Complex dynamics of the formation of spatially localized standing structures in the vicinity of saddle-node bifurcations of waves in the reaction-diffusion model of blood clotting

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Local activation in a one-dimensional three-component reaction-diffusion model of blood clotting may lead to a formation of spatially localized standing structures (peaks) via several complex scenarios. In the first scenario, two concentration pulses first propagate from the site of activation, then stop and transform into peaks [Zarnitsina *et al.*, Chaos **11**, 57 (2001)]. Here, we examine this scenario, and also describe a different scenario of peak formation. In this scenario, two trigger waves propagate initially in opposite directions away from the site of activation. Then they stop and change direction of propagation toward each other to the activation site, where they interact and form a peak. Both of these scenarios of stable peak formation are observed in the vicinity of saddle-node bifurcation and may be viewed as a memory of the extinct wave modes.

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INTRODUCTION

One of the well known solutions for one-dimensional reaction-diffusion models is a stationary, spatially localized standing structure, referred to below as a "peak"[1–3]. In two-component models of excitable media, stable peaks exist if the diffusion coefficient for one of the variables (usually called the inhibitor) exceeds the diffusion coefficient for the other variable (usually called the activator) [1]. The dynamics of peak formation in previously described activator-inhibitor models is simple: the peak is rapidly generated at the site of activation in response to a local increase in the activator concentration. However, in a three-component model of excitable media, the blood clotting (BC) model, there are two other complex scenarios of peak formation in addition to the simple scenario (Fig. 1).

The complex transient processes of peak formation via these two scenarios initially resemble either autowaves (scenario 1) or trigger waves (scenario 2). In the first scenario [4,5], spatially localized pulses resembling autowaves start propagating from the site of activation [Fig. 1(b)]. Soon, however, they stop and convert into standing peaks. In the second scenario [Fig. 1(c)], the peak is generated directly at the site of activation [5]. However, its formation is preceded by an expansion in the form of two trigger waves, and then by a shrinkage of the excitation zone back to the initial activation site. In this study, we demonstrate that both complex scenarios are observed in the domain of a parameter space where stable peak solutions are found, which is adjacent to the boundary of a saddle-node bifurcation of autowaves or trigger waves, respectively. Stable wave solutions exist on the other side of this boundary, while at the bifurcation line the stable waves disappear. We also provide evidence suggesting that the proximity to the saddle-node bifurcations is essential for the formation of peaks via these two scenarios.

THE BC MODEL

This model was originally developed to describe the spatial dynamics of blood clotting [4], and is shown in a one-dimensional form below:

$$\frac{\partial u_1}{\partial t} = D\frac{\partial^2 u_1}{\partial x^2} + K_1 u_1 u_2 (1-u_1)\frac{(1+K_2\, u_1)}{(1+K_3\, u_3)} - u_1,$$

$$\frac{\partial u_2}{\partial t} = D\frac{\partial^2 u_2}{\partial x^2} + u_1 - K_4\, u_2,$$

$$\frac{\partial u_3}{\partial t} = D\frac{\partial^2 u_3}{\partial x^2} + K_5\, u_1^2 - K_6\, u_3. \tag{1}$$

The variables in this model correspond to the concentrations of certain important blood clotting factors. By analogy with activator-inhibitor models, we call u_1 the activator and u_3 the inhibitor. The variable u_2 may be viewed as the catalyst of the activator's production. The molecular weights of blood clotting factors described in this model are roughly the same, so their diffusion coefficients are set equal $(D=1)$. Equations (1) contain six constants K_1–K_6, which are combinations of the rate constants for individual reactions of the clotting cascade [4]. We varied only the key parameters K_5 and K_6, which describe the inhibitor's production and inactivation, respectively, while the remaining four parameters were kept constant ($K_1=6.85$, $K_2=13.5$, $K_3=2.36$, and $K_4=0.078$). For all values of the parameters the BC model has a trivial solution corresponding to a stable trivial spatially uniform state $(0,0,0)$ with threshold properties. This means that the nontrivial regimes are observed only when the threshold is exceeded.

In order to find stable solutions of the BC model and to analyze the dynamic modes, we solved Eqs. (1) over a relatively long segment, using a simple explicit difference

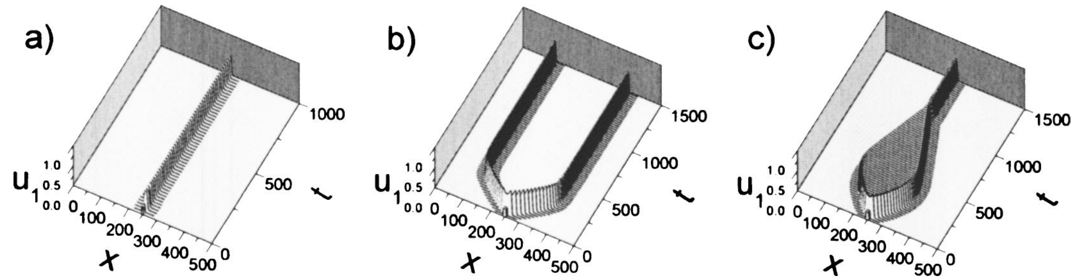

FIG. 1. The simple and complex dynamics of peak formation in the BC model in response to a local, above-threshold activation ($K_1=6.85$, $K_2=13.5$, $K_3=2.36$, $K_4=0.078$, and $D=1$): (a) peak formation at the site of activation (simple dynamics) ($K_5=27$, $K_6=0.076$); (b) scenario 1 of peak formation; the initial stage resembles an autowave ($K_5=17.35$, $K_6=0.05$); (c) scenario 2 of peak formation; the initial stage resembles on waves ($K_5=20$, $K_6=0.0635$).

scheme with no-flux boundary conditions for space step $h=0.25$ and time step $\tau=0.01$. The results obtained were qualitatively similar to those obtained for smaller step sizes. We focused our study on the dynamic behavior induced by an increase in the activator's concentration above the threshold within a small part of the segment (referred to below as a local above-threshold activation). Such activation imitates the initiation of blood clotting [4,6]. Steady-state solutions corresponding to peaks and waves, which travel at a constant speed without changes in wave form, were obtained by numerically solving the nonlinear ordinary differential equations derived from Eqs. (1). This approach allows one to obtain both stable and unstable solutions. The stability was examined by perturbing the solutions and using them as initial conditions to solve Eqs. (1) in time. If the solution is unstable, this procedure leads to its disappearance. Since the initial stages of the complex scenarios of peak formation resemble wave solutions, we examined mutual positions of the domains corresponding to stable peaks and to stable stationary waves. The results of these calculations are presented as one-parameter bifurcation diagrams. Using these diagrams we also analyzed the location of the domains where peaks are formed via complex dynamics relative to the peaks and stationary wave domains.

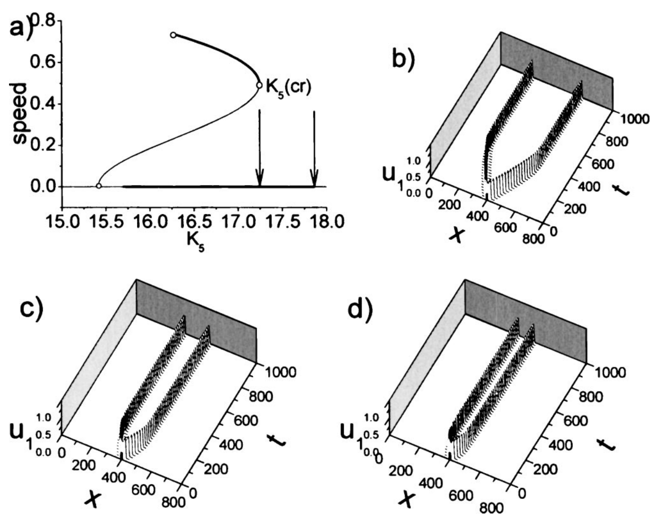

FIG. 2. First complex scenario of peak formation. (a) The one-parameter bifurcation diagram for autowaves with K_5 as the bifurcation parameter ($K_1=6.85$, $K_2=13.5$, $K_3=2.36$, $K_4=0.078$, $K_6=0.05$, and $D=1$). The speed value assigned to peak solutions is zero. The branches of stable and unstable solutions are depicted with thick and thin lines, respectively. (b)–(d) Peak formation in response to a local above-threshold activation for supracritical values of the bifurcation parameter: (b) $K_5=17.3$, (c) $K_5=17.5$, and (d) $K_5=17.8$.

COMPLEX SCENARIO 1 FOR PEAK FORMATION

This is observed near the saddle-node bifurcation boundary of the autowave solutions. As in other known models of excitable media, the BC model (1) has a solution in the form of stable or unstable spatially localized, constant-amplitude pulses that propagate at a constant speed (autowaves) [2,7–9]. Figure 2(a) shows a typical bifurcation diagram, which depicts the mutual positions of the peak and autowave solutions in the BC model. The speed of the autowave is plotted as a function of constant K_5 (and for $K_6=0.05$), and the stationary peak solutions correspond to zero speed. The right boundary of the existence range for stable autowaves is formed by a saddle-node bifurcation, where the branch for stable autowave solutions merges with that for the unstable autowaves. The autowave width increases upon approaching the left boundary of the stable branch. Stable autowaves and peaks coexist for $16.29<K_5<17.25$, although the autowaves dominate in this region. Since autowaves are generated in response to above-threshold activation, these solutions are readily obtained by calculating the behavior of the system (1) as a function of time. The peaks can be obtained by choosing the initial spatial distributions of model variables in a form resembling the peak.

The complex dynamics of peak formation via scenario 1 are obtained in the model for the range of parameters within the area between two arrows on Fig. 2(a). There are no autowave solutions within this region. Its left boundary corresponds to the parameter value $K_5(\mathrm{cr})(K_5\sim 17.25)$ for the saddle-node bifurcation of autowaves, while the right boundary coincides with the end of the stable peak domain. When K_5 is slightly above the critical value $K_5(\mathrm{cr})$, the autowaves disappear, but the initial response of the system resembles the extinct autowave. Figure 2(b) shows an example of peak formation for parameters that are within this region and slightly outside the autowave domain. Two pulses are generated at the site of activation and propagate away from it at

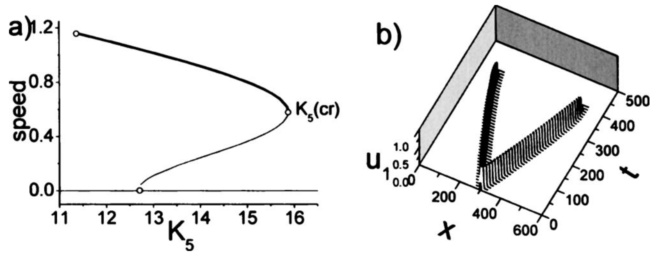

FIG. 3. Transient dynamics of pulse formation, propagation, and disappearance near the saddle-node bifurcation in the absence of peak solutions. (a) The one-parameter bifurcation diagram with K_5 as the bifurcation parameter ($K_1=6.85$, $K_2=13.5$, $K_3=2.36$, $K_4=0.078$, $K_6=0.04$, and $D=1$). (b) Pulse formation, propagation, and destruction in response to a local above-threshold activation for a supracritical value of $K_5=15.9$.

approximately constant speed and with minor variations in shape. After some time, they stop and convert into peaks. Thus, the initial stage of peak formation closely resembles the autowave regime, although the resemblance diminishes for parameters farther away from the autowave domain. For example, the distance that excitation pulses travel before converting into peaks becomes progressively shorter [Figs. 2(b)–2(d)].

DYNAMIC BEHAVIOR OF THE MODEL NEAR THE SADDLE-NODE BIFURCATION IN THE ABSENCE OF PEAK SOLUTIONS

Since peak formation by scenario 1 is preceded by propagation of autowavelike pulses, we wanted to examine the requirements for such behavior in more detail. For example, we wanted to determine whether such propagating pulses could be obtained in the model for parameter regions close to the saddle-node bifurcation boundary of autowaves, but where peak solutions do not exist. Figure 3(a) shows the one-parameter bifurcation diagram for $K_6=0.04$ and in the K_5 range where stable peaks are absent. The autowave solution disappears at $K_5(\mathrm{cr})\sim 15.87$ via a saddle-node bifurcation, and for $K_5>K_5(\mathrm{cr})$ the trivial, spatially uniform solution is the only stable solution to Eqs. (1) [Fig. 3(a)]. We found that in this parameter range a local, above-threshold activation immediately generates two excitation pulses, which propagate in opposite directions away from the site of activation. After traveling over some distance, both pulses disappear precipitately and the medium settles down to a stable, spatially uniform state [Fig. 3(b)]. As in the case described in the previous section, the traveled distance becomes progressively shorter with increasing K_5, and the wave forms diverge from the autowave. Therefore, propagation of autowavelike pulses can occur in the vicinity of the saddle-node bifurcation boundary, and in the parameter range where stable peak solutions do not exist. This strongly suggests that the initial dynamics of peak formation via scenario 1 is determined by the proximity of the stable peak domain to the boundary of saddle-node bifurcations.

COMPLEX SCENARIO 2 OF PEAK FORMATION

This is observed in the vicinity of saddle-node bifurcations of trigger waves. Another type of stationary wave solution to model (1) is a trigger wave. For some model parameters it can disappear via a saddle-node bifurcation. The trigger waves are observed if there are two stable spatially uniform states, the lower and upper. The trigger wave propagates at a constant speed without changes in the wave form and switches medium between these two states; either from the lower spatially uniform steady state into the upper steady state (on waves), or it returns the medium to the lower state (off waves) [7,10].

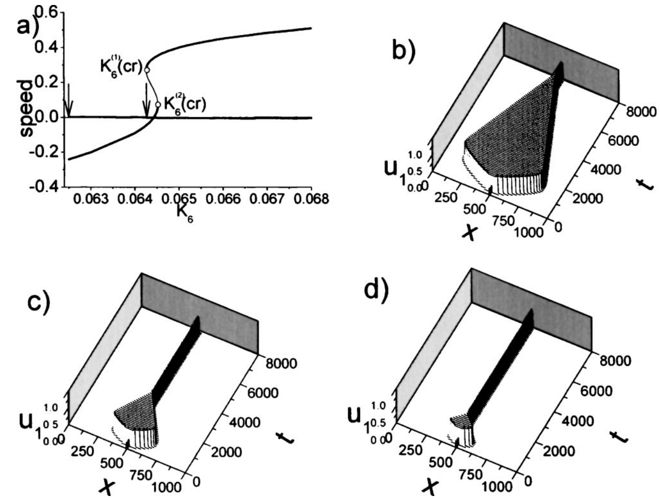

FIG. 4. Second complex scenario of peak formation. (a) The one-parameter bifurcation diagram for trigger waves with K_6, as the bifurcation parameter ($K_1=6.85$, $K_2=13.5$, $K_3=2.36$, $K_4=0.078$, $K_5=20.0$, and $D=1$); (b)–(d) peak formation in response to a local, above-threshold activation for (b) $K_6=0.0642$, (c) $K_6=0.064$, and (d) $K_6=0.63$.

In the BC model there is a small parameter range where the domain of the stable peak solutions borders the area of the saddle-node bifurcation of the trigger waves. We found that such proximity to the bifurcation boundary leads to an unusual transient process during peak formation. The bifurcation diagram in Fig. 4(a) shows mutual positions of the peak and trigger wave solution domains. The trigger wave diagram is S shaped and consists of three branches in which positive and negative speeds correspond to the on waves and off waves, respectively. At large K_6 only the on waves exist, while for small K_6 only the off waves are observed. There are two saddle-node bifurcation points $K_6^{(1)}(\mathrm{cr})$ and $K_6^{(2)}(\mathrm{cr})$ at which the branch of the unstable wave solutions merges with the branches of the stable wave solutions. In response to a local above-threshold activation, two on waves are generated and they travel in opposite directions for all parameter values within the domain of their existence and stability. A thick horizontal line at zero speed indicates the peak solutions. As seen in Fig. 4(a), the right boundary of the peak solutions domain coincides with $K_6^{(1)}(\mathrm{cr})$ where two on waves (stable and unstable) arise via a saddle-node bifurcation. In this region (the parameter range between the two arrows), the second complex scenario of peak formation is observed. Although at $K_6<K_6^{(1)}(\mathrm{cr})$, there are no solutions in the form of a stationary on wave, the initial response to the activation closely resembles the on waves [Fig. 4(b)]. Two on-wave-

like modes begin to propagate in opposite directions away from the activation point. Soon they stop and transform into off waves, which exist stably in this parameter range [Fig. 4(a)]. Then the off waves run backward to merge at the original activation site and form a peak [Fig. 4(b)]. As for the autowavelike pulses described above, the travel span of the on-wave-like modes from the activation site depends on the distance between $K_6^{(1)}(\mathrm{cr})$ and the corresponding K_6. For K_6 closer to $K_6^{(1)}(\mathrm{cr})$, the time during which the excitation zone expands is longer, and the travel distance of the on waves is bigger [Figs. 4(b)–4(d)].

DISCUSSION

There are several interesting, complex regimes observed in the BC model [11–13], some of which include the formation of peaks [4,6]. Peaks are found in a small area of the parameter space, but their formation may occur via intricate dynamics. Importantly, such dynamic behavior is observed whenever the stable peak domains border the saddle-node bifurcation boundary of the wave domain. The proximity within the parameter space of the standing peak domain to the saddle-node bifurcation line (surface) is one of the distinctive features of the BC model.

Both complex scenarios of peak formation described above are characterized by two distinct stages. During the first, in response to a local above-threshold activation, wave modes are generated. These running waves closely resemble the stationary wave solutions (autowaves or trigger waves) which exist on the other side of the saddle-node bifurcation boundary. The closer the parameters are to the bifurcation boundary, the greater the resemblance, and the longer the duration of the first stage. Since the events during the first stage are largely determined by the general properties of Eqs. (1), such as the continuous dependence of their solutions (over a finite time interval) on the model parameters (see [14,15]), we believe that a similar phenomenon is likely to be found in other reaction-diffusion models. In contrast, the events of the second stage of peak formation bear no resemblance to the modes seen on the other side of the bifurcation boundary. These processes cannot be predicted or explained from the general properties of the equations. Rather, they are determined only by the stable solutions that exist for given parameters and for given initial conditions.

The characteristic property of the BC model is that the initial conditions used (a local, above-threshold activation) are always in the basin of attraction of the wave solution. Asymptotically, at large t, this solution represents two waves that move without changes in the wave form in opposite directions along an infinite straight line. After a parameter change causes this mode to disappear, the trajectory in the infinite dimensional space starts from the initial conditions, continues along the same path as prior to the parameter change, and through the area which previously contained the attractor. After leaving this area, the trajectory tends to another attractor, which might be a peak solution, a spatially uniform state, a trigger off wave, or something else. The complex dynamics of peak formation described in this study deserve close attention as an example of how the proximity of a domain of one type of solution to the bifurcation line (surface) where the stable and unstable branches of another type of solution merge, can lead to the appearance of unusual dynamic modes.

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[1] S. Koga and Y. Kuramoto, Prog. Theor. Phys. **63**, 106 (1980).
[2] A. Ito and T. Ohta, Phys. Rev. A **45**, 8374 (1992).
[3] B. S. Kerner and V. V. Osipov, *Autosolitons: A New Approach to Problems of Self-Organization and Turbulence* (Kluwer, Dordrecht, 1994).
[4] V. I. Zarnitsina, F. I. Ataullakhanov, A. I. Lobanov, and O. L. Morozova, Chaos **11**, 57 (2001).
[5] See EPAPS Document No. E-PLEEE8-70-005409 for video files showing different scenarios of peak formation in the BC model presented in Figs. 1(a)–1(c). A direct link to this document may be found in the online article's HTML reference section. The document may also be reached via the EPAPS homepage (http://www.aip.org/pubservs/epaps.html) or from ftp.aip.org in the directory /epaps/. See the EPAPS homepage for more information.
[6] F. I. Ataullakhanov, V. I. Zarnitsyna, A. Yu. Kondratovich, E. S. Lobanova, and V. I. Sarbash, Usp. Fiz. Nauk **172**, 671 (2002) [Phys. Usp. **45**, 619 (2002)].
[7] V. A. Vasiliev, Y. M. Romanovskii, D. S. Chernavskii, and V. G. Yakhno, *Autowave Processes in Kinetic Systems* (VEB Deutscher Verlag der Wissenschaften, Berlin, 1987).
[8] M. Mimura and M. Nagayama, Chaos **7**, 817 (1997).
[9] M. Or-Guil, J. Krishnan, I. G. Kevrekidis, and M. Bär, Phys. Rev. E **64**, 046212 (2001).
[10] A. Hagberg and E. Meron, Nonlinearity **7**, 805 (1994).
[11] V. I. Zarnitsina, A. V. Pokhilko, A. I. Lobanov, O. L. Morozova, and F. I. Ataullakhanov, Int. J. Bifurcation Chaos Appl. Sci. Eng. **12**, 1985 (2002).
[12] A. I. Lobanov, T. K. Starozhilova, V. I. Zarnitsina, and F. I. Ataullakhanov, Mat. Model. **15**, 14 (2003).
[13] E. S. Lobanova and F. I. Ataullakhanov, Phys. Rev. Lett. **91**, 138301 (2003).
[14] Y. Nishiura and D. Ueyama, Physica D **130**, 73 (1999).
[15] Y. Nishiura and D. Ueyama, Physica D **150**, 137 (2001).