bromide ion ($HBrO_2$) works as an activator, while the bromide ion (Br^-) works as an inhibitor, and the dynamics is well reproduced with the mathematical model named Oregonator [28–30], though there may be still some discrepancies between actual experiments and simulation results.

BZ reaction medium poured into a petri dish or a filter paper immersed with BZ reaction medium is considered to be a pseudo two-dimensional reaction-diffusion system, that is to say, spontaneous pattern formation occurs; spiral patterns as

well as target patterns, *i.e.*, chemical waves propagating with the shape of concentric rings, are seen. Using the reaction-diffusion equation with the above-mentioned Oregonator model, the patterns observed in the experiments are well reproduced, and therefore, the Oregonator model has been widely adopted for the reproduction of spatio-temporal pattern formation in BZ reaction.

Next, myocardial cells are considered. As described above, a heart is a tissue composed of a large number of cardiomyocytes, which can be regarded as excitable activator-inhibitor systems, though activators and inhibitors do not correspond to specific substances. Actually, activator concentration corresponds to the membrane potential of cardiomyocytes, and inhibitor concentration is the recovery process of ion localization by pumps on the cell membrane [2]. Therefore, a cardiac tissue can be regarded as a continuous excitable media in a macroscopic scale. A group of cells named a pacemaker is located at a sinoatrial node, and these cells exhibit oscillatory behavior, which initiates a wave propagating on an excitable media, which induces a regular contraction enabling blood circulation.

Unpinning of spiral waves anchored to obstacles

Here we would like to discuss how to eliminate spiral patterns in an excitable system. Considering that the center of a spiral wave is a phase singularity point, what we have to do to eliminate a spiral wave is, (1) to apply strong external force that greatly changes the local behavior of the medium, (2) to collide with a phase singularity point with the opposite chirality, or (3) to shift the phase singularity point across the medium boundary. The mechanism of AED is also discussed based on the dynamics of phase singularity points on excitable media [2,31,32]. Actually, there have been a number of studies to eliminate spiral waves with more moderate stimulation, which does not significantly change the local dynamics. Therefore, the most important thing is to shift the position of phase singularity points for a homogeneous excitable field. However, if there is an obstacle, *i.e.*, a region with no excitability, a spiral is easily anchored to the obstacle. In detail, a travelling wave can generate a pair of phase singularity points that become spiral cores. If one of the cores are trapped and the other is shifted in space, and then a spiral wave is anchored to the obstacle. It is also known that the location of the core of a spiral wave is affected by the obstacle, and the core position can shift to the obstacle [33,34]. Once anchored, it is difficult to be unpinned from the obstacle. Therefore, we investigated the manner how an anchored spiral wave can be unpinned from the obstacle. After unpinning from the obstacle, the previous knowledge can be adopted on the pair elimination of spiral waves or the shift out of the boundary of the field.

There are two types of obstacles existing in excitable fields. The first one is an obstacle without inflow or outflow at the boundary, which we call a "hard" obstacle. Mathematically, the boundary of the obstacle obeys the Neumann boundary condition for concentration field. The second one is a "soft" obstacle, which has diffusive interaction across the boundary, and thus excitability is repressed. Mathematically, the local dynamics are different inside and outside the obstacle, and an increase in activator concentration is suppressed within the obstacle.

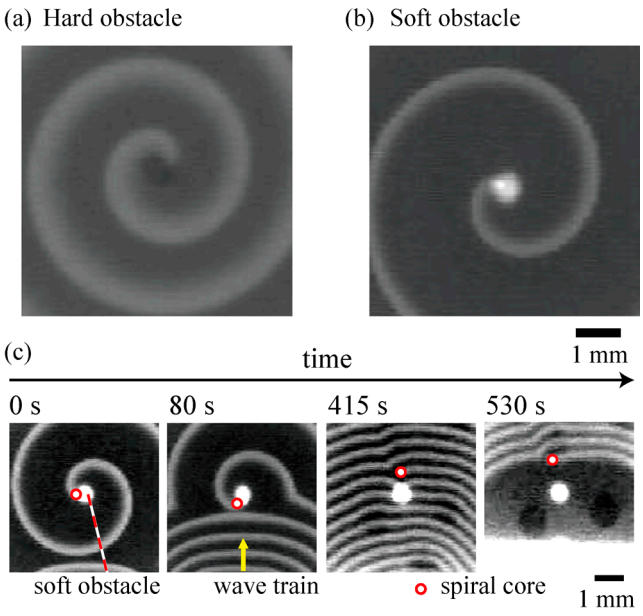

Figure 2 Experimental observation of high-frequency unpinning in the excitable BZ reaction. (a) and (b) Pinned spirals on hard and soft obstacles, respectively. (c) An example of the unpinning process of a spiral anchored on a soft obstacle. The wave train approaching from the bottom led to unpinning at t~400 s. The unpinned spiral wave was forced to drift upward together with subsequent traveling waves. The waves of the train were suppressed by strong light illumination of 60 klx at t~470 s to verify detachment of the spiral, *i.e.*, accomplishment of the unpinning. Reproduced with permission from Figure 6 in reference [13].

We reported that a spiral wave anchored by these two kinds of obstacles can be unpinned by the chemical waves generated with the periodic stimuli at high frequency in the peripheral part, *i.e.*, high frequency pacing. We confirmed that this method can work in actual experiments using a rat-derived cardiomyocyte culture system and BZ reaction system [12]. The chemical waves generated by high frequency pacing had shorter wave length than the spiral wave anchored to the obstacle, and in such a case they unpinned the spiral wave from the obstacle. After unpinning, the phase singularity point of the spiral wave was shifted and disappeared by the collision with the outer boundary.

In the BZ reaction system, we realized these two kinds of obstacles, *i.e.* hard and soft obstacles, and demonstrated the unpinning of the spiral wave anchored to the obstacle as shown in Figure 2; A hard obstacle was realized in a filter paper immersed with BZ medium after dropping a fine oil droplet onto the filter paper, while a soft obstacle was real-

ized by using photosensitive BZ reaction with a small circular region with high light intensity of the light illumination with a liquid-crystal projector controlled by personal computer [13]. In order to theoretically approach the mechanism on the unpinning of spiral waves anchored to an obstacle, we discussed using Oregonator model corresponding to BZ reaction mentioned above. As the result of numerical calculation, there is a threshold for the frequency of high frequency pacing above which a spiral wave can be unpinned from the obstacle. We found that such a threshold frequency is lower for a soft obstacle than that for a hard one. It was also found that the threshold is higher for the obstacle with larger size.

Discussion

First, we consider the unpinning of a spiral wave anchored to a hard obstacle. To discuss analytically, the shape of a chemical wave is characterized by a curve that connects the points at which the activator concentration suddenly increases in time. This curve is often called a front of the chemical wave. So far, Tyson discussed the shape of the front of a spiral wave in a uniform excitable field using the Eikonal approximation in which the local propagation velocity of the front depends only on its curvature [13–15]. It is known that the front of a chemical wave orthogonally intersects with a boundary of the hard obstacle considering that there is no diffusive interaction at the boundary of the obstacle, which corresponds to the Neumann boundary condition for the time evolution of chemical concentration. Based on this boundary condition, we discussed the front shape of a spiral wave anchored to a hard obstacle. One of important characteristics of propagation of chemical waves is that the velocity of the following front is affected by the distance from the preceding front. The shorter the distance is, the slower it is. In addition, when the distance is less than a certain threshold distance, the following wave cannot propagate [35,36]. Such a relationship between the wave length of the chemical waves and the propagation speed is called the dispersion relation. Based on such dispersion relation, the condition for unpinning of a spiral wave anchored to a hard obstacle can be discussed; whether the velocity of the chemical wave induced by high frequency pacing but modified by the curvature effect is greater or smaller than a certain threshold velocity is important to determine the success or failure of unpinning.

On the while, at the soft obstacle boundary, the front of a chemical wave is not orthogonal to the boundary of the obstacle. In order to apply the discussion for a hard obstacle, we considered a virtual obstacle such that the front of a spiral wave was orthogonal to the boundary of the virtual obstacle. It was found that the spiral wave was unpinned from the obstacle when the front speed in the vicinity of this virtual obstacle became almost the same value as in the case of a hard obstacle as shown in Figure 3.

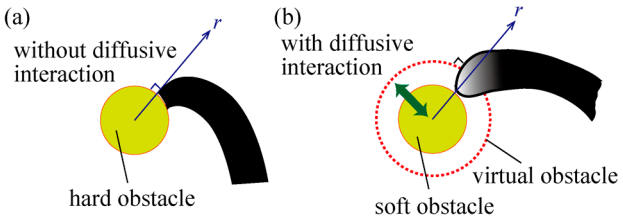

Figure 3 Schematic diagram for a hard obstacle (a) and a soft obstacle (b). The black region indicates a region with high activator concentration. Reproduced with permission from Figure 4 in reference [13].

In the next section, we will introduce fundamental but important results on the behavior of the chemical wave anchored to a soft and hard obstacles, especially noticing dispersion relation.

Numerical results on the chemical wave anchored to obstacle

We performed numerical calculation on the chemical wave propagation to obtain fundamental knowledge related to the mechanism of unpinning. We adopted the Oregonator for the photosensitive BZ reaction [28–30,37]:

$$\frac{\partial u}{\partial t} = \frac{1}{\varepsilon}\left[u(1-u)-(fv+\phi(\mathbf{r}))\frac{u-q}{u+q}\right]+D\nabla^2 u, \tag{5}$$

$$\frac{\partial v}{\partial t} = u-v, \tag{6}$$

where u and v are variables which correspond to the concentrations of the activator and inhibitor, respectively. In the actual BZ reaction, u corresponds to the concentration of $HBrO_2$, and v corresponds to that of the oxidized catalyst $Ru(bpy)_3^{3+}$. ε, f, and q are the parameters which determine the characteristics of the BZ reaction. In detail, ε determines the inverse of excitation time scale, *i.e.*, the rate of rapid increase in u, and q corresponds to the order of minimum value of u in the time course. By changing f, the system can shift between an oscillatory state and an excitable state. ϕ corresponds to the light intensity, and D is the diffusion constant of the activator. The parameters were set as follows: $\varepsilon = 0.1$, $f = 2$, $q = 2\times10^{-3}$, and $D = 1$. Here it should be noted that the Oregonator model uses the dimensionless values and, for example, $D = 1$ means the scales of space and time are rescaled such that D becomes 1. Under the above conditions, we confirmed that a spiral wave exhibited rigid rotation with a radius and period of $R_{free} = 1.6$, and $T_{free} = 7.44$. The calculations were performed in cylindrical coordinates using the explicit method, and the discretized time step and mesh sizes were $\Delta t = 2\times10^{-5}$, $\Delta r = 0.1$, and $\Delta\theta = \pi/200$. The Neumann boundary condition was adopted for the boundary corresponding to the periphery, whose radius was set to be 15, though the outer boundary did not play an important role in the unpinning of a spiral wave. As for a hard obstacle,

the Neumann boundary condition was also adopted at the boundary of the obstacle at $|\mathbf{r}| = R$ and $\phi(\mathbf{r}) = \phi_{\mathrm{med}}$ for all region, while for a soft obstacle, we set $\phi(\mathbf{r})$ as

$$\phi(\mathbf{r}) = \begin{cases} \phi_{\mathrm{obs}}, & |\mathbf{r}| \le R, \\ \phi_{\mathrm{med}}, & |\mathbf{r}| > R, \end{cases} \tag{7}$$

where R is the radius of a circular obstacle. We set $\phi_{\mathrm{med}} = 0.01$ and $\phi_{\mathrm{obs}} = 0.02$ or 0.2.

We initialized a wave propagating counterclockwise, and measured the angular velocity for a hard obstacle, and soft obstacles with $\phi_{\mathrm{obs}} = 0.02$ and 0.2. The snapshots are shown in Figure 4. In both cases, a chemical wave was rotating anchored to the obstacle. The angular velocity was the highest for a wave anchored to the hard obstacle. As for the wave anchored to the soft obstacle, the angular velocity was higher for smaller ϕ_{obs}. In Figure 5, we show the radius-dependence of the angular velocity of the chemical wave anchored to each obstacle. For each R, the angular velocity was the highest for a hard obstacle, and it was higher for the lower ϕ_{obs} in the same way as shown in Figure 4. There existed a threshold radius below which a chemical wave was not anchored to the obstacle. The threshold radius for a chemical wave anchored to a soft obstacle and the corresponding angular velocity were almost the same as the rotating radius and angular velocity of a free spiral. On the other hand, the threshold radius was larger and corresponding angular velocity was higher for a chemical wave anchored to a hard obstacle. This seems to be because the chemicals can diffuse across a soft obstacle though the dynamics inside the soft obstacle affects to some extent, while the chemicals cannot go through a hard obstacle and the dynamics of a spiral wave is perfectly changed.

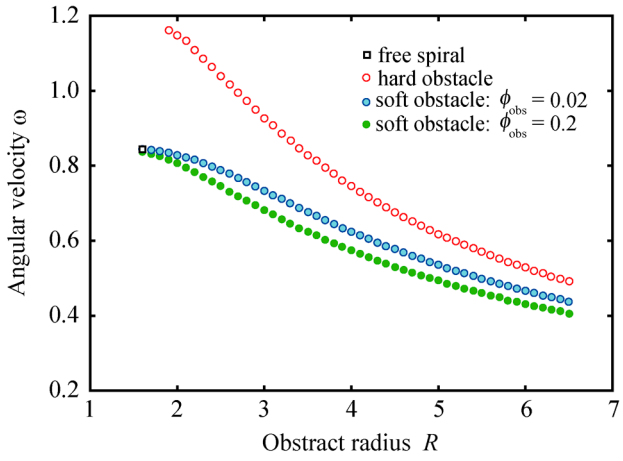

Figure 5 Dependence of angular velocity ω of a chemical wave anchored to an obstacle with a radius of R. Red open circle, blue circle filled with cyan, and green filled circle correspond to the chemical waves anchored to a hard obstacle, soft obstacle with $\phi_{\mathrm{obs}} = 0.02$, and that with $\phi_{\mathrm{obs}} = 0.2$, respectively. For the radius R smaller than 1.6 (for a soft obstacle) and 1.9 (for a hard obstacle), the chemical wave was not anchored to the obstacle. The radius of the core and angular velocity for a free spiral ($R_{\mathrm{free}} = 1.6$, and $\omega_{\mathrm{free}} = 2\pi/T_{\mathrm{free}} = 0.845$) are shown with a open black square.

The difference between a chemical wave anchored to a hard obstacle and that to a soft one measured in numerical calculation is important for whether unpinning by high frequency pacing succeeds or not. In the previous work, we have shown that the chemical wave anchored to a hard obstacle

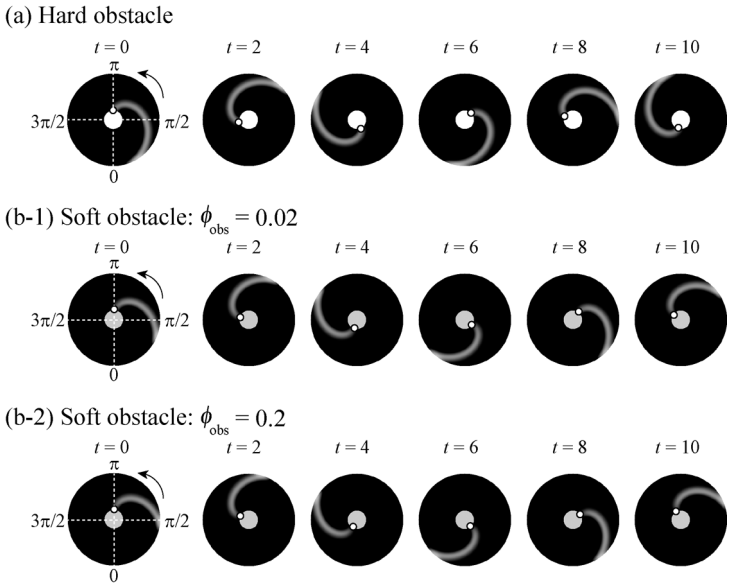

Figure 4 Snapshots obtained by numerical calculation based on Eqs. (5) and (6). We considered a circular obstacle with a radius of $R = 3$. The waves anchored to (a) a hard obstacle, (b-1) a soft obstacle with $\phi_{\mathrm{obs}} = 0.02$, and (b-2) a soft obstacle with $\phi_{\mathrm{obs}} = 0.2$ are shown. The angular velocity was highest for a hard obstacle. For a soft obstacle, the angular velocity was higher for smaller ϕ_{obs}.

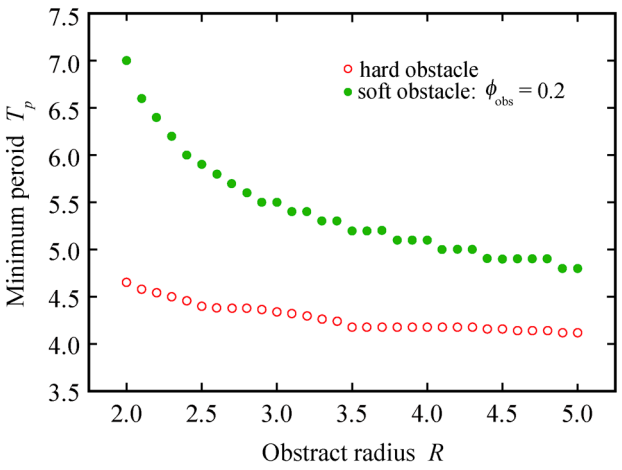

Figure 6 Numerical results on unpinning and elimination of a spiral wave anchored to an obstacle by incoming wave train. The minimum wave train period T_p for unpinning and elimination is plotted as a function of the obstacle radius R for a hard obstacle (red open circle) and a soft obstacle for $\phi_{obs} = 0.2$ (green filled circle). The parameters for the Oregonator model were the same as those used in Figures 3 and 4. Modified with permission from Figure 2 in reference [13].

needs higher frequency (shorter period) for the unpinning of the spiral wave from the obstacle as shown in Figure 6. This is because the velocity of the waves anchored to a hard obstacle is higher as shown in Figure 5, and the unpinning of the spiral wave from a hard obstacle needs higher frequency pacing in order to decrease the velocity of the wave to the certain threshold velocity.

Summary

Research on the unpinning of a spiral wave from an obstacle in a reaction-diffusion system is a fundamental topic, but it may contribute to pathology and/or medical care, through the similarities as reaction-diffusion systems. In the present paper, we introduce some fundamental knowledge and then show the numerical results on the relation between angular velocity and the obstacle radius for a chemical wave anchored to a hard and soft obstacle. The numerical results well correspond to the results for the success or failure of unpinning of an anchored spiral wave by high frequency pacing performed in the previous study. Theoretical work on the dynamics of spiral waves on excitable reaction-diffusion systems can suggest possible methods to unpin the anchored spiral waves to an obstacle. We need to consider the quantitative comparison between mathematical model and actual systems, and at the same time, we have to develop an actual system that can be used in cure considering the efficiency and safeness to human body based on such theoretical studies. We hope that our study will help to develop novel, safe, and more efficient ways of unpinning of a spiral wave with less damage.

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Conflicts of Interest

Authors declare no competing financial interests

Author Contributions

H. K. and M. T. contributed to review the studies on unpinning of a chemical wave, M. T. performed numerical calculation, and H. K. wrote the manuscript.

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