# Interaction function of coupled bursting neurons*

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The interaction functions of electrically coupled Hindmarsh–Rose (HR) neurons for different firing patterns are investigated in this paper. By applying the phase reduction technique, the phase response curve (PRC) of the spiking neuron and burst phase response curve (BPRC) of the bursting neuron are derived. Then the interaction function of two coupled neurons can be calculated numerically according to the PRC (or BPRC) and the voltage time course of the neurons. Results show that the BPRC is more and more complicated with the increase of the spike number within a burst, and the curve of the interaction function oscillates more and more frequently with it. However, two certain things are unchanged: $\phi = 0$, which corresponds to the in-phase synchronization state, is always the stable equilibrium, while the anti-phase synchronization state with $\phi = 0.5$ is an unstable equilibrium.

**Keywords:** phase response curve, burst phase response curve, interaction function, phase locking

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## 1. Introduction

The Kuramoto model was originally motivated by the phenomenon of collective synchronization and now is the most popular model to be used in the coupled oscillating neurons to study the collective states among diverse groups of neurons.[1,2] Collective synchronization was first studied mathematically by Wiener,[3,4] but his approach has turned out to be wrong. The pioneering work was begun by Winfree,[5] who formulated the problem in terms of a huge population of interacting limit-cycle oscillators. Then Kuramoto promoted Winfree's work and put his intuition about phase models on a firmer foundation.[6] In the Kuramoto model, the interaction between the coupled oscillators is described by the simplest possible case of purely sinusoidal coupling. However the simple sinusoidal interaction function is far from sufficient in wide ranges of experimental situations.[7–10] For example, the coupling of Hodgkin–Huxley (HH) model neurons, which is one of the most important models in computational neuroscience representing real spiking neurons of the brain, needs at least three Fourier modes when they couple electrically.[11] Since the interaction function in the Kuramoto model is insufficient, how can we know the real interaction function which changes from model to model and experiment to experiment? One way of obtaining the interaction function is appealing to the theory of weakly coupled oscillators[12–14] which indicates that interaction function takes the form of a convolution of an intrinsic property of the oscillator, the phase response curve (PRC), and the coupling mechanism between any two such identical oscillators.[15–17] As it is pointed out in Ref. [18], when applied to electrically coupled regularly oscillating neurons, the coupling mechanism is easily specified: It is proportional to the difference of the voltage time course. Once the interaction function is available we could use it to analyze the phase-locking states and their stability property. Synchronization is an important phenomenon in coupled neurons because different synchronization regimes may correspond to different cognitive and pathological states.[19–21] We also can use the interaction function between coupled neurons to further investigate the phase synchronization of the system.

The PRC of an oscillating neuron measures the phase shifts in response to stimuli delivered at different times in its cycle.[22] PRC is an effective tool to predict the phase-locking behavior in the networks of neurons and to understand the mechanisms that underlie this behavior. In general, however, the PRC is difficult to compute analytically and is often computed numerically.[23–26] There are two basic ideas for numerical computation of PRC. One of them is based on direct computation of the oscillator response to short pulses delivered at different phases of the oscillator.[25] Another idea is to linearize the system around the stable limit cycle and solve the linear adjoint equations.[23,24,26] In this way, we could conveniently obtain the PRC normalized by the amplitude of the impulse due to an infinitesimally small perturbation, which is also called the infinitesimal phase response curve (iPRC). For tonic spiking neurons, there are two kinds of curves according to their different shapes termed type 1 and type 2.[27] Type-1 PRCs are wholly positive or wholly negative, i.e., the perturbations can only cause the phase advancing or delaying. Meanwhile type-2 PRCs have both positive and negative portions, so their response can be both phase advancing and phase delaying. However, this classification is not suitable for

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bursting neurons because they have complex phase response properties[28] and their shapes of PRC are rather rough.

In a previous study,[18] the authors have investigated the nature of the interaction function for coupled oscillating neurons and some degree of generalization has been achieved by using several critical parameters. However, they only considered the case of tonic spiking neurons based on the HH model. As we know bursting activity is apparently different from spiking and the shapes of PRC are totally different, so we want to know what the interaction function will be like for coupled bursting neurons. In this paper, we investigate the interaction function of Hindmarsh–Rose (HR) neurons[29–31] which can exhibit diverse bursting activities. We organize our study as follows: we first introduce the models and the method we adapted to compute the interaction function. Next we present some analytical expressions for interaction function and use the interaction function curves to analyze the phase-locking behaviors between the two coupled neurons. Finally, we compare the results and give the conclusions.

## 2. Model and methods

### 2.1. Neuronal model

In this paper, we focus on a particular model of neuronal bursting, the Hindmarsh–Rose(HR) model. It was originally proposed to give a bursting type with long inter-spike intervals of real neurons and now is widely used to simulate the firing behaviors of the real neuron. The model is expressed by the following three ordinary differential equations

$$\begin{aligned}\dot{x} &= y - ax^3 + bx^2 - z + I,\\ \dot{y} &= c - dx^2 - y,\\ \dot{z} &= r[s(x-\chi) - z],\end{aligned}$$

where the variable $x$ is the membrane potential, $y$ represents the fast current of $Na^+$ or $K^+$, and $z$ associates with the slow current, like currents of $Ca^{2+}$. We employ the parameter set $a = 1$, $b = 3$, $c = 1$, $d = 5$, $r = 0.006$, $\chi = -1.6$, and the parameter $I$, which means the stimulus current that enters into the neuron from the external environment, is taken as a control parameter to get different firing patterns.

As the bifurcation parameter $I$ is increased, the states of the neuron will change from quiescent state to bursting, and then to tonic spiking. One can reference the bifurcation diagram of the interspike interval (ISI) and the corresponding time course of the membrane potential in Ref. [32].

### 2.2. Phase response curve (PRC) and burst phase response curve (BPRC)

The PRC is an intrinsic property of the oscillator and defined as the steady phase shift of an oscillation relative to the unperturbed oscillation as a function of the perturbation to the oscillator.[33] It provides useful information for understanding the oscillator's behavior when the oscillator is subjected to external stimuli or signals from other oscillators. There are two fundamental firing modes in the neuron: tonic spiking and bursting. Tonic spiking is marked by continuous firing of action potentials, normally at a fixed rate, while bursting is characterized by relatively slow, periodic alternation between periods of spiking and periods of quiescent state. The PRC is originally used for the spiking case, and it is periodic with the same period as that of the neuron. Then the PRC was extended to the bursting case by Sherwood *et al.*[28] and they called it burst phase response curve (BPRC) to avoid confusion. It demonstrates the shift in the timing of the onset of the active segment of a neuron's next burst cycle due to perturbation at a particular phase of its current burst cycle. BPRC is different from PRC, for example, it is possible for a perturbation to change the timing of the next spike (of the perturbed burst cycle) without changing the timing of the next full burst cycle. However for the PRC case, the change in timing of the onset of the next spike is precisely the relevant quantity in measuring phase response.

In what follows, we give a comparison of the PRC and BPRC for the HR neuron when $I$ take different values. The results are depicted in Fig. 1 and calculated by Viktor's method.[22] Firstly, we compare two cases of spiking-1 ($I = 4.0$) and bursting-1 ($I = 1.4$) firing patterns. Apparently, they are totally different. The PRC corresponding to spiking-1 ($I = 4.0$) is continuous and smooth as a whole and it has both positive and negative parts which means phase advancing and delaying, while the BPRC corresponding to bursting-1 ($I = 1.4$) changes more roughly and irregularly. At the firing time the curve has a sharp spike while in the other time it gently closes to zero. The difference between their shapes causes them to have different properties. Then we take a look at all the bursting cases and find the BPRC have the following interesting properties: (i) the phases are obviously advanced or delayed when the perturbations are added near the firing time in the burst, while in the other time the phase responses are almost equal to zero, and (ii) the phases responses are always delayed during spikes except the last spike in the burst and the amplitudes of these phase response peaks become bigger and bigger. For the last spike, the phase response has a sharp advancement opposite to all the former cases, maybe because it is the time to end the spiking state and begin the quiescent state. Sherwood *et al.* explained the particular shape of BPRC for HR neuron using isochron geometry of fast subsystem, which demonstrated that the shape of BPRC may be closely related to the intrinsic structure properties of the system itself. One can get more details in Ref. [28].

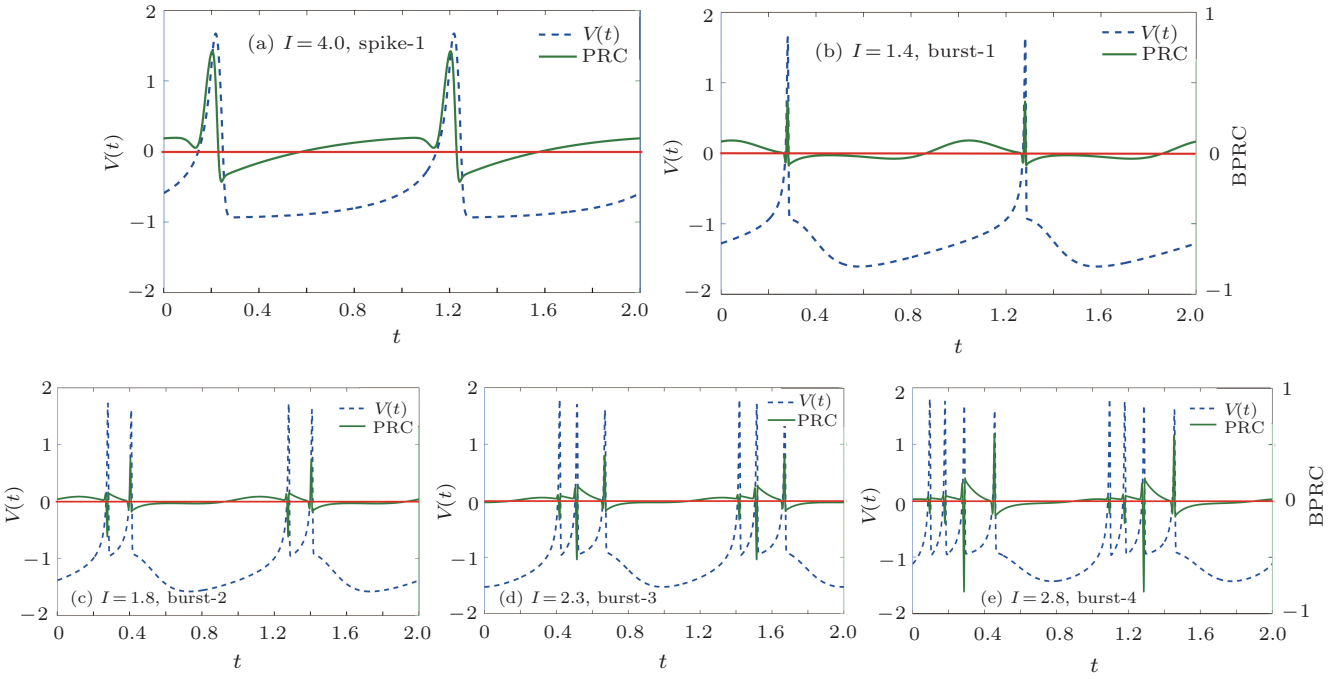



**Fig. 1.** (color online) The voltage time course and PRC or BPRC for two periods and the period is normalized to be 1. The green line represents the PRC or BPRC and the blue dashed line represents the voltage time course of the HR neuron. (a) $I = 4.0$, spike-1; (b) $I = 1.4$, burst-1; (c) $I = 1.8$, burst-2; (d) $I = 2.3$, burst-3; (e) $I = 2.8$, burst-4.

### 2.3. Method of computing the interaction function

If the coupling of two neurons is sufficiently weak, the possibly high-dimensional system can be reduced to a network of coupled phase models.[34,35] The phase evolution equations corresponding to a pair of weakly coupled identical neurons are as follows:[14]

$$\begin{aligned} \mathrm{d}\theta_1/\mathrm{d}t &= \omega_0 + KH(\theta_2 - \theta_1), \\ \mathrm{d}\theta_2/\mathrm{d}t &= \omega_0 + KH(\theta_1 - \theta_2), \end{aligned}$$

where $\omega_0$ is the oscillating frequency of each neuron in the absence of coupling, $K$ is the coupling coefficient, and $H(\cdot)$ is the interaction function, which is given by the following expression for the electrical coupling:

$$H(\phi) = \frac{1}{T}\int_0^T Z(t)[V(t+\phi) - V(t)]\mathrm{d}t,$$

where the phase difference $\phi$ ranges from 0 to $T$. For convenience, we usually normalize the period $T$ to be 1. $Z(t)$ is the PRC or BPRC of the coupled neurons and $V(t)$ represents the membrane voltage course of the neuron. Once the interaction function is known, it is convenient to analyze the collective behavior of the coupled neurons. In the following section, we will calculate $H(\phi)$ numerically and analyze the synchronization state of coupled neurons by it.

Obviously, $H(\phi)$ is a periodic function depending only on the phase difference $\phi = \theta_2 - \theta_1$. The dynamic equation of the phase difference can be obtained as follows:

$$\frac{\mathrm{d}\phi}{\mathrm{d}t} = K(H(-\phi) - H(\phi)) = KG(\phi).$$

The stable solutions of this equation give the stable synchronization states of the coupled neurons. Note that the function $G(\phi)$ ($G$-function) can be used to determine the phase-locking behavior of the coupled neurons. The zeros of $G$-function are phase-locking states of the coupled neurons. If $\phi = 0$ is a stable solution, it implies that the synchronous solution is a steady state of the system, and the stability of the steady state is determined by the derivative of $G(\phi)$. The conditions for the stability of the fixed point are:

$$G(\phi) = 0$$

and

$$\frac{\mathrm{d}G(\phi)}{\mathrm{d}\phi} < 0.$$

According to the above conditions, we can easily identify the synchronization state and judge its stability with the curve of $G$-function we derived numerically.

## 3. Results

In this section, we give the interaction function of the electrically coupled HR neurons numerically when the parameter $I$ is chosen as the controlling parameter. Furthermore, we analyze the synchronization state of the neurons by $G$-function, which dominates the phase-locking activities.

Firstly, the simplest case with the external stimulus current being $I = 4.0$ is considered. In this case, the single HR neuron exhibits stable period-1 spiking. Then the curve of the interaction function derived by the phase reduction technique and the curve of the $G$-function are depicted in Fig. 2. It is obvious that the curve of the interaction function is very smooth

as a whole, and it is steep when the phase difference is small and steady for the larger phase difference. In order to judge the synchronization state of the coupled neurons, the $G$-function is also presented in Fig. 2(b).

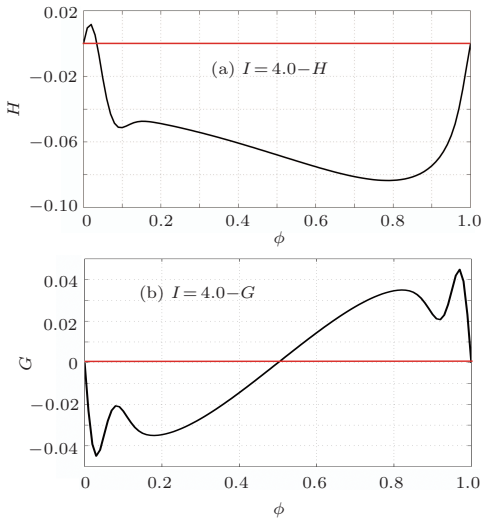



**Fig. 2.** (color online) (a) The curve of the interaction function and (b) the curve of $G$-function for $I=4.0$.

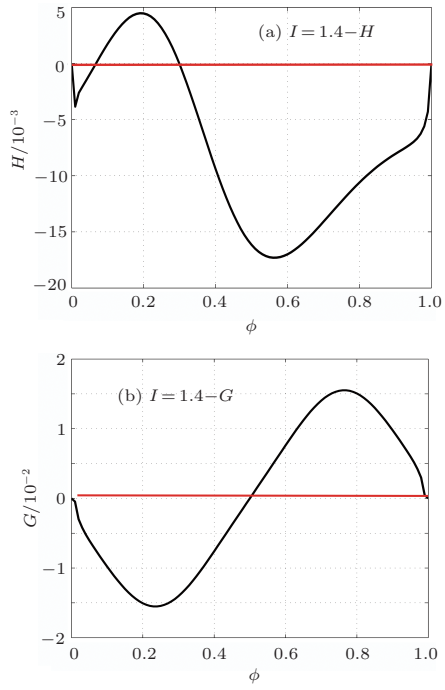



**Fig. 3.** (color online) (a) the curve of the interaction function and (b) the curve of $G$-function for $I=1.4$.

It is concluded that there are two zero points on the curve. $\phi=0$ is the stable fixed point which corresponds to the stable in-phase synchronization state, while the anti-phase synchronization state which corresponds to $\phi=0.5$ is unstable. It means that two electrically coupled spiking neurons will always reach in-phase synchronization.

Secondly, we consider the situation when $I=1.4$, with which the HR neuron exhibits period-1 bursting. The curve of the interaction function derived by the phase reduction technique and the curve of the $G$-function are presented in Fig. 3. The BPRC has significant difference with the PRC above. There is an impulse response at the time of neuron firing and the curve is softer at the other time. Nevertheless, the curve of the interaction function is steadier and more regular than that of the spiking case. The curve of $G$-function looks simpler and it just looks like a reversed sine curve. Similarly, the function $G(\phi)$ also has two zero points and $\phi=0$ is the stable equilibrium while the antiphase difference $\phi=0.5$ is unstable. It also implies that two electrically coupled bursting neurons will reach in-phase synchronization.

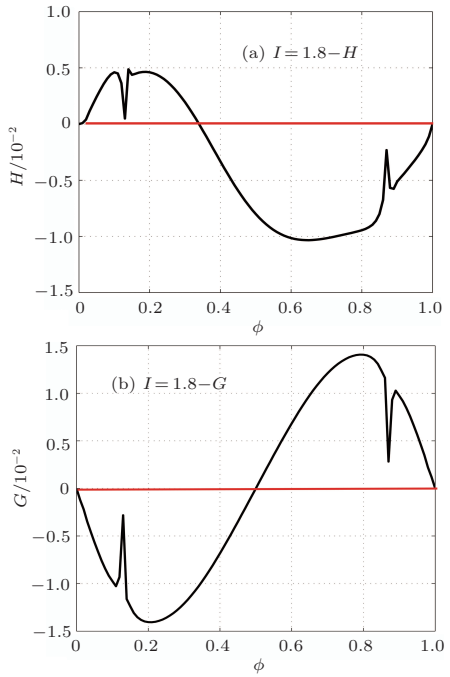



**Fig. 4.** (color online) (a) The curve of the interaction function and (b) the curve of $G$-function for $I=1.8$.

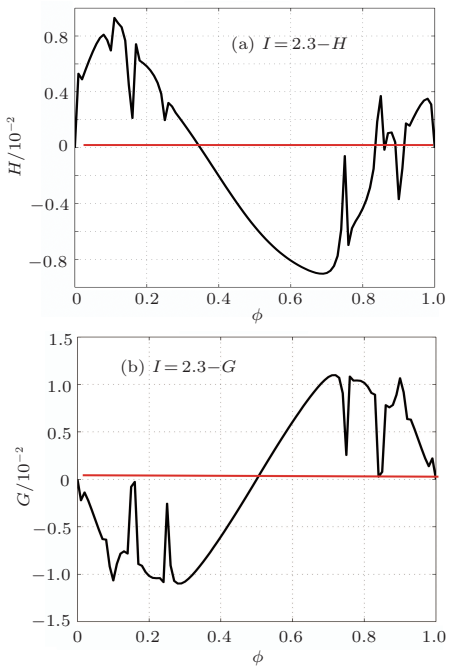



**Fig. 5.** (color online) (a) The curve of the interaction function and (b) the curve of $G$-function for $I=2.3$.

Finally, we consider more complex cases when the neuron shows period-2, period-3, and period-4 bursting with $I = 1.8$, $I = 2.3$, and $I = 2.8$. The numerical results are depicted in Figs. 4–6. It is obvious that as the stimulus current increases, the neuron fires more spikes per burst and the BPRC becomes more complicated and irregular. The curves of the interaction function and $G$-function are no longer as smooth as the situation when $I = 1.4$.

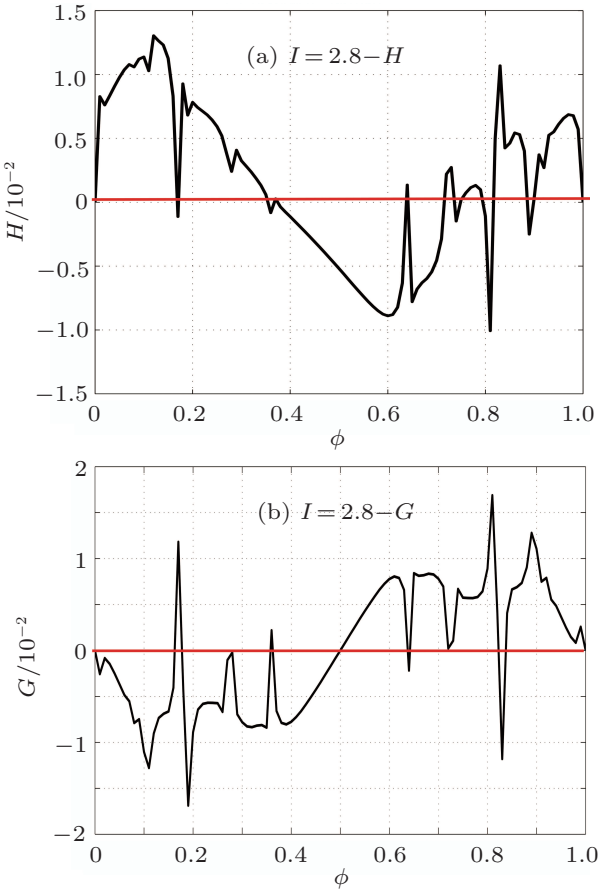



**Fig. 6.** (color online) (a) The curve of the interaction function and (b) the curve of $G$-function for $I = 2.8$.

For the simple bursting such as burst-2 and burst-3, the function $G(\phi)$ also has two zero points and $\phi = 0$ is the stable equilibrium while the antiphase difference $\phi = 0.5$ is unstable. It means that in-phase synchronization is the final state of two electrically coupled neurons. It is notable that new equilibriums of $G$-function appear when $I = 2.8$. Some of them are stable and others are unstable, which means that multistable synchronous states exist for coupled bursting neurons. However, two certain things are unchanged: $\phi = 0$, which corresponds to the in-phase synchronization state, is always the stable equilibrium, while the anti-phase synchronization state with $\phi = 0.5$ is an unstable equilibrium. In short, the curves of $G$-function for different bursting types have some common properties. That is, the curves of $G$-function look like sine curve with the parameter $I$ changing from $I = 1.4$ to $I = 2.8$. But more oscillations appear with the increase of the spike number within one burst, which is quite different from the situation of tonic spiking.

## 4. Conclusion and discussion

In this paper, we mainly investigated the interaction function of electrically coupled bursting neurons by the theory of PRC. PRC is an effective tool to predict the phase-locking behavior in the network of neurons and to understand the mechanisms that underlie this behavior. However, it is only effective for spiking neurons. It is well known that bursting plays important roles in communication between neurons. For the bursting neuron, BPRC is defined to describe the effect of the input impulse on the next firing timing. Then by applying the method of phase reduction, we can obtain the interaction function of coupled bursting neurons by its BPRC numerically. Furthermore, the stability of the synchronization state for coupled bursting neurons can be judged by $G$-function. Results show that the impulse number of the BPRC is the same as the spiking number of the bursting, and only the last impulse of the BPRC is positive and nearly coincides with the spiking, while all the others are rightly opposite to the spiking. The BPRC is more and more complicated with the increase of the spike number within a burst, and the curve of the interaction function oscillates more and more frequently with it. For spiking and simple bursting (burst-1, burst-2, and burst-3), the coupled neuron system only has two equilibriums: $\phi = 0$ is stable and $\phi = 0.5$ is unstable. Thus the system will exhibit monostability with the phase-locking state $\phi = 0$. But for the case of burst-4, new equilibriums emerge in the system and a multistable synchronous state exists. However, two certain things are unchanged: $\phi = 0$, which corresponds to the in-phase synchronization state, is always the stable equilibrium, while the anti-phase synchronization state with $\phi = 0.5$ is an unstable equilibrium.

It is well known that the chemical synapse is the main coupling mode in a neuronal network; we will do some similar work on the chemically coupled bursting neurons in the future. Also we hope the work would give some insight into the synchronization of coupled neurons and even the complex neuronal network.

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