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Stability of neuronal pulses composed of concatenated unstable kinks

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We demonstrate that a traveling pulse solution, emerging from the concatenation of two unstable kinks, *can* be stable. By means of stability analysis and numerical simulations, we show the stability of neuronal pulses (action potentials) with increasing refractory periods, which decompose into two (radiationally) unstable kinks in the limit. These action potentials are solutions of an ultrarefractory version of the FitzHugh-Nagumo system.

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Pulses which bifurcate from the concatenation of a front kink and a back kink (with the same speed and direction) arise in a variety of physical systems. A model of CO oxidation on a platinum [Pt(110)] surface yields such solitary pulses near the onset of spatiotemporal chaos [1]. Sneyd *et al.* [2] found that their model of traveling calcium (Ca^{2+}) waves in pancreatic acinar cells is also of this type. A mode-locked laser with a multiple quantum well saturable absorber produces traveling flat-top pulses formed by linking together a front and back [3]. In a neuronal system, an action potential (or electrical pulse) held in a refractory, quiescent phase can be viewed as a conjoining of a generalized front (including the activation, excited and inactivation phases of the action potential) and a generalized back (consisting only of the final, recovery phase).

Since it is believed that neuronal systems communicate through action potentials, numerous studies have been conducted to analyze and ‘‘decode’’ neuronal signals [4]. In particular, Berry and Meister [5] experimentally and analytically found that extended, neuronal refractory periods may in fact enhance neural precision. Herein, we consider a model which effectively captures the dynamics of a neuronal system having a long and variable refractory period. The ultrarefractory FitzHugh-Nagumo system exhibits an action potential with a long (refractory) quiescent phase. If the refractory latent phase is prolonged indefinitely, the action potential with a widening quiescent phase will decompose in the limit into two (generalized) kinks, as shown in Fig. 1.

The issue of interest is the *stability* of these pulse solutions with elongating intermediary (quiescent) states, *in relation to* the stability of their limiting behavior: two coexisting kinks. It is known that pulse solutions bifurcating from two *stable* kinks may be either stable or unstable (depending on the first derivative of the Evans' function) [6]. A more intriguing question of recent interest is: Will the concatenation of two *unstable* kinks *necessarily* produce an *unstable* pulse? Nii [7], and Sandstede and Scheel [8] independently showed a case where such pulses experience a particularly severe instability. A cascade of unstable bound states accumulates, as the latent state between the front and back increases. On the other hand, Zimmerman *et al.* [1] obtained numerical results suggesting that the pulses may be stable even though the kinks are unstable.

In this article, we show that the seemingly paradoxical scenario of a *stable* pulse bifurcating from two *unstable* kinks can, and indeed does, occur. By studying the ultrarefractory FitzHugh-Nagumo system, we show that a stable pulse emerges from linking together two kinks with unstable continuous spectrum. Independently, Sandstede and Scheel [8] analytically showed, in this setting, the possibility of no unstable eigenvalues being created.

Before analyzing the stability of the solutions of the ultrarefractory FitzHugh-Nagumo system, we first briefly discuss the known dynamics of the FitzHugh-Nagumo equations which will be relevant in our analysis [9]. The model formulated independently by FitzHugh [10] and Nagumo *et al.* [11] qualitatively describes the spatial propagation of an action potential along a nerve axon. The system is

$$\begin{aligned} u_t &= u_{xx} + f(u) - w, \\ w_t &= \epsilon(u - \gamma w), \end{aligned} \tag{1}$$

where $\epsilon \ll 1$, $\gamma \ll 1$, and $f(u) = u(u-a)(1-u)$, for some $a \in (0,0.5)$. The fast, one-dimensional (1D) excitatory variable u mimics the neuron's membrane potential. The slow, inhibitory variable w captures the channel gating kinetics quantitatively described by the Hodgkin-Huxley model [12].

By introducing the moving frame $\xi = x - ct$, where c is the speed of the wave, the traveling wave solutions of Eq. (1) satisfy the ordinary differential equations (ODEs):

$$\begin{aligned} u' &= v, \\ v' &= -cv - f(u) + w, \\ w' &= -\frac{\epsilon}{c}(u - \gamma w), \end{aligned} \tag{2}$$

where $' = \mathrm{d}/\mathrm{d}\xi$. In the traveling wave phase space given by Eq. (2), at a particular speed c, there exists a homoclinic orbit based at the origin [13]. The homoclinic H_p corresponds to the traveling pulse solution of Eq. (1). Figure 2(a) shows the

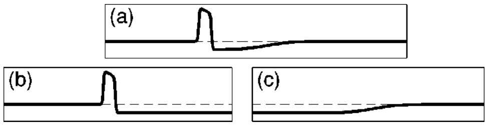

FIG. 1. (a) An action potential with a prolonged refractory, quiescent phase can be viewed as a concatenation of (b) a generalized front and (c) a generalized back. The rest state is denoted by a dashed line.

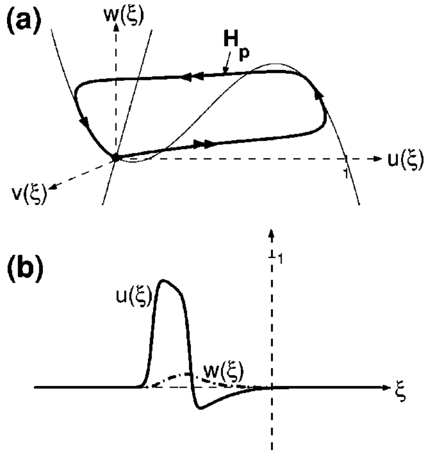

FIG. 2. The 2D traveling pulse solution of the FitzHugh-Nagumo equations, for $0<\epsilon\ll 1$, is depicted twice: (a) As the homoclinic orbit H_p in the 3D traveling wave phase space, where the thin solid lines correspond to the nullclines on the $\{v=0\}$ plane. (b) As functions of ξ. The pulse solution has two components: an excitatory (u) and an inhibitory (w). The double arrows in (a) indicate ''fast'' dynamics, and the single arrows, ''slow.''

two distinct scales of the system: slow (as H_p passes near $\mathcal{C}=\{(u,0,w):w=f(u)\}$, along its right then left-hand branches) and fast (as the orbit shoots across in the u-direction, between the left and right-hand branches of $\mathcal{C}$). The two scales are equivalently manifested in the fast and slow amplitude changes of the waves in Fig. 2(b). The action potential $u(\xi)$ has quick activation and inactivation phases, but a slow excited phase and a slow return to rest. Because of the singular nature of Eq. (1), it is possible to show the existence of a unique homoclinic orbit H_p, and to determine the stability of the pulse solution corresponding to H_p [6].

The ultra-refractory FitzHugh-Nagumo system has the same, fast excitatory behavior as (1), but with different slow, inhibitory dynamics:

$$\begin{aligned} u_t &= u_{xx}+f(u)-w, \\ w_t &= \epsilon[\alpha(w-\beta)^2+\beta^2(u-\alpha)], \end{aligned} \tag{3}$$

where $\alpha=0.1$, $\beta=0.01p$, and $f(u)$ is as before. The bifurcation parameter p controls the opening of the parabola, as seen in Fig. 3. Such a system might result from the reduction of a conductance-based neuron model [14] which incorporates various Ca^{2+} currents [15], in addition to the sodium (Na^{+}) and potassium (K^{+}) currents included in the Hodgkin-Huxley model. The parameter p should modulate according to the membranous currents considered. The effect of modulating p is to vary the length of the refractory period of the action potential. The longer the relative refractory phase of a neuron, the harder it is for the neuron to fire again; the longer the absolute refractory period of a neuron, the more time before a neuron may fire at all [16].

Setting $\xi=x-ct$, the traveling wave solutions of Eq. (3) satisfy

$$\begin{aligned} u' &= v, \\ v' &= -cv+w-f(u), \\ w' &= -\frac{\epsilon}{c}[(w-0.01p)^2+0.001p^2(u-0.1)]. \end{aligned} \tag{4}$$

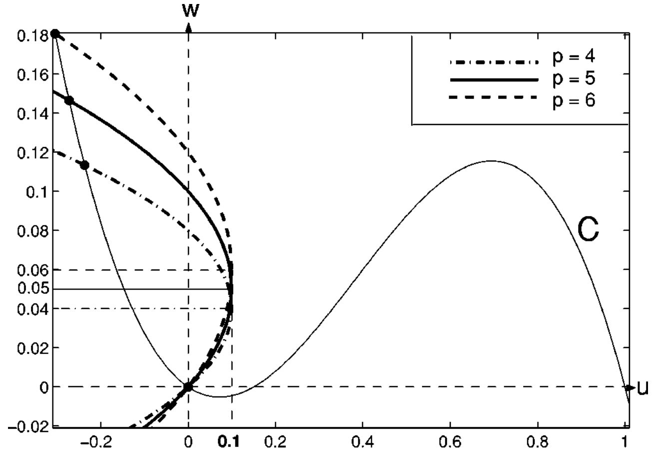

FIG. 3. The vertex of each parabola is located at $u=\alpha=0.1$ and $w=\beta=0.01p$. The critical points occur whenever the quadratic nullclines (for varying values of p) cross the cubic nullcline $\mathcal{C}$.

As depicted in Fig. 3, on the $\{v=0\}$ plane, the inhibitory nullcline crosses the excitatory nullcline $\mathcal{C}$ at (0,0,0) and $(\hat{u}(p),0,\hat{w}(p))$. As p decreases, the latter critical point moves down along the left-hand branch of $\mathcal{C}$, closer to the homoclinic orbit H_r. See Fig. 4.

Let p^* be the value at which

$$(\hat{u}(p^*),0,\hat{w}(p^*))=(u^*,0,w^*)$$

is a point contained on the homoclinic orbit corresponding to the pulse solution of Eq. (3). Since $(u^*,0,w^*)$ is a critical point, the homoclinic orbit H_r is now actually a heteroclinic loop (or cycle). One heteroclinic orbit [from (0,0,0) to $(u^*,0,w^*)$] corresponds to a generalized front solution of Eq. (3), while the other, ''shorter'' heteroclinic orbit [from $(u^*,0,w^*)$ back to (0,0,0)] corresponds to a slow, generalized back solution. For any small ϵ, there exists a bifurcation value $p^*(\epsilon)$. When $p>p^*(\epsilon)$, (4) has a homoclinic orbit corresponding to an action potential of (3); but when p

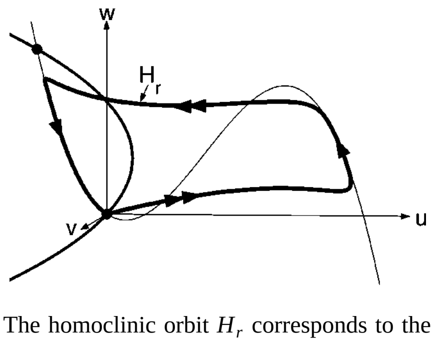

FIG. 4. The homoclinic orbit H_r corresponds to the pulse solution of Eq. (3). On the $\{v=0\}$ plane, the parabolic, w-nullcline crosses the cubic u-nullcline at two critical points: (0,0,0) and $(\hat{u}(p),0,\hat{w}(p))$.

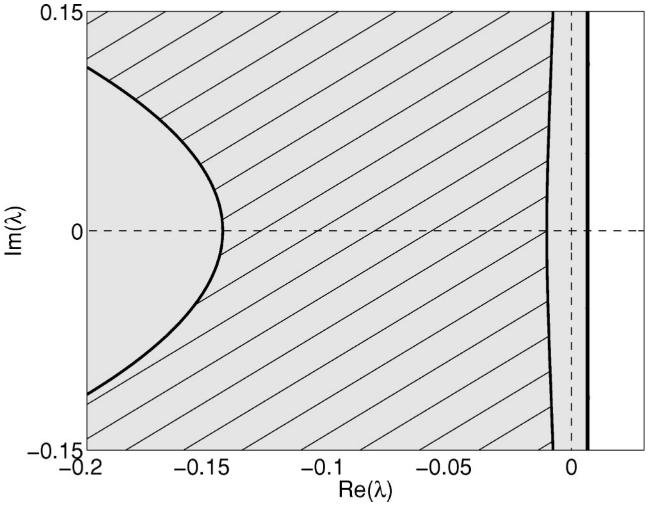

FIG. 5. The continuous spectrum of either the front or back wave solutions for $\epsilon=0.05$, $p=4.114$, $c=0.48$, and $a=0.15$, is shown. $\sigma_c((0,0))$ consists of the striped region; and the shaded region corresponds to $\sigma_c((u^*,w^*))$. Notice that $\sigma_c((0,0))\subset\sigma_c((u^*,w^*))$; and that $\sigma_c((u^*,w^*))$ extends into the (unstable) right-half plane.

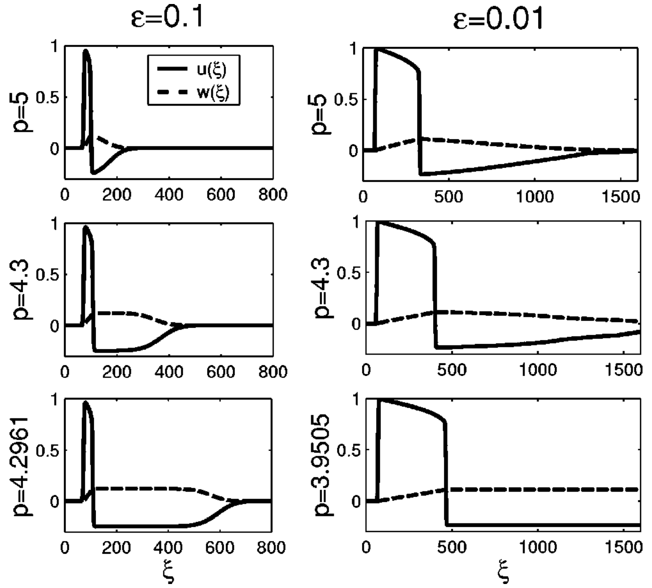

FIG. 6. For fixed ϵ, the quiescent states of the pulse solutions lengthen as p decreases. As ϵ decreases, the pulses experience a larger disparity between their slow and fast phases, in addition to lengthening latent states.

$=p^*(\epsilon)$, a heteroclinic loop for (4) exists instead. The parameter pair $(\epsilon,p^*(\epsilon))$, where the bifurcation from a homoclinic orbit to a heteroclinic loop occurs, is called a *T*-point [17]. A *T*-point bifurcation has been experimentally observed in a simple electrical circuit [18].

We are first interested in the stability of the two (generalized) kinks of Eq. (3). Using the argument in [6], we can show that neither kink solution has an eigenvalue in the unstable, right-half plane when $0<\epsilon\ll 1$. *If* either of the kinks had an unstable bound state, then the composite pulse solution would also have an unstable eigenvalue [19]. Since the kinks have no unstable eigenvalues, the pulse is not automatically unstable.

The continuous spectrum of a solution is associated with the far field steady states of that solution. If either of the asymptotic states of a wave is unstable, the wave itself suffers a radiation instability. Evans [20] showed that in some circumstances, the continuous spectrum can be located by calculating the eigenvalues of the corresponding critical points in the traveling wave phase space. In particular, since the critical point $(u^*,0,w^*)$ yields two eigenvalues with negative real parts and one eigenvalue with positive real part (when $c>0$), the continuous spectrum of (u^*,w^*) is unstable. Since both kinks have (u^*,w^*) as an asymptotic state, both kink solutions are radiationally *unstable*. This is consistent with the fact that kinks are not observed in neuronal systems.

We next calculate the continuous spectrum emitted from the steady state $(0,0)$. By numerically calculating the dispersion relation of (3) evaluated at $(0,0)$, we find that the continuous spectrum of $(0,0)$ is bounded in the (stable) left half-plane, for any small $\epsilon>0$. See Fig. 5. This fact does not affect the stability of the kinks, because they have already been shown to possess an unstable continuous spectrum. However, it does show that the pulse solution has no unstable continuous spectrum [since the rest state $(0,0)$ is the only asymptotic state of the pulse]. Thus we need only check for eigenvalues in order to fully determine the stability of the pulse solution.

Finding the eigenvalues of the pulse solution of Eq. (3) for $0<\epsilon\ll 1$ and $p>p^*(\epsilon)$ again follows the same argument as for the stability of the pulse solution of the original FitzHugh-Nagumo equations in [6]. The argument entails calculating the spectrum of each of the reduced systems for $\epsilon=0$ [these are the same systems for Eqs. (1) and (3)]; demonstrating that the eigenvalues for the full system, when $0<\epsilon\ll 1$, are nearby the eigenvalues of the reduced systems; and calculating that the right-most eigenvalue is a simple eigenvalue at the origin. In this manner, the ultra-refractory FitzHugh-Nagumo system is shown to generate *stable* pulse solutions (with varying refractory lengths) for any small ϵ and $p>p^*(\epsilon)$; though at the T-points $(\epsilon,p^*(\epsilon))$, the solutions of (3) have instead been shown to be two radiationally *unstable* kink solutions.

To verify numerically that the pulses are able to maintain their stability for all $p>p^*(\epsilon)$, we implement a Crank-Nicholson difference scheme with the modification that the nonlinear terms are evaluated using linearly extrapolated values of the solution at the two previous time steps [21]: $U^j_{\text{xtp}}=(1+\sigma)U^j-\sigma U^{j-1}$, where $\sigma=0.45$. This three-level scheme (in time) is conditionally stable. Since we are not interested in how the solutions change with varying a, we fix $a=0.15$. Either periodic or Neumann boundary conditions yield the same results (as long as the pulses are kept away from the boundaries).

The general procedure used for generating pulse solutions of Eq. (3) for fixed $\epsilon\in[0.01,0.1]$ and $p>p^*(\epsilon)$ is as follows: We first use the stable pulse solution generated by Eq. (3) for $p=p_1\gg p^*(\epsilon)$ as an initial condition for solving the system for $p=p_2<p_1$. We continue in this manner, each time using the solution for $p=p_{n-1}$, as an initial condition to solve Eq. (3) for $p=p_n<p_{n-1}$. As p decreases, the critical point $(\hat{u}(p),0,\hat{w}(p))$ approaches $H_r(\epsilon,p)$. The effect of the approaching equilibrium point on the pulse solutions of Eq. (3) is shown in Fig. 6. The quiescent state (between the inactivation and recovery phases of the action potential) elongates dramatically as p decreases. Because for each (ϵ,p), the pulses $(u(\xi),w(\xi))$ have a small domain of attraction (in function space), and they change drastically as p_n monotonically decreases to $p^*(\epsilon)$ [i.e., $p_n \downarrow p^*(\epsilon)$], the way to continue generating stable pulse solutions for smaller p-values is to choose $\{p_n\}$ so that $|p_n-p_{n-1}|\downarrow 0$ as $p_n \downarrow p^*(\epsilon)$.

Figure 6 also shows that the lengths of the latent states of the pulse solutions depend on ϵ. As ϵ decreases, the system becomes increasingly singular; the disparity between the solitary wave's slow and fast phases becomes more pronounced. Because the continuous spectrum of the constant vector function (u^*,w^*) extends into the right half-plane for a distance of $\mathcal{O}(\epsilon)$ from the imaginary axis, we only consider a pulse to be stable in computations, if it propagates unchanged for times of $\mathcal{O}(1/\epsilon)$. Thus any instability associated with the quiescent phase would have sufficient time to manifest itself.

The widening quiescent states of the pulses translate to longer refractory periods of the action potentials. This, in turn, decreases the maximal frequency in wave trains generated by a neuron. The ultra-refractory FitzHugh-Nagumo system (3) also appears to be an excellent coincidence detector [22]. Because of the shape of the inhibitory nullcline, a neuron modeled by (3) would be much more sensitive to input timing.

In conclusion, we have both analytically and numerically demonstrated that the pulse solutions of the ultra-refractory FitzHugh-Nagumo system, with widening quiescent phases, do not lose their stability as they approach their limit: two radiationally unstable kink solutions. The system accounts for variable refractory periods in neurons, and therefore provides a mechanism for controlling the precision and maximal frequency of wave trains. Furthermore, we believe that this is an important result for traveling wave solutions in any physical context: Though a traveling pulse solution is formed by concatenating two radiationally *unstable* kinks (of the same speed and direction), the resulting pulse *may still be stable*.

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