Targeting characteristic wave properties in reaction-diffusion systems by optimization of external forcing

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We consider the targeted manipulation of reaction-diffusion waves by optimization of an external forcing parameter. As an example, we present numerical results for the FitzHugh-Nagumo system exploiting model-based optimization capable of targeting characteristic wave properties such as wavelength, shape, and propagation speed by spatiotemporally controlling electric current. The conceptual basis of our approach is optimal control of periodic orbits in a wave-variable coordinate system. The results are transferred back to the partial differential equation context and validated in numerical simulations. The whole procedure is applicable to any reaction-diffusion model.

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I. INTRODUCTION

Dynamic pattern formation processes are the basis for many aspects of the high degree of structure and organization in nature. Nonlinear chemical and biochemical reaction processes far from equilibrium coupled with diffusion underly most mechanisms for spatiotemporal pattern formation and self-organization. The general aspect of controlling and manipulating such complex systems is important from the operational point of view in technical processes [1] and in biological systems [2]. Model-based control techniques have been developed specifically for this task over the past years [3–6]. However, these have been applicable only to static self-organized patterns so far, not including propagating waves. In [7], control techniques have been applied to stabilize existing but unstable moving fronts in the FitzHugh-Nagumo system. Here, we present a computational approach for specific targeting of characteristic wave properties in reaction-diffusion systems by appropriate control stimuli and demonstrate its applicability using the FitzHugh-Nagumo system as an example.

Specific potential example applications of such control approaches are the improvement of self-propagating high-temperature synthesis or frontal polymerization [1]. By using predefined input of heat or concentrations, the quality of the resulting product could be favorably influenced. In biology, impressing observations have been made suggesting that biochemical oscillations govern the activity of cellular immune responses [8], and, more importantly, diverse and dynamically regulated spatiotemporal waves, likely to be of the reaction-diffusion type, also seem to play an important role [9]. Since biological information processing is believed to be encoded at least partially in properties such as propagation speed, wavelength, intensity, and shape of propagating activation signals [8] and activity patterns, the study of manipulation of biochemical waves and their dynamic regulation seems to be of general interest.

In this article, we consider computational techniques for the targeted control of one-dimensional reaction-diffusion waves. An additional motivation to study these kind of control problems is the application for the study of inverse problems with the aim to identify potential dynamic input stimuli that lead to an observed or desired system output in the form of a measurable system readout. By computing the external influence needed to induce a specific oscillation shape, for instance, it is possible to discover what these interactions might be. This approach was illustrated successfully in [10] for ordinary differential equation (ODE) models of glycolysis.

The situation for oscillatory and excitable reaction-diffusion systems is somewhat different, as, by virtue of being represented by a partial differential equation (PDE), the behavior of the models takes place within an infinite-dimensional space, albeit usually only on a finite-dimensional manifold. However, in certain cases, the problem can be reduced to the targeted control of an ODE, using the so-called wave variable. This transformed system does not necessarily inherit the stability properties of the original model. Furthermore, as illustrated by the large number of publications dealing with special cases, no general mathematical theory exists that can link phase plane analysis to wave shape and wave velocity explicitly. This state of affairs suggests an experimental computational approach.

Self-organizing structures often occur in chemical and biochemical networks. Studying the effect of influence parameters on dynamics and the other way around—achieving a desired behavior by computing an appropriate amount of influence—is a key for understanding the mechanisms behind self-organization.

It is important to emphasize that our focus is on the computation of a specific forcing that produces predetermined properties, as are wave speed, length, or shape. In that point, it differs from other approaches (see [11], and the review in [12] and references therein), where the effects of given forcings are studied theoretically, and fairly complex behavior is investigated. Probably, combining both approaches would al-

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low for the targeted control of far more complex and subtle properties, a matter that shall be investigated in future work.

Since the most famous oscillating chemical reaction, the Belousov-Zhabotinsky reaction, was discovered in 1951, the importance of investigating related phenomena has been realized, especially in biological systems [13]. Following this insight, the interaction of reaction dynamics with diffusion effects under nonequilibrium conditions was found to be generally important for spatiotemporally self-organized behavior, cf. [14]. One of the most prominent early biological examples linking experimental observation of self-organization and mathematical modeling is the work by Hodgkin and Huxley on the electric signaling in nerve cells of the squid giant axon [15]. In this model, the components of the system describe electric currents occurring in an axon.

The Hodgkin-Huxley model is a standard model for studies concerning wave propagation and theoretically well understood [16], including its dispersion relation [17]. Numerous publications have appeared in the past years, treating external control of oscillatory or pattern forming dynamical systems. These extend from (sub)excitable systems [18] to feedback control of instabilities [19] and optimal control to target specific patterns [3,20].

We introduce our technique for computing the dynamic input to a system in the next two sections. To simplify matters, we do so on a concrete example: the bidiffusive FitzHugh-Nagumo system, which is a simplified version of the Hodgkin-Huxley model. We then illustrate the performance of the methodology in a few carefully selected examples, validating our results by performing simulations on the original PDE model. Our experimental studies suggest that, for this approach to work correctly, the parameter used to control the system must be restricted in order to avoid bifurcations.

II. MODEL EQUATIONS

Let us consider the FitzHugh-Nagumo equations [21], which present a simplified version of the Hodgkin-Huxley model [22]. They are also widely used for control studies of self-organization [23]. In a reduced form, we have a two-component dimensionless system, describing qualitatively the original full system,

$$\frac{\partial u}{\partial t} = D_1 \Delta u + u - u^3 - v + I_a,$$

$$\frac{\partial v}{\partial t} = D_2 \Delta v + \varepsilon(u - \gamma v + \delta). \qquad (1)$$

v and u denote hypothetical variables, u can be identified with voltage, and v can be understood as combined force trying to reach a rest state [24]. I_a denotes an applied current from the outside. These PDE of parabolic type present a standard example for a reaction-diffusion system displaying self-organized wave propagation. We restrict ourselves here to the spatially one-dimensional case. In these equations, it is not possible to influence the characteristic properties we are interested in only by using a constant input parameter I_a.

We introduce the "wave variable" $z=x-ct$ with the fixed wave speed c, obtaining the following system of ordinary differential equations:

$$-cu' = D_1 u'' + u - u^3 - v + I_a,$$

$$-cv' = D_2 v'' + \varepsilon(u - \gamma v + \delta), \qquad (2)$$

where the prime denotes differentiation with respect to z. Since we take the diffusion coefficients to be nonzero, we have to transform these equations into a system of first order.

A periodic wave train solution of Eq. (1) transforms into a periodic orbit solution of Eq. (2) and vice versa. To obtain a traveling wave solution of Eq. (1) with a given property, we will set up an optimal control problem, where the value of I_a is used as forcing parameter for controlling the wavelength, wave speed, and wave shape. We first consider a set of parameters for which Eq. (1) is in an oscillatory regime ($D_1=1$, $D_2=0.01$, $\varepsilon=0.01$, $\gamma=0.5$, $\delta=0$) and try to impose a chosen wavelength or wave speed. Under these conditions, for any wavelength a wave with specific wave speed, amplitude, and form exists in the uncontrolled case. For example a wave with velocity $c\approx 2.7$ and an amplitude of approximately 0.7 for both u and v is associated with a wavelength $L=20$.

With the choice of parameters we ensure that the nullclines of system (1) without diffusion intersect only once in an unstable fixed point with a stable limit cycle surrounding it [17,22]. The algebraic sign in Eq. (2) changes in comparison to Eq. (1), and thus the nullclines are reflected with respect to the u axis. The intersection point of the nullclines becomes a stable fixed point.

III. OPTIMAL CONTROL OF THE TRANSFORMED SYSTEM

For setting up the optimal control problem we use system (2) and formulate the square deviation between properties of the desired wave (characterized by the desired wavelength, velocity, or shape) and the controlled system output as objective functional to be minimized. Exemplarily, we provide the mathematical formulation only for the case of wavelength targeting. We denote the actual wavelength by L and the desired wavelength by L^* and want to solve the optimal control boundary value problem

$$\min_{u_1,u_2,v_1,v_2,I_a,L} F := (L - L^*)^2 \qquad (3a)$$

subject to

$$\frac{du_1}{dz} = u_2,$$

$$\frac{du_2}{dz} = \left(\frac{1}{D_1}\right)[-(u_1 - u_1^3 - v_1) - cu_2 - I_a],$$

$$\frac{dv_1}{dz} = v_2,$$

$$\frac{dv_2}{dz} = \left(\frac{1}{D_2}\right)[-\varepsilon(u_1 - \gamma v_1 + \delta) - cv_2], \tag{3b}$$

which is just the first-order transformation of Eq. (2), and

$$u_i(0) = u_i(L), \quad i = 1,2,$$

$$v_i(0) = v_i(L), \quad i = 1,2,$$

$$v_1(0) = 1,$$

$$v_2(0) = 0, \tag{3c}$$

which are the periodicity constraints together with a “phase condition” to exclude simple translations of the solution, and finally the restrictions

$$L_{\min} \leq L \leq L_{\max},$$

$$0 \leq z \leq L,$$

$$u_{i,\min} \leq u_i \leq u_{i,\max}, \quad i = 1,2,$$

$$v_{i,\min} \leq v_i \leq v_{i,\max}, \quad i = 1,2,$$

$$I_{a,\min} \leq I_a \leq I_{a,\max}, \tag{3d}$$

which are additional constraints with arbitrary values of lower and upper bounds which are required for the numerical reason to optimize on a compactum. Should the secondary variable, v, be nondiffusive, the first order transformation becomes obsolete and, to adapt the problem formulation, one could choose the accordant right-hand side of the model equation to be equal to 0 at $z=0$ instead of $v_2(0)$.

The cases with different objective functionals will be treated analogously to this one, replacing the wavelength by propagation velocity or wave shape, respectively. For wavelength targeting we choose control constraints $I_a \in [-0.455, 0.455]$ in order to ensure that the system dynamics remains in the oscillatory regime, since a Hopf bifurcation occurs at $I_a = \pm 0.4763$ for the chosen parameter values (as computed with XPPAUT [25]).

To solve this problem we use the optimal control package MUSCOD-II, which is based on a multiple shooting technique, cf. [26,27], where the interval $[0, L]$ is discretized into several subintervals by defining multiple shooting nodes as gridpoints. After parametrization of the control function on the multiple shooting grid, the corresponding ODE is solved independently on each subinterval. For continuity of the solution additional equality constraints are introduced at the multiple shooting nodes. The resulting nonlinear optimization problem is solved using a sequential quadratic programming algorithm.

(i) In the first example we control the wavelength. Selected results are shown in Fig. 1. A wavelength increase from 15 up to 25 can be achieved by applying a switching control function for I_a within the control bounds imposed. The wave speed is fixed to $c=2.5$. We use three equidistant multiple shooting intervals and a piecewise constant control function parametrization, as this seemed to be flexible enough to achieve our optimization goals. The control function switches three times to obtain the desired wavelength.

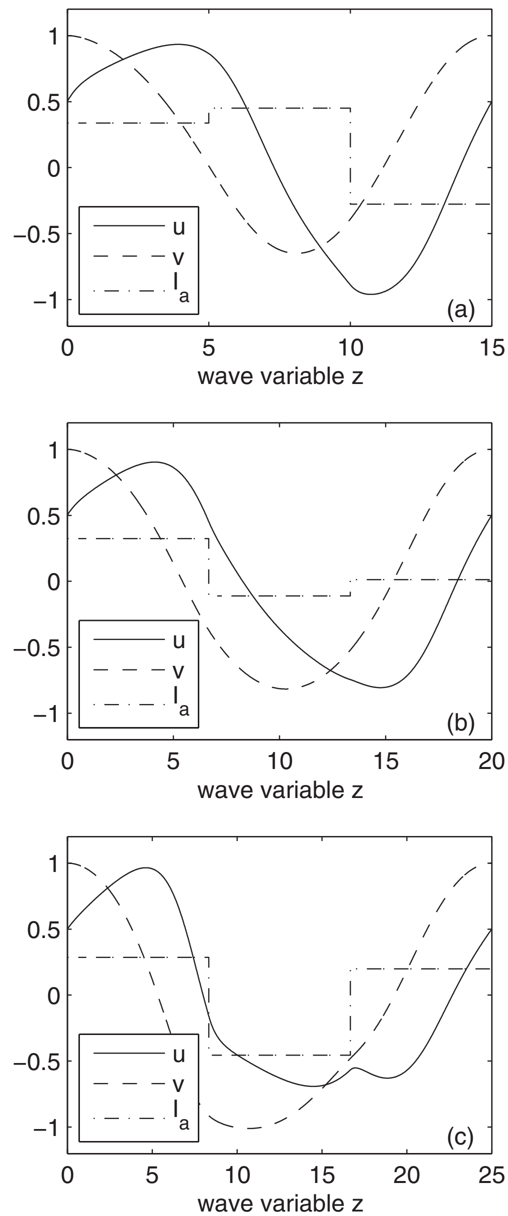

FIG. 1. Numerical solution results of problem (3a)–(3d) for target wavelengths (a) $L^*=15$, (b) $L^*=20$, and (c) $L^*=25$. The continuous line represents u, the broken line v, and the dash-dotted line the control I_a. Parameter values for system (1): $D_1=1$, $D_2=0.01$, $\varepsilon=0.01$, $\gamma=0.5$, $\delta=0$. The objective functional values are 7.31×10^{-12}, 2.16×10^{-13}, and 4.50×10^{-11}.

(ii) In Fig. 2 we present results for influencing the wave speed. The same conditions as for scenario (i) are used. Three multiple shooting intervals and a piecewise constant function make it possible to target wave velocities between $c=2.12$ and $c=3.35$. A fixed wavelength $L=20$ is chosen. We show the maximum range of reachable velocities under the given constraints. In the second multiple shooting interval the influence parameter nearly catches the bound of ± 0.455, where the oscillatory domain is ending.

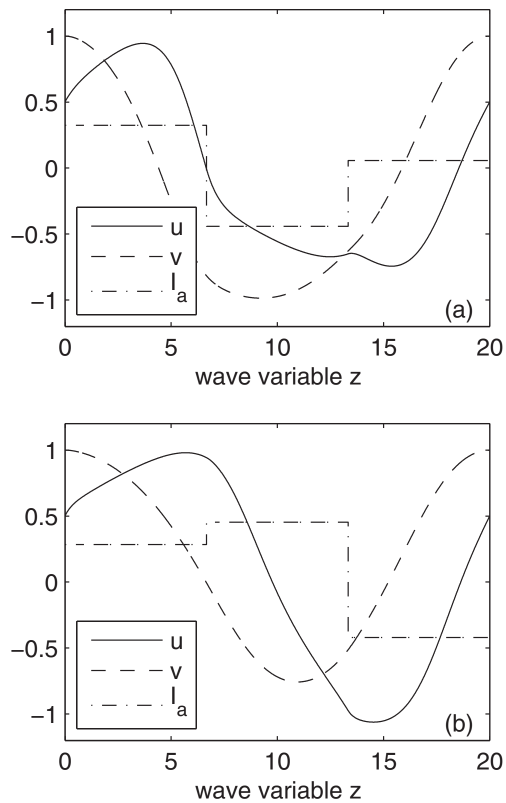

FIG. 2. Numerical solution results of problem (3a)–(3d) for target wave speed (a) $c^*=2.12$, (b) $c^*=3.35$. Changes in problem formulation: Objective function $(c-c^*)^2$, with c^* desired wave speed, $c_{\min}\leq c\leq c_{\max}$, $L=20$ is fixed. All other parameters as in Fig. 1. Objective functional values are 5.14×10^{-10} and 1.15×10^{-10}, respectively.

(iii) The most challenging control objective we treat is the targeting of a sine profile for the second variable v, just to make a choice, with a fixed amplitude of 1.9, fixed wavelength $L=20$, and fixed wave speed $c=2.5$. To achieve an accurate adjustment to a sine function, we use cubic splines for the input I_a on five multiple shooting intervals (see Fig. 3). We allow $I_a\in[-10,10]$ and thereby cover both the oscillatory and excitable regime. We make the following modification of the objective functional (3a):

$$\min_{u_1,u_2,v_1,v_2,I_a,L} F := \int_0^{20}\left[v_1(z) - 1.9\times\sin\left(\frac{2\pi z}{20}\right)\right]^2 dz. \quad (4)$$

The constraints (3b)–(3d) are mostly the same, however we have no initial value constraint for $v_2(0)$ here, changed the initial value for v_1 into $v_1(0)=0$ (as given by the sine function), and introduced a periodicity constraint for I_a.

IV. VALIDATION OF WAVE TARGETING IN NUMERICAL SIMULATIONS

To verify that the waves predicted for the optimally controlled system indeed exist and are stable in the context of the original FitzHugh-Nagumo PDE model, we transfer the output data of the optimization into the context of a numerical PDE simulation. For the simulation we discretize (1) first in space using finite differences, and then solve the resulting ODE system using a backward differentiation formula (BDF) method, implemented in DAESOL [28,29]. The total length of the one-dimensional spatial domain is chosen to coincide with the wavelength and periodic boundary conditions are imposed. We choose an equidistant grid width of 0.1 and use the optimal trajectory output of MUSCOD-II (as a spatial profile in the wave variable $z=x-ct$ at time $t=0$) after linear interpolation on the grid points as spatially distributed initial values. The control variable I_a moves with the wave velocity c, defined or computed in the optimization process. This ensures that I_a from the wave-variable coordinate system takes the correct value in space at the right time. The wave moves together with the control function from the left to the right as illustrated by the snapshots in Fig. 4.

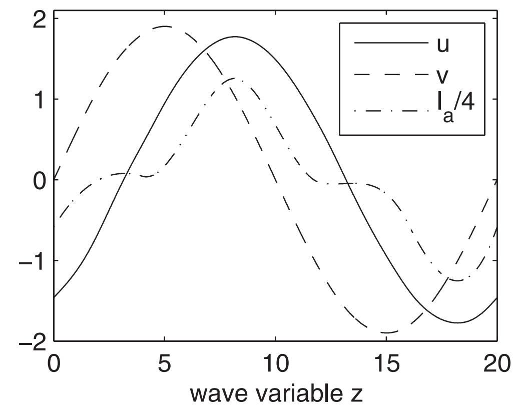

FIG. 3. Numerical results for problem (4): Targeting a sine-shaped wave for v. Here, we use piecewise cubic splines as control parametrization. Parameters as in control scenarios (i) and (ii). Value of the objective function: 1.05×10^{-4}.

As we can see in Fig. 4, the induced wave is indeed stable and propagates in the computed shape without change. Figure 5 shows the PDE simulation corresponding to example (ii) targeting a desired wave speed. Also in the third case study, where we controlled the wave of v to a sine shape and pushed the amplitude to an extreme value of 1.9, the wave propagates through space without changing shape, as can be concluded from Fig. 6.

To confirm the stability of all these waves, we computed Floquet multipliers for the discretized PDE system in order to theoretically determine stability properties. The monodromy matrix was computed for one full transition of the wave through space for each grid point meaning one period of the periodic wave train. Computations were done by internal numerical differentiation implemented in the code DAESOL [28,29]. In all cases presented above, the absolute values of the Floquet multipliers are smaller than 1. This is strong evidence that the waves are stable in all control scenarios.

V. SUMMARY

We present in this paper a generally applicable and robust numerical approach to the specific targeting of wavelength,

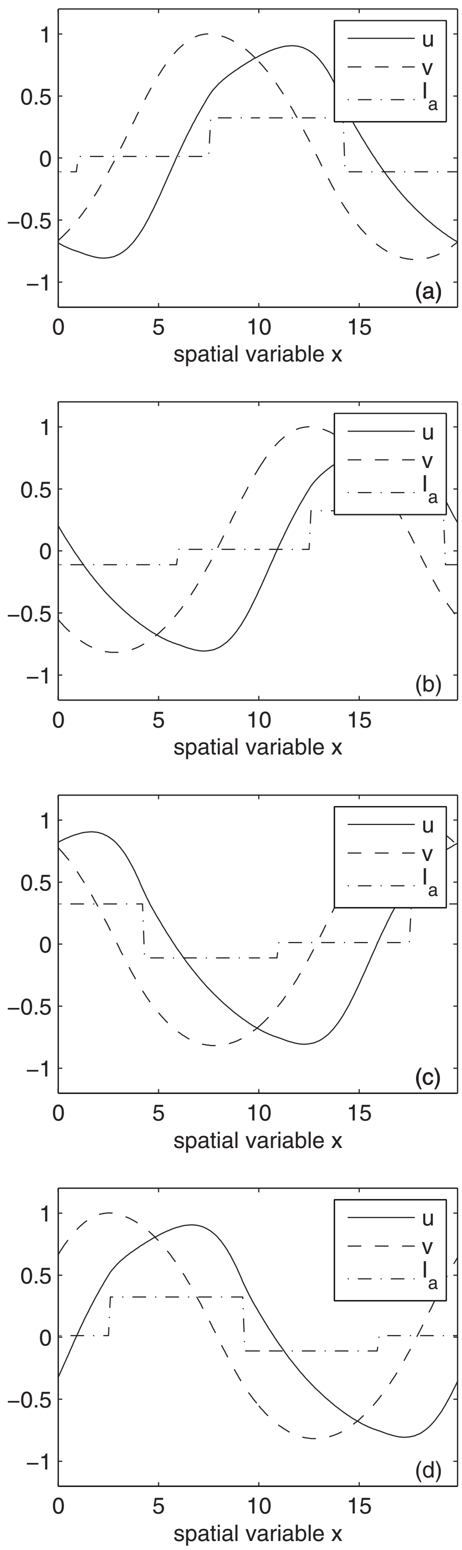

FIG. 4. PDE of control scenario (i) (wavelength): Conditions and parameters as in Fig. 1(b), $L=20$. Snapshots are presented at different points in time, (a) $t=75$, (b) 125, (c) 175, (d) 225. Numerical integration was performed using DAESOL [28,29]. Spatial grid width 0.1. Optimal trajectory output of MUSCOD-II in the wave variable z for $t=0$ linearly interpolated on the grid points as initial values. Between two successive pictures the wave has crossed space already six times.

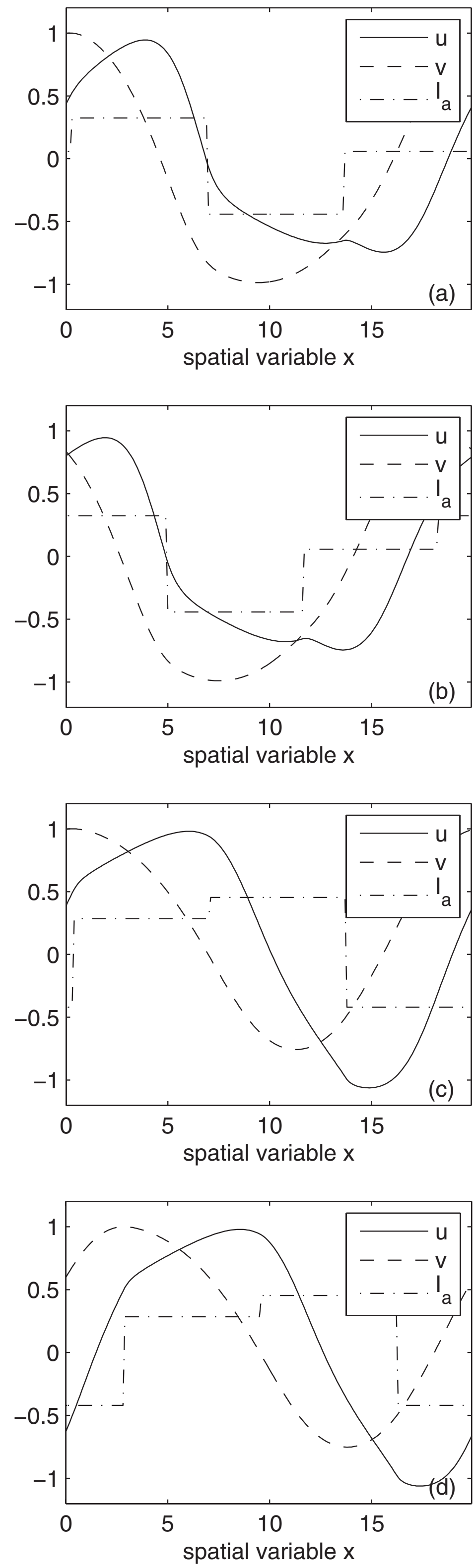

FIG. 5. PDE of control scenario (ii) (wave propagation speed): Conditions and parameters in (a) ($t=0.1$), (b) ($t=150.1$) as in Fig. 2(a), $c=2.12$, and in (c) ($t=0.1$), (d) ($t=150.1$) as in Fig. 2(b), $c=3.35$. Transfer of optimal control output into the PDE simulation as described in Fig. 4. In the first case, the wave crosses the domain nearly 16 times between the two snapshots without changing shape, and in the second case it does so more than 25 times.

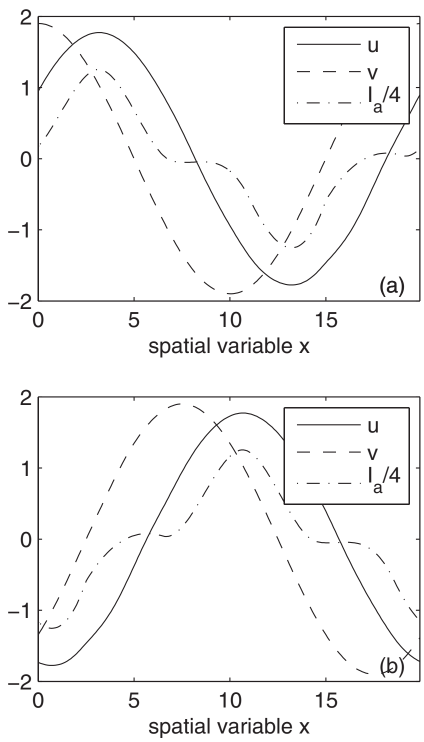

FIG. 6. PDE of control scenario (iii) (sine-shaped v with amplitude 1.9) at (a) $t=150$ and (b) $t=225$.

velocity, amplitude, and shape in reaction-diffusion systems by external forcing. Of course, also other objective functions are conceivable, e.g., including the control force. We predefine a desired behavior and compute the necessary influence for achieving this behavior numerically, using the wave variable. In contrast to former approaches, which applied a periodic forcing and studied its influence on spatiotemporal dynamics (see [12] for a review), our approach can be used to compute control function which influence the model system obtaining a desired behavior. The details of this additional external forcing can be interpreted as a dynamic difference between the model and an observed behavior. For a demonstration of the capability of this method we have applied it to the FitzHugh-Nagumo system, assuming a piecewise constant or piecewise cubic external control parametrization, and show results for various control scenarios.

Our aim was to apply a control function as easy as possible and restricted ourselves to piecewise constant functions with a minimal number of equidistant intervals. The computed control functions are dependent on the number of these intervals and the optimal solution is not unique since the optimization problem is underdetermined. An extension of the range of controlability, e.g., allowing stronger influence or refining the resolution of the input, and choosing a larger number of subintervals may result in a greater range of achievable output, but there exists no general theory right now.

Transfer of results into numerical simulations of the FitzHugh-Nagumo PDE system and stability analysis confirmed the existence of stable traveling wave trains with the desired properties.

An interesting possibility to test these methods in a real-world scenario would be to use the Belousov-Zhabotinsky system, where a source of light can be used to influence the reaction. Since fairly accurate reaction-diffusion models exist, we predict that it may be possible to compute an illumination regime that induces a desired wave speed, length, or shape within a certain range.

Our approach is applicable to reaction-diffusion PDE systems in general. Even in the case of unstable waves a straightforward extension to the use of nonlinear model predictive control [30,31] within our optimization framework could be used to stabilize wave propagation.

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