Firing-rate resonance in a generalized integrate-and-fire neuron with subthreshold resonance

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Neurons that exhibit a peak at finite frequency in their membrane potential response to oscillatory inputs are widespread in the nervous system. However, the influence of this subthreshold resonance on spiking properties has not yet been thoroughly analyzed. To this end, generalized integrate-and-fire models are introduced that reproduce at the linear level the subthreshold behavior of any given conductance-based model. A detailed analysis is presented of the simplest resonant model of this kind that has two variables: the membrane potential and a supplementary voltage-gated resonant variable. The firing-rate modulation created by a noisy weak oscillatory drive, mimicking an in vivo environment, is computed numerically and analytically when the dynamics of the resonant variable is slow compared to that of the membrane potential. The results show that the firing-rate modulation is shaped by the subthreshold resonance. For weak noise, the firing-rate modulation has a minimum near the preferred subthreshold frequency. For higher noise, such as that prevailing in vivo, the firing-rate modulation peaks near the preferred subthreshold frequency.

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I. INTRODUCTION

Advances in recordings, in visualization techniques, and in computational modeling capabilities [1,2] have made notable progress possible towards the understanding of the dynamics of neural assemblies. Neuronal synchronization and oscillations have been studied in vivo and in vitro in slices of neural tissues and analyzed theoretically with the help of computer simulations [3]. The properties of the single cell and of the synaptic couplings between different cells are both thought to play a role in the observed dynamics. In particular, it has been found that the subthreshold membrane potential response of neurons subjected to a small oscillatory drive depends on the drive frequency and can be peaked at particular frequencies. Examples include trigeminal root ganglion neurons [4], neocortical neurons [5,6], hippocampal pyramidal cells [7,8] and interneurons [8], and others [9]. It has long been known that this resonance phenomenon can be related to the neuronal ionic channel characteristics and can be accurately modeled using the classic Hodgkin-Huxley conductance-based description [10,11]. In order to assess the functional significance of this subthreshold resonance, it is important to determine its relation to spike emission, and particularly to examine the case of a neuron embedded in a neural structure under heavy synaptic bombardment, as is the case in vivo. In a previous paper [12], numerical simulations of conductance-based models under noisy oscillatory drive were performed to address this question. It was found that, for a sufficient level of noise, the modulation of the spike rate at the driving frequency was related to the subthreshold resonance curve. The classic Lapicque or leaky integrate-and-fire (IF) model [13,14] has been useful for understanding in simple terms the properties of more detailed spiking neuron models and of real neurons and neuronal networks [15–17]. However, the leaky integrate-and-fire model cannot describe subthreshold resonance. This motivated the introduction [12,18] of a generalized integrate-and-fire (GIF) model to describe more accurately these types of subthreshold properties. As for conductance-based models, the spike rate resonance curve of the GIF model was found to be peaked at the firing-rate frequency for low noise and around the subthreshold resonance for stronger noise regimes.

The aim of the present work is to present an analytic computation of the spike rate modulation and phase for the GIF model and a detailed analysis of the findings of Ref. [12]. The GIF model and its relation to linearized conductance-based models are first recalled in Sec. II. The main characteristics of the model for constant input or weak oscillatory drive without noise are given in Sec. III. The general perturbative framework of the computation for noisy inputs and the main results are then described in Sec. IV. They are first explained using a simple but representative case in Sec. IV A. The general lowest-order computation is then dealt with in Sec. IV B. It is found here that a sufficient level of noise is necessary for the subthreshold resonance to be seen in the firing-rate modulation. This interplay of noise and oscillations is reminiscent of stochastic resonance [19]. However, as discussed in Sec. IV C, the two phenomena are quite different since, for instance, the usual leaky IF model displays stochastic resonance [20] but not the subthreshold and firing-rate resonance studied here. A discussion of the results and some perspectives of the present work are provided in the concluding section. The results of some higher-order computations are described in the Appendix.

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II. SUBTHRESHOLD DYNAMICS AND THE GIF MODEL

A. Subthreshold response of conductance-based models

The response of neurons to a small oscillatory current has been tested in a number of experiments. In several cases, a peak response has been observed at a frequency that depends on the particular neuron type under examination. This resonance phenomenon is well accounted for by the conductance-based description of a single compartment neuron. In this classic Hodgkin-Huxley description [10,11], with an injected current $I_{app}(t)$, the potential difference across the cell membrane $V = V_{in} - V_{out}$ is given by

$$ C \frac{dV}{dt} = g_L(E_L - V) - \sum_j I_j(V,\{x_k\}) + I_{app}(t), \quad (1) $$

where $C$ denotes the membrane capacity, $g_L$ and $E_L$ are the conductance and reversal potential of a passive leak current, the $I_j$'s are a set of ionic currents associated with active conductances (by convention, positive values are associated with outward currents), and $I_{app}$ is the externally applied current. The $I_j$'s are generally taken to be functions of the potential and of $N$ additional activation and inactivation variables $\{x_k, k = 1, \ldots, N\}$, with time course

$$ \frac{dx_k}{dt} = \frac{x_k^\infty(V) - x_k}{\tau_k(V)}, \quad (2) $$

where both the relaxation times $\tau_k(V)$ and the steady-state values $x_k^\infty$ depend on $V$. For a small injected current $I_{app}(t)$, the departure $v(t)$ of the membrane potential from its resting value $V_0$ is described by the linearized version of Eqs. (1) and (2)

$$ C \frac{dv}{dt} = -gv - \sum_k g_k w_k + I_{app}(t), $$

$$ \tau_k \frac{dw_k}{dt} = v - w_k, \quad k = 1, \ldots, N, \quad (3) $$

where $g$ is the sum of all the steady-state conductances, $\tau_k$ is the relaxation time of $x_k$ at the resting potential, $\tau_k = \tau_k(V_0)$, and $g_k$ measures the strength of the steady-state current flow change due to the $x_k$ variation following a small modification of the steady-state potential value,

$$ g = g_L + \sum_j \frac{\partial I_j}{\partial V}|_{V_0}, $$

$$ g_k = \sum_j \frac{\partial I_j}{\partial x_k} \left. \frac{dx_k^\infty}{dV} \right|_{V_0}. \quad (4) $$

Variable $w_k$ measures the departure of the activation or inactivation variable $x_k$ from its value at the steady-state potential.

Without variables $w_k$, Eq. (3) is equivalent to a simple electric RC circuit. In this case, the amplitude of the potential oscillation induced by an injected alternating current decreases monotonically with the frequency of the current. Variables $w_k$ add effective inductances into this electric circuit analogy and can give rise to a nonmonotonic frequency response curve. Adding a single $w_k$ is already sufficient to produce a peak response [9], a resonance, at a particular frequency and more complex responses can be obtained with several variables [12].

B. The GIF model

The effect of a subthreshold resonance on the spike rate can be directly examined by supplementing the subthreshold dynamics (3) with a threshold for spike emission in the spirit of the usual leaky integrate-and-fire neuron description [14,2]. That is, a GIF model is defined by using Eq. (3) as long as the potential $v$ is below a threshold $\theta$. When $v$ reaches $\theta$, a spike emission is registered, $v$ is reset to a lower value $V_r$ and the linear evolution (3) resumes [18]. In principle, the supplementary variables $w_k$ could also be reset at the spike emission time when $v = \theta$. For simplicity, it is chosen here to leave them unaffected. This is appropriate for variables that have slow dynamics relative to the spike duration and it has also the advantage of keeping to a minimum the number of parameters in the model. In neural structures, a neuron receives a continuous barrage of inputs arriving at a large number of synapses. This is modeled here as a constant mean injected current $I_0$ plus a fluctuating Gaussian part $\eta(t)$ of amplitude $\Delta$, $(\langle \eta(t) \eta(t') \rangle = \Delta \delta(t-t')$. We thus consider the following two-variable GIF model:

$$ C \frac{dv}{dt} = -gv - g_1 w + I_0 + \eta(t) + I_{osc}(t), \quad v < \theta \quad (6) $$

$$ \tau_1 \frac{dw}{dt} = v - w, \quad (7) $$

where $I_{osc}(t)$ is a small oscillating test current. When $v$ reaches $\theta$, it is instantaneously reset to $V_r < \theta$. The noise strength is more intuitively measured by the amplitude $\sigma_v$ of membrane potential fluctuations than by $\Delta$. Without the threshold condition, the two are easily related

$$ \sigma^2_v = \langle (v - \langle v \rangle)^2 \rangle = \frac{\Delta}{2C} \frac{C + g \tau_1 + g_1 \tau_1}{(g + g_1)(C + g \tau_1)}. \quad (8) $$

An example of the dynamics is shown in Fig. 1.

The present study focuses on computing the spike rate in this model with the particular aim of analyzing the influence of the subthreshold resonance on the input-output transfer function for this neuron. In the presence of a small oscillating input current $I_{osc}(t) = I/2 \exp(i\omega t) + c.c.$, the instantan-
neous firing-rate \( r(t) \), averaged over a population of independent neurons or over many trials for a single neuron, shows a weak modulation

\[
r(t) = r_s + \frac{1}{2} [\hat{r}(\omega) \exp(i\omega t) + \text{c.c.}],
\]

where \( r_s \) is the time-independent spike rate in the absence of the weak drive (c.c. stands for the complex conjugate terms). Modulation \( \hat{r}(\omega) \), or signal gain (e.g., Ref. [21]), measures the amplification of the frequency \( \omega \) in the output signal and its phase. It is one of the main factors determining synchronization at the network level [17]. It will be computed in the following sections under various conditions, in order to determine when and how it is modified by subthreshold resonance.

Before considering the effect of noise, the main characteristics of the deterministic two-variable GIF model are described.

III. THE DETERMINISTIC GIF MODEL

A. Subthreshold dynamics of the two-variable model

The subthreshold dynamics of the two-variable model is identical to the dynamics of a general two-variable conductance-based model for small excursions around some holding voltage.
FIG. 3. The phase diagram of the GIF model in the $\alpha = g \tau_i / (C, \beta = g \tau_i / C)$ parameter plane. Models in the black region have no stable rest state. Models represented by parameters above the dotted line have a subthreshold resonance. Those above the dashed-dotted line have complex eigenvalues $\xi_{\pm}$. As explained in the text, models in the gray region are of type I, whereas those in the white region are of type II. The subthreshold resonance curves of the models corresponding to the points marked by the different symbols (circle, triangle, square, diamond) are drawn in Fig. 2.

The response amplitude $|Z(\omega)|$ displays a peak at a finite nonzero frequency $\omega_p$ (Fig. 2) when $\beta^2 + 2\beta + 2\alpha \beta > 1$ with

$$\omega_p = \sqrt{(\beta^2 + 2\beta + 2\alpha \beta)^{1/2} - 1}. \tag{14}$$

The parameter domain where $|Z(\omega)|$ displays a peak at finite frequency overlaps with domain $\beta > (\alpha - 1)^2/4$, where Eq. (12) has complex roots with $\beta > 1/4$. A resonant response occurs in the more restricted case, when the time scale of the supplementary variable $w$ is sufficiently slow, for $\beta > \sqrt{2} - 1$. The resonant peak grows with $\beta$. In particular, for $\beta \gg 1$, the maximal response amplification, $Q = |Z(\omega_p)/Z(0)|$, is equal to $\beta$ at the peak frequency $\omega_p \sim \beta$ and the peak width is of order $1 / \omega_p$.

3. Periodic firing regimes

In order to analyze the GIF-neuron firing rate and its dependence on current $I_0$, periodic firing regimes (i.e., limit cycles) are now considered. Between a reset of the potential at $v = V_r$, and the next spike emission when $v$ reaches $\theta$ a period $T$ later, the dynamics is a simple superposition of exponentials controlled by the two eigenvalues $\xi_{\pm}$,

$$v = \frac{I_0}{g + g_1} + a \exp(\xi_+ t) + b \exp(\xi_- t).$$

FIG. 4. Firing rates $r_s(I)$ as a function of the normalized injected current $I = (I_0, I_g - \theta)(\theta - V_r)$ for two zero-leak GIF models $(g = 0)$ with different $\beta$ parameters. The full lines correspond to the exact firing rates as given by Eq. (17). Top panel: type-I model with $\beta = 0.1$. The low frequency approximation of Eq. (18) (dotted line) is shown as well as the high frequency approximation $r_s \tau_i = \beta (T + 1/2)$ (dashed line). Bottom panel: type-II model with $\beta = 5$. The dotted line corresponds to the large $\beta$ approximation Eq. (20) and the shaded area is the region in which a quiescent and a firing state coexist.

$$w = \frac{I_0}{g + g_1} + \frac{a}{1 + \xi_+} \exp(\xi_+ t) + \frac{b}{1 + \xi_-} \exp(\xi_- t). \tag{15}$$

The constants $a, b$ are determined by requiring that $v$ starts from $V_r$ at $t = 0$ and ends at $\theta$ at $t = T$. They are given in term of period $T$ as

$$a = \frac{1}{\exp(\xi_+ T) - \exp(\xi_- T)} \left[ \frac{\theta - I_0}{g + g_1} \right],$$

$$-e^{\xi_- T} \left( V_r - \frac{I_0}{g + g_1} \right),$$

$$b = \frac{-1}{\exp(\xi_+ T) - \exp(\xi_- T)} \left[ \frac{\theta - I_0}{g + g_1} \right],$$

$$-e^{\xi_+ T} \left( V_r - \frac{I_0}{g + g_1} \right). \tag{16}$$

Since $w$ is not modified when a spike is emitted, the period $T$ is obtained by the periodicity condition $w(0) = w(T)$, which gives

$$\frac{I_0}{g + g_1} = V_r - \frac{\theta - V_r}{\xi_+ - \xi_-} \left[ \frac{1 + \xi_+}{1 - \exp(\xi_+ T)} - \frac{1 + \xi_-}{1 - \exp(\xi_- T)} \right]. \tag{17}$$

The solutions of Eq. (17) correspond to periodic solutions where $v$ goes from $V_r$ to $\theta$ during period $T$, that is to neurons periodically emitting spikes at a rate $r_s(I_0) = 1/(\tau_1 T)$ in di-
dimensional units. However, the condition that \( u(t) \) should remain below \( \theta \) during its motion has not been taken into account in Eq. (17). Among the solutions of Eq. (17), only those which satisfy this condition correspond to real solutions. The simpler zero-leak case is analyzed first.

(a) The zero-leak case \((\alpha=0)\). In the parameter range \( 0<\beta<1/4 \), the two eigenvalues \( \xi_{\pm} \) are real and negative, \( \xi_{-}<-1/2<\xi_{+}<0 \). For \( T\to+\infty \), the slower relaxation dominates and Eq. (17) can be approximately written as

\[
\frac{I_0}{g_1} - \theta = \frac{\theta - V_r}{\xi_{-} - \xi_{+}} (1 + \xi_{+}) \exp(\xi_{+} T). \tag{18}
\]

The right-hand-side (rhs) of Eq. (18) is positive, so a periodic state appears above the threshold \( I_0/g_1 = \theta \) with a logarithmically long period \( T\sim|\ln(I_0/g_1-\theta)| \). This is a kind of type-I behavior, analogous to that of the usual IF neuron.

The situation is different for \( \beta>1/4 \) when the two eigenvalues are complex \( \xi_{\pm} = -1/2\pm i\xi_2 \). Then, Eq. (17) reads, for \( T\to+\infty \),

\[
\frac{I_0}{g_1} - \theta = (\theta - V_r) \exp(-T/2) \left[ \cos(\xi_2 T) + \frac{\sin(\xi_2 T)}{2\xi_2} \right]. \tag{19}
\]

The rhs in Eq. (19) oscillates and takes both positive and negative signs for \( T \) large while decaying to zero. Thus, solutions to Eq. (17) exist below \( I_0/g_1 = \theta \). The smallest solution \( T \) of Eq. (17) gives a potential \( u(t) \) that remains below \( \theta \) and corresponds to a real periodic regime. So, for \( \beta>1/4 \), a steady and a periodically firing state coexist in a range of applied currents: a type-II behavior. The firing rate as a function of applied current is displayed in Fig. 4, for several values of \( \beta \). The domain of coexistence and the firing-rate are easily estimated for \( \beta>1 \). Then \( \xi_{\pm} = \sqrt{\beta}, T\sim 1/\sqrt{\beta} \), and expansion of Eq. (17) in inverse powers of \( \beta \) gives

\[
\frac{I_0}{g_1} - \theta = \frac{\theta - V_r}{\xi_{-} - \xi_{+}} (1 + \xi_{+}) \exp(\xi_{+} T). \tag{20}
\]

The expression within square brackets on the rhs of Eq. (20) attains its minimum for \( \xi_{2} T = \pi \). So, for large \( \beta \), the steady periodically firing state coexists with the steady-state in the interval

\[
\frac{V_r + \theta}{2} + \frac{(\theta - V_r) \pi}{8\sqrt{\beta}} + \ldots \leq \frac{I_0}{g_1} \leq \theta. \tag{21}
\]

It appears at the lower end of the interval with the finite period \( T\approx \pi/\sqrt{\beta} \). The lower bound \( (V_r + \theta)/2 \) in Eq. (21) can easily be understood. When \( \beta\to+\infty \), the dynamics of the \( w \) variable is much slower than the dynamics of the potential and \( w \) simply relaxes to the average of \( u \). For a constant \( \omega \), the dynamics of \( v \) is linear in time and the mean of \( v \) in a periodically firing state is simply the average between the reset and threshold potentials. Putting \( \omega = (\theta + V_r)/2 \) in Eq. (10) immediately gives that a periodically firing state exists only if \( I_0/g_1 \) is larger than \((\theta + V_r)/2 \). The period (with \( \tau_1 \) as the time unit) in the same limit is simply obtained as

\[
T = \frac{C(\theta - V_r)}{\tau_1[I_0 - g_1(\theta + V_r)/2]} \text{ for } \beta\gg 1, \tag{22}
\]

which corresponds to Eq. (20) for \( T\xi_{2} \ll 1 \).

(b) The general non-zero-leak case \((\alpha\neq 0)\). When \( \alpha \neq 0 \), a similar analysis can be performed and is briefly summarized here. When \( T\to+\infty \), Eq. (17) gives back the threshold \( I_0 = (g + g_1)\theta \). Two types of behavior can be distinguished by considering how \( I_0 \) departs from \((g + g_1)\theta \) for \( T\gg 1 \): (1) the periodic state exists only for \( I_0>(g + g_1)\theta \) and starts with infinite period at the threshold \( I_0=(g + g_1)\theta \), i.e., a type-I behavior, or (2) a periodic state coexists with the steady state for some range of current below the threshold \( I_0=(g + g_1)\theta \), i.e., a type-II behavior. In the parameter range \((\alpha - 1)^2>4\beta \), \( \xi_{\pm} \) are real and negative (with \( \xi_{-} < \xi_{+} \)). For large \( T \), the slower relaxation \( \xi_{+} \) dominates and Eq. (17) gives

\[
\frac{I_0}{g_1} - \theta = \frac{\theta - V_r}{\xi_{-} - \xi_{+}} (1 + \xi_{+}) \exp(\xi_{+} T). \tag{23}
\]

The neuron is of type I when the prefactor of the exponential in Eq. (23) is positive whereas it is of type II when the prefactor is negative.

The prefactor has the same sign as \( 1 + \xi_{+} \). It is positive for \( \beta<0 \) as well as for \( \beta>0 \) and \( \alpha<1 \) and negative for \( \beta>0 \), \( \alpha>1 \).

In the parameter range \((\alpha - 1)^2<4\beta \), \( \xi_{+} \) and \( \xi_{-} \) are complex conjugates and the obtained correction in the analog of Eq. (17) is oscillatory. This indicates the existence of periodic firing regimes below \( I_0/(g + g_1) \) and correspond to type-II behavior.

The region of type-II behavior exactly corresponds to the parameter region delimited in Ref. [12], where after a current step, the membrane potential overshoots before relaxing to the new holding potential. The different regions are displayed in Fig. 3. It should be noted that in general the type-II behavior does not necessarily correspond to the existence of complex roots: a difference of exponentials can provide the overshoot leading to type-II behavior.

4. Firing-rate resonance

In this section, the firing-rate modulation by a small time-varying current is considered. The analysis is limited to the computation of the linear response. It amounts to generalizing the well-known analysis for the IF neuron [22] to the slightly more complicated two-variable GIF model. The aim is to investigate how the subthreshold resonance modifies the rate response function.

The neuron is submitted to the injected current \( I_0 + I_{osc}(t) \). The constant current \( I_0 \) is sufficiently large, so that in the absence of \( I_{osc}(t) \) the neuron emits spikes periodically at times \( t=nT+t_0, n = \ldots, -1, 0, 1, \ldots \). For a collection of
neurons, \( t_0 \) varies independently from neuron to neuron and the spike emission probability per unit time, \( r_s \), is time independent. The effect of the small time-varying component is to slightly displace the spike times from \( t \) to \( t + d(t) \). This produces a modulation in time of the spike rate,

\[
r(t) = r_0[1 - d'(t)].
\]

(24)

In order to obtain the rate modulation, it remains to determine \( d(t) \) for the two-variable GIF model. With an injected current with a small time-varying component, Eq. (10) becomes

\[
dv{v}{t} = -\alpha v - \beta w + [I_0 + I_{osc}(t)] \frac{\tau_1}{C}.
\]

(25)

At the linear level, the time-varying current can be decomposed in Fourier components and it is sufficient to consider \( [I_{osc}(t) = \hat{I}/2 \exp(i\omega t) + c.c. \). A particular solution to Eqs. (25) and (11) is given by

\[
v = \frac{1}{2} [(\hat{I} \frac{\tau_1}{C}) v_p \exp(i\omega t) + c.c.],
\]

\[
w = \frac{1}{2} [(\hat{I} \frac{\tau_1}{C}) w_p \exp(i\omega t) + c.c.],
\]

with

\[
v_p(\omega) = \frac{1 + i\omega}{(1 + i\omega)(\alpha + i\omega) + \beta},
\]

\[
w_p(\omega) = \frac{1}{(1 + i\omega)(\alpha + i\omega) + \beta}.
\]

(26)

Function \( v_p = Z(\omega)C/\tau_1 \) is a dimensionless form of the impedance \( Z(\omega) \). Between the \( n \)th spike at time \( t_n \) and the \( (n+1) \)th spike at time \( t_{n+1} \), the complete solution can be written as

\[
v = \frac{I_0}{g + g_1} + a_n \exp[\xi_+(t - t_n)] + b_n \exp[\xi_-(t - t_n)] + \frac{1}{2} [(\hat{I} \frac{\tau_1}{C}) v_p \exp(i\omega t) + c.c.],
\]

(27)

The forcing perturbs \( a_n, b_n, t_{n+1} - t_n \) and \( w(t_n) \), the value of \( w(t) \) at the spike time, away from their steady limit cycle values. At linear order, one can write

\[
a_n = a + 1/2 \left[(\hat{I} \frac{\tau_1}{C}) \hat{a} \exp(i\omega t_n) + c.c.\right],
\]

\[
b_n = b + 1/2 \left[(\hat{I} \frac{\tau_1}{C}) \hat{b} \exp(i\omega t_n) + c.c.\right],
\]

\[
w(t_n) = w_0 + 1/2 \left[(\hat{I} \frac{\tau_1}{C}) \hat{w} \exp(i\omega t_n) + c.c.\right],
\]

and

\[
t_{n+1} - t_n = \frac{1}{2} \left[(\hat{I} \frac{\tau_1}{C}) \hat{T} \exp(i\omega t_n) + c.c.\right].
\]

The \( n \)th spike time \( t_n \) and the value of \( w \) at \( t_n \) determine the constants \( a_n \) and \( b_n \) in the time interval \([t_n, t_{n+1}], \) i.e., they give \( \hat{a} \) and \( \hat{b} \) as linear functions of \( \hat{w} \) and \( \hat{T} \). The knowledge of \( a_n \) and \( b_n \) in turn determines the \((n+1) \)th spike time and the value \( w(t_{n+1}) \). This provides two supplementary equations that determine \( \hat{w} \) and \( \hat{T} \).

Explicitly, one obtains

\[
\hat{a} = \frac{1}{\xi_- - \xi_+} \left[(1 + \xi_+)v_p + (1 + \xi_+)(1 + \xi_-)(\hat{w} - w_p)\right],
\]

(29)

\[
\hat{b} = \frac{1}{\xi_+ - \xi_-} \left[(1 + \xi_-)v_p + (1 + \xi_-)(1 + \xi_-)(\hat{w} - w_p)\right].
\]

(30)

Then \( \hat{T} \) is determined by the condition that the \((n+1) \)th spike occurs when \( v \) reaches \( \theta \),

\[
\hat{T} = -\frac{\hat{a} \exp(\xi_+ T) + \hat{b} \exp(\xi_- T) + v_p \exp(i\omega T)}{a \xi_+ \exp(\xi_+ T) + b \xi_- \exp(\xi_- T)}
\]

\[
= \kappa_1 (\hat{w} - w_p) + \kappa_2 v_p,
\]

(31)

where the two constants \( \kappa_1 \) and \( \kappa_2 \) are given by

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This gives the evolution of $w$ from one spike to the next,

$$\dot{w} \exp(i\omega T) = \lambda_L \dot{w} + \mu v_p + \exp(i\omega T) - \lambda_L w_p,$$

(34)

with

$$\lambda_L = \frac{(a \xi_+ + b \xi_-) \exp((\xi_+ + \xi_-) T)}{a \xi_+ \exp(\xi_+ T) + b \xi_- \exp(\xi_- T)}.$$

(35)

$$\mu = \frac{a \xi_+}{1 + \xi_+} \exp(\xi_+ T) - \exp(i\omega T) + \frac{b \xi_-}{1 + \xi_-} \exp(\xi_- T) - \exp(i\omega T)$$

(36)

Equation (34) expresses $w(t_{n+1})$ (its lhs) as a function of $w(t_n)$ and the effective forcing on $w$, $\mu v_p + (1 - \lambda_L) w_p$, coming from the imposed oscillating current (its rhs). In the absence of forcing, constant $\lambda_L$ controls the free evolution of small perturbations around the limit cycle: it is the discrete Lyapunov exponent giving the (unforced) limit cycle stability. Equation (34) determines $\dot{w}$ as

$$\dot{w} = \frac{\mu v_p + \exp(i\omega T) - \lambda_L w_p}{\exp(i\omega T) - \lambda_L}.$$

(37)

Substituting this expression back in Eq. (31) with formulas (32)–(36) for the constants, gives the simple expression of $\dot{T}$,

$$\dot{T} = v_p(\omega) \left[ \frac{a \xi_+ \exp(\xi_+ T)}{\exp(\xi_+ T) - \exp(i\omega T)} \right.$$  

$$+ \frac{b \xi_- \exp(\xi_- T)}{\exp(\xi_- T) - \exp(i\omega T)} \right]^{-1},$$

(38)

where $T$ is given by Eq. (17) and $a$ and $b$ are given by Eq. (16) or by the equivalent formulas

$$a = \frac{(\theta - V_r)(1 + \xi_+)}{[\xi_+ - \xi_-][1 - \exp(\xi_- T)]},$$

$$b = \frac{(\theta - V_r)(1 + \xi_-)}{[\xi_- - \xi_+][1 - \exp(\xi_+ T)]}.$$

(39)

These expressions permit a comparison of the zero frequency limit of Eq. (38) with a direct differentiation of Eq. (17) and a check that

$$\dot{T}(\omega = 0) = \frac{C}{\tau_1} \frac{dT}{dT_0}.$$

(40)

After determining the variation $\dot{T}$ of the interspike interval, the time displacement of the $n$th spike at linear order follows by summation,

$$d(t_n) = \frac{I \tau_1}{2C} \sum_{m=-\infty}^{n-1} \{ \dot{T} \exp[i\omega(mT + t_0)] + \text{c.c.} \}$$

$$= \frac{I \tau_1}{2C} \frac{\dot{T}}{\exp(i\omega T) - 1} \exp(i\omega t_n) + \text{c.c.}.$$  

(41)

As usual, the summation is performed by supposing that the perturbation is created slowly, that is, by adding a small negative imaginary part to the forcing frequency $\omega$. Finally, when the spike rate is written as $r_s + 1/2[\dot{r} \exp(i\omega t) + \text{c.c.}]$ [Eq. (9)], the modulation amplitude $\dot{r}$ is obtained as

$$\frac{\dot{r}}{r_s} = -\frac{\tau_1}{C} \left( \frac{i\omega}{\exp(i\omega T) - 1} \right) \dot{T},$$

(42)

where $\dot{T}$ is explicitly given by Eq. (38). Expressions (38) and (42) generalize to the two-variable GIF model, the well-known formula [22] for the usual IF model. It is recovered for $\beta = 0$ when the additional variable has no influence on the membrane potential dynamics. In this case, one has $\xi_+ = -\alpha$ and $\xi_- = -1$ so that $b = 0$ [Eq. (39)]. Equation (38) with $v_p = 1/(\alpha + i\omega)$, then reads $\dot{T} \times (1 - \exp((\alpha + i\omega)T)) / (\alpha + i\omega)$, which gives back Knight’s formula [22].

Equation (42) is plotted in Fig. 5 together with the results of direct numerical simulations for two cases where the GIF model displays subthreshold resonance. As for the usual leaky IF model, sharp resonance peaks are seen for frequencies that are multiples of the firing-rate. They arise from the vanishing of the denominator in formula (42). However, in this deterministic case, the GIF firing-rate resonance curve
has no peak at the subthreshold resonance frequency. For $g > 0$, it exhibits instead a suppression around the subthreshold resonance frequency.

For comparison with the following sections, the limiting form of $\hat{r}$ when $t_1$ is long in comparison with other time scales is worth noting. Then, the dynamics of $w$ does not play a significant role in most of the driving frequency range. Explicit expressions can be obtained by taking the limits of the above expressions when $\alpha, \beta \to +\infty, T \to 0$ with $\alpha/\beta$ and $\beta T$ fixed. For $g \neq 0$, one obtains the expression for a usual IF neuron with leak conductance $g$ and a resonance peak of well-defined limiting form around the firing-rate frequency. The limit is not uniform in a low frequency range that tends to zero with $\tau_1$ (where the slow dynamics of $w$ does play a role). The zero-leak case is special in that the firing-rate resonance curve of the allied zero-leak IF model has no peak at the firing-rate frequency $\tau_1$. For $g = 0$, one obtains, in the limit $\tau_1 \to +\infty$ with $\omega T$ fixed,

$$
\frac{\dot{r}}{r_s} = \frac{T \tau_1}{C(\theta - V_f)} \left( 1 + \frac{\beta T^2}{[1 - \exp(-i \omega T)]^2} \right).
$$

For any finite $1/\tau_1$, the firing-rate response exhibits resonance peaks centered on the firing-rate frequency and its harmonics. However, the firing-rate response is modified by these resonances only in frequency intervals of width tending to zero such as $\frac{\tau_1}{\omega - 2\pi n \approx \sqrt{\beta} T}$.

**IV. STEADY AND MODULATED SPIKE RATES WITH NOISY INPUTS**

In a number of previous studies [14,16,17,23–25] on neuron firing-rates and modulation using the IF model with...
noise, it has been found convenient to transform the stochastic description of neuron dynamics into a Fokker-Planck equation for the distribution of its membrane potential. In the present case, Eqs. (6) and (7) give a Fokker-Planck equation for the distribution \( P(v,w,t) \) of the membrane potential and the supplementary variable \( w \),

\[
\frac{\partial P}{\partial t} = \frac{1}{C} \frac{\partial}{\partial v} \left[ (g v + g_1 w - I_0 - I_{osc}(t)) P \right] + \frac{1}{\tau_1} \frac{\partial}{\partial w} [(w-v)P] + \frac{\Delta}{2C^2} \frac{\partial^2}{\partial v^2} P, \tag{44}
\]

with an absorbing boundary condition at threshold \( P(\theta,v,t) = 0 \). At the reset potential \( v = V_r \), the distribution is continuous, but it has a discontinuous first derivative arising from the reinjected probability current

\[
\frac{\partial}{\partial v} P(v,w,t)|_{v=V_r} = \frac{\partial}{\partial v} P(v,w,t)|_{v=V_r} = \frac{\partial}{\partial v} P(v,w,t)|_{v=\theta}. \tag{45}
\]

The instantaneous firing-rate \( r(t) \) is simply related to the total probability current through the threshold,

\[
r(t) = -\frac{\Delta}{2C^2} \int_{-\infty}^{+\infty} dw \frac{\partial}{\partial v} P(\theta,v,t). \tag{46}
\]

Without the threshold condition, the stationary solution \( \{I_{osc}(t) = 0\} \) of Eq. (44) is a simple Gaussian,

\[
P(v,w) = \frac{C + g \tau_1}{\pi \Delta} \sqrt{(g + g_1)/\Delta} \exp \left\{ -\frac{C + g \tau_1}{\Delta} (g + g_1) \right\}
\times \left\{ \frac{w - I_0}{g + g_1} + \frac{C}{\tau_1} (w-v)^2 \right\}. \tag{47}
\]

Finding the solution to Eq. (44) with the threshold and reinjection boundary conditions is less easy. In the usual case of the IF model, the problem is similar to Kramer’s well-known computation of the thermal escape from a one-dimensional potential well \([26]\) and reduces to solving an ordinary differential equation. In the present two-dimensional nonpotential case, obtaining an exact solution to Eq. (44) appears to be a difficult task even in the stationary case. Instead of attempting this, a perturbative approach is developed here in the limit where the supplementary variable \( w \) evolves on a long time scale. This is a limit where subthreshold resonance is well developed. It is also relevant for subthreshold resonance in real cells \([12]\) since most of them show preferred frequencies of a few Hertz \([5, 9, 27, 31]\). When \( w \) evolves slowly as compared to the membrane potential \( v \), it stays near the time-averaged potential \( \langle v \rangle \) and the analysis of Eq. (44) can be reduced to that of an effective one-variable model. The analysis is first illustrated using a simple self-consistent approach in the zero-leak case \((g = 0)\). The general case is then dealt with in Sec. IV B using a direct expansion of the Fokker-Planck Eq. (44), which also provides a systematic means of computing higher perturbative orders as shown in the Appendix.

### A. The zero-leak case

The GIF model of Eq. (6,7) with zero leak \((g = 0)\) is analyzed in this section in the limit \( \tau_1 \to + \infty \).

#### 1. Steady firing-rate

The steady firing-rate is considered first \((with I_{osc}(t) = 0)\). When \( \tau_1 \to + \infty \), the relaxation of the supplementary variable \( w \) is driven by the time average of potential and in the stationary state \( w = \langle v \rangle \). The membrane potential dynamics reduces to the single Eq. (6) with \( w \) replaced by \( \langle v \rangle \). The steady-state distribution of the membrane potential \( P_s(v) \) thus obeys

\[
(g_1(v) - I_0) \frac{\partial}{\partial v} P_s + \frac{\Delta}{2C} \frac{\partial^2}{\partial v^2} P_s = 0, \tag{48}
\]

with the absorbing boundary condition at the threshold potential \((P_s(\theta) = 0)\) and the reinjection condition at the reset potential \(V_r\). Multiplication of Eq. (48) by \( v \) and integration from \( v = - \infty \) to the threshold \( v = \theta \) directly relates the mean steady spike rate \( r_s \) and the average potential \( \langle v \rangle \),

\[
r_s = \frac{I_0 - g_1 \langle v \rangle}{C(\theta - V_r)}. \tag{49}
\]

where expression (46) for \( r_s \) and boundary condition (45) have been used to evaluate the boundary terms.

The full solution to Eq. (48) is also easily obtained and reads

\[
P_s(v) = \frac{1}{\theta - V_r} \left\{ 1 - \exp \left[ \frac{2C(g_1(v) - I_0)}{\Delta} (\theta - v) \right] \right\}, \quad V_r < v < \theta \\
P_s(v) = \frac{1}{\theta - V_r} \left\{ 1 - \exp \left[ \frac{2C(g_1(v) - I_0)}{\Delta} (\theta - V_r) \right] \right\} \times \exp \left[ \frac{2C(g_1(v) - I_0)}{\Delta} (V_r - v) \right], \quad v < V_r. \tag{50}
\]

The membrane potential distribution \( P_s(v) \) depends on the average membrane potential \( \langle v \rangle \), which remains to be determined. It is obtained in a self-consistent way by writing

\[
\langle v \rangle = \int_{-\infty}^{+\infty} dv \; v \; P_s(v) = \frac{\theta + V_r}{2} + \frac{\Delta}{2C(g_1(v) - I_0)}. \tag{51}
\]

The last equality can be derived by integrating the exact expression (50) or again directly from Eq. (48), by multiplying it by \( v^2 \) and integrating from \( v = - \infty \) to the threshold \( v = \theta \). The simple self-consistent quadratic equation (51) has two roots, one larger and one smaller than \( I_0/g_1 \). Only the smaller one is compatible with a normalizable \( P_s(v) \) [Eq. (50)] and with a positive spike rate [Eq. (49)]. One, therefore, obtains
Numerical simulation and the lines show the analytic result of Eq. 2. Results of direct simulations. The model parameters are \( \tau_1 \) and \( \tau_0 \) when all other parameters are fixed (\( \beta = \tau_1 g_1 / C \)). (a) \( C / g_1 = 5 \), \( I_0 / g_1 = -1.5 \) mV, \( \Delta (C g_1) = -10 \) mV \(^2\) (a high noise, low current case). (b) \( C / g_1 = 10 \), \( I_0 / g_1 = -4 \) mV, \( \Delta (C g_1) = 1 \) mV \(^2\) (a low noise, high current case). The symbols are the results of direct simulations. The large \( \tau_1 \) result of Eq. (53) and its first correction, Eq. (A14), are shown for comparison (dashed lines). The firing rate of a classic IF neuron with leak \( g_1 \) gives the small \( \tau_1 \) approximation (dotted lines). (c) shows the firing rate as a function of the normalized injected current \( I = (I_0 / g_1 - \theta) / (\theta - V_\text{r}) \) for four noise levels. The symbols are the results of direct numerical simulation and the lines show the analytic result of Eq. (53). No noise, bold line; \( \Delta (C g_1) = 1 \) mV \(^2\), triangles and dash-dotted line; \( \Delta (C g_1) = 5 \) mV \(^2\), stars and dashed line; \( \Delta (C g_1) = 10 \) mV \(^2\), circles and dotted line [\( \tau_1 = 100 \) ms and other model parameters as in (a)].

When \( \Delta = 0 \), Eqs. (52) and (53) reduce to the simple noiseless expressions, \( \langle v \rangle = I_0 / g_1, r_s = 0 \) for \( I_0 < g_1 (\theta + V_r) / 2 \) and \( \langle v \rangle = (\theta + V_r) / 2, r_s = (I_0 - g_1 (\theta + V_r) / 2) / C (\theta - V_r) \) for \( I_0 > g_1 (\theta + V_r) / 2 \). One obtains again that the noiseless neuron has a periodically firing state when \( I_0 > g_1 (\theta + V_r) / 2 \), namely, for a smaller injected current than that which is required to bring its resting potential above the threshold (i.e., \( I_0 > g_1 (\theta + V_r) / 2 \)). Moreover, for \( \tau_1 \rightarrow +\infty \), Eq. (53) shows that as soon as this periodic firing regime exists, it is selected by an infinitesimal noise.

As shown in Fig. 6, results of direct simulations of the stochastic GIF model tend toward the limiting values (52) and (53) when \( \tau_1 \) increases. Higher order corrections to these lowest order estimates are obtained in the Appendix and are also plotted in Fig. 6.

### 2. Spike rate modulation by a small oscillatory current: Direct linearization

When the neuron is submitted to an additional small oscillatory current injection, \( I_{\text{osc}}(t) = \hat{I} / 2 \exp(i \omega t) + i.c.c. \) in Eq. (44), its spike rate acquires a small modulation at the forcing frequency \( r(t) = r_s + 1 / 2 \hat{I} \exp(i \omega t) + i.c.c. \). The aim here is to compute this modulation and to determine whether and under which conditions it displays a peak at the subthreshold resonance frequency. We first proceed straightforwardly and obtain the result for a fixed driving frequency \( \omega \) in the limit \( \tau_1 \rightarrow +\infty \). It is then shown that the procedure needs some refinement to capture the subthreshold resonance for \( \omega \sim g_1 / \tau_1 C \).

As discussed above, when \( \tau_1 \rightarrow +\infty \), the relaxation of the supplementary variable \( w \) is driven by the time average of the potential \( w = \langle v \rangle \) and Eq. (6) reduces to the single-variable Fokker-Planck equation for the potential distribution,

\[
\partial_t P = \frac{1}{C} \left[ g_1 \langle v \rangle - I_0 - I_{\text{osc}}(t) \right] \partial_v P + \frac{\Delta}{2 C^2} \partial_v^2 P. \tag{54}
\]

The modulation due to the small oscillatory current \( I_{\text{osc}}(t) \) is obtained by linearizing Eq. (54) around the steady-state so-
The solution to Eq. (55) is easily obtained. First, comparison with the steady-state Eq. (48) provides a particular solution to the linear inhomogeneous Eq. (55) equal to $i \partial_\omega P_r l/(C \omega)$. Second, in the present zero-leak case, the linear Eq. (55) has constant coefficients and its solution is simply obtained as a superposition of exponentials $\exp(\lambda \pm v)$ with

$$\lambda_{\pm} = \frac{C}{\Delta}[I_0 - g_1(v)] \pm \sqrt{(g_1(v) - I_0)^2 + 2i\Delta \omega}], \quad \text{Re}(\lambda_{\pm}) > 0. \tag{56}$$

Taking into account the boundary conditions (45) and matching the function expressions in the two intervals $v < V_r, V_r < v < \theta$, one obtains

$$\hat{P}(v) = \frac{i}{\omega} \left[ \frac{2C r_s}{\Delta} \exp[\lambda_+(v - \theta)] + \frac{1}{C} \partial_e P_s \right], \quad v < v < \theta$$

$$\hat{P}(v) = \frac{i}{\omega} \left[ -1 + \exp[\lambda_+(V_r - \theta)] \exp[\lambda_+(v - V_r)] \right] + \frac{1}{C} \partial_e P_s \right], \quad v < V_r. \tag{57}$$

The corresponding spike rate modulation $1/2[\hat{r}^{IF}[\exp(i \omega t) + \text{c.c.}]$ and mean voltage amplitude are simply

$$\hat{r}^{IF} = -\frac{C}{\omega} \left[ \frac{\Delta \omega}{(\theta - V_r)^2} \frac{r_s}{\omega} \sqrt{1 + 2i \frac{\Delta \omega}{C^2(\theta - V_r)^2} \frac{r_s}{\omega} - 1} \right]. \tag{58}$$

$$\hat{\omega}^{IF} = \int_{-\infty}^{\theta} dv \, v \hat{P}(v)$$

$$= \frac{i}{\omega} \left[ (\theta - V_r)\hat{r}^{IF} - \frac{1}{C} \right]$$

$$= \frac{C(\theta - V_r)^2}{\Delta} \frac{r_s^2}{\omega^2} \left[ \sqrt{1 + 2i \frac{\Delta \omega}{C^2(\theta - V_r)^2} \frac{r_s}{\omega} - 1} \right]$$

$$- \frac{i}{C \omega}. \tag{59}$$

The superscript IF has been added to emphasize that the results are identical to what would have been obtained for a simple zero-leak IF model with injected current $I_0 - g_1(v) = C(\theta - V_r) r_s$. Therefore, modulation $\hat{r}^{IF}(\omega)$ is a monotonically decreasing function of frequency $\omega$ and does not display any sign of the subthreshold resonance, as shown in Fig. 7.

It can be noted that the deterministic peak at the firing-rate frequency, which exists for small noise for any finite $\tau_1$ [Eq. (43)], is also missed by the lowest-order $\tau_1 = \infty$ approximation. This is peculiar to the $g = 0$ case and comes from the fact that the firing-rate resonance curve of the allied zero-leak IF model itself is special in not having a peak at the firing-rate frequency [22] as recalled previously.

The characteristic frequency $\tau_1/K$ appears in Eq. (58), where $K$ denotes the dimensionless ratio

$$K = \frac{\Delta}{2C^2(\theta - V_r)^2 r_s}. \tag{60}$$

For further use below, we note the spike rate and mean voltage expansions for frequencies small compared to $\tau_1/K$,

$$\hat{r}^{IF} = \frac{1}{C(\theta - V_r)} \left[ 1 - iK \frac{\omega}{r_s} - 2 \left( \frac{K \omega}{r_s} \right)^2 + \cdots \right],$$

$$\hat{\omega}^{IF} = \frac{K}{Cr_s} \left[ 1 - i2K \frac{\omega}{r_s} + \cdots \right]. \tag{61}$$

The corresponding expansions in the opposite frequency range $\omega \gg \tau_1/K$ read

$$\hat{r}^{IF} = e^{-i \pi/4} \frac{\sqrt{r_s}}{C(\theta - V_r)} \sqrt{\frac{\omega K}{\omega K + \cdots}},$$

$$\hat{\omega}^{IF} = \frac{1}{C \omega} \left[ -i + e^{i \pi/4} \sqrt{\frac{r_s}{\omega K}} \sqrt{\omega K + \cdots} \right]. \tag{62}$$

3. **Spike rate modulation by a small oscillatory current:**

**The low frequency regime**

Considering the zero frequency limit provides a hint that the perturbative result of Eq. (58) does, however, not entirely describe the spike rate modulation dependence on frequency. On one hand, when $\omega \rightarrow 0$, Eq. (58) gives the limiting behavior

$$\lim_{\omega \rightarrow 0} \hat{r}^{IF} = \frac{1}{C(\theta - V_r)}. \tag{63}$$

On the other hand, the spike rate modulation induced by a very slowly changing injected current should be given by the variation of the steady-state firing-rate with a change in the constant current from $I_0$ to $I_0 + I_{osc}(t)$,

$$\lim_{\omega \rightarrow 0} \frac{d \hat{r}}{d I_0} = \frac{1}{C(\theta - V_r)} \left[ 1 - g_1 \frac{d(I)}{d I_0} \right] \left( \frac{1}{2C(\theta - V_r)} \frac{\Delta \omega}{\sqrt{|I_0 - g_1(\theta + V_r)/2|^2 + 2g_1^2/C}} \right). \tag{64}$$

$$\lim_{\omega \rightarrow 0} \frac{\hat{r}}{d I_0} = \frac{1}{2C(\theta - V_r)} \left( \frac{1}{\sqrt{|I_0 - g_1(\theta + V_r)/2|^2 + 2g_1^2/C}} \right). \tag{65}$$
where the last two equalities follow from Eqs. (49) and (58). Since the average membrane potential $\langle v \rangle$ depends on the injected current $I_0$, results (63) and (64) are different. The origin of the discrepancy is that they correspond to different limiting procedures (see Fig. 7). The perturbative result (63) is obtained by first computing the limit of $\hat{r}(\omega)$ when $\tau_1 \rightarrow +\infty$ at a fixed nonzero frequency and then taking the limit $\omega \rightarrow 0$. Contrary to this, Eq. (64) corresponds to first setting

FIG. 7. Firing-rate resonance curves in the zero-leak case. (A) Modulus of the firing-rate modulation $\hat{I} \hat{r}(\omega)$. (B) Phase of the firing-rate modulation. The triangles are the results of direct numerical simulation; the lines correspond to the analytic formula (73). (C) Samples of membrane potential traces. In (A) and (B), symbols are the results of direct numerical simulations, the dotted lines show the large $\tau_1$ analytic expression (58), and the thick lines show the refined expression (73). The zero-noise result (42) is also shown for comparison (dashed lines). Three different noise and injected current conditions are shown. $I=0.02$ with (a) $\Delta=0.01, I_0=0.35$; (b) $\Delta=0.1, I_0=0.31$; and (c) $\Delta =0.5, I_0=0.14$. The other model parameters are $C=1, g=0.1, \tau_1=100$ (units as in Fig. 6). As noise increases, the peak shifts from the firing-rate frequency around 20 Hz in (a) to the subthreshold resonance frequency of about 5 Hz in (c).
\( \omega = 0 \) and then evaluating the limit of \( \hat{r}(0) \) when \( \tau_1 \to +\infty \). The two results differ because \( \hat{r}(\omega) \) has a rapid variation near \( \omega = 0 \) in a small frequency range that tends to zero when \( \tau_1 \to +\infty \), as a consequence of the fact that the subthreshold resonance \( \sim \sqrt{\gamma_1/\tau_1 C} \) also tends to zero in this limit.

This being noted, the previous calculation can be refined so that it correctly interpolates between the two frequency regimes \( \omega \ll \sqrt{\gamma_1/\tau_1 C} \) and \( \omega \gg \sqrt{\gamma_1/\tau_1 C} \). A simple approach is presented here. A more systematic way of proceeding is presented in Sec. IV B.

As previously, we consider the limit \( \tau_1 \gg 1 \) with a weak driving term but at frequency \( \omega \) that is arbitrarily slow. In this case, the potential \( v \) has short time fluctuations but also slow oscillations at frequency \( \omega \). Averaging on a time that is long for the random fluctuations but short compared to the period \( 2\pi/\omega \) of the oscillation gives

\[
\langle v \rangle = v_0 + \frac{1}{2} [\hat{I}v_1 \exp(i\omega t) + \text{c.c.}].
\]

Integration of Eq. (7) provides the corresponding expression for \( w \),

\[
w(t) = v_0 + \frac{1}{2} \left[ \hat{I}v_1 \exp(i\omega t) + \text{c.c.} \right].
\]

Since \( w \) is no longer a fluctuating variable, Eq. (6) reduces as before to a single-variable Fokker-Planck equation

\[
\partial_t P = \frac{1}{C} \left[ g_1 w(t) - I_0 - I_{osc}(t) \right] \partial_v P + \frac{\Delta}{2C^2} \partial_v^2 P,
\]

where \( w(t) \) is given by Eq. (67). Expanding \( P(v,t) \), as above, under the form \( P(v,t) = P_s(v) + 1/2[\hat{P}(v) \exp(i\omega t) + \text{c.c.}] + \cdots \), gives a modified equation for \( \hat{P} \),

\[
-i\omega \hat{P} + \frac{1}{C} (g_1(v)-I_0) \partial_v \hat{P} + \frac{\Delta}{2C^2} \partial_v^2 \hat{P} = \frac{1}{C} \left[ 1 - \frac{g_1 \hat{v}_1}{1 + i\omega \tau_1} \right] \partial_v P_s.
\]

Equation (69) is identical to Eq. (55) except that the homogeneous rhs of these two linear equations differ by a constant proportionality factor. The solution to Eq. (69) is therefore obtained by multiplying the solution to Eq. (55) by the same factor (this is also consistent with the boundary conditions at threshold and reset). In particular, this gives the two relations

\[
\hat{v}_1 = \int_{-\infty}^{\theta} dv \, v \hat{P}(v) = \left[ 1 - \frac{g_1 \hat{v}_1}{1 + i\omega \tau_1} \right] \hat{v}_1^{IF},
\]

\[
\hat{r} = -\frac{\Delta}{2C^2} \partial_v \hat{P}(v) \bigg|_{v=\hat{v}_1} \sim \left[ 1 - \frac{g_1 \hat{v}_1}{1 + i\omega \tau_1} \right] \hat{r}^{IF}.
\]

where \( \hat{v}_1^{IF} \) is the previously computed oscillation amplitude [Eq. (59)]. Equation (70) self-consistently determines the amplitude of the average potential oscillations

\[
\hat{v}_1 = \frac{1 + i\omega \tau_1}{1 + i\omega \tau_1 + g_1 \hat{v}_1^{IF}}.
\]

Together with Eq. (72), this also completes the determination of the spike rate modulation amplitude (to lowest order)

\[
\hat{r} = \frac{1 + i\omega \tau_1}{1 + i\omega \tau_1 + g_1 \hat{v}_1^{IF}} = \frac{1 + i\omega \tau_1}{1 + i\omega \tau_1 + g_1 (1 - (\theta - V_s) \hat{r}^{IF})/[i\omega \tau_1]}.
\]

where Eq. (59) has been used to obtain the second equality. Equation (73) gives that the firing-rate modulation amplitude is maximal at a nonzero frequency \( \omega_{pf} \). It is compared with the results of direct numerical simulations in Fig. 7. The analytic long \( \tau_1 \) result misses the resonance at the firing frequency that is captured by the noiseless expression, Eq. (42). For low noise, this resonance is dominant and the approximation poorly describes the numerics in this frequency range. For higher noise, the resonance at the firing frequency disappears and the dominant modulation lies around the subthreshold resonance frequency. Equation (73) then describes the numerical data quite well (see Fig. 7 lower panels).

The frequency \( \omega_{pf} \) corresponding to the maximal spike rate modulation can be estimated simply when the subthreshold frequency is much smaller than the characteristic frequency \( r_s/K \) (which approximately corresponds to the parameters chosen in Fig. 7) or in the opposite case when it is much larger. In the first case, we consider the frequency range \( 1/\tau_1 \ll \omega \ll r_s/K \), where the different terms of Eq. (73) can be expanded as follows [Eq. (61)]:

\[
|\hat{r}| = |\hat{r}^{IF}(0)| = \left[ 1 + \frac{1}{\omega^2 \tau_1^2} \right] \times \left[ 1 + 4K^2 \gamma_1 \frac{1}{r_s^2 \tau_1 C} + \left( \frac{\omega}{\gamma_1} \right)^2 \frac{1}{\gamma_1^2} \frac{1}{r_s^2 \tau_1 C} + \cdots \right]
\]

\[
\times \left[ 1 - 3 \left( \frac{K \omega}{r_s} \right)^2 + \cdots \right]
\]

\[
= |\hat{r}^{IF}(0)| \left[ 1 + 4K^2 \gamma_1 \frac{1}{r_s^2 \tau_1 C} - \left( 2r_s C/g_1 + K \right) \frac{1}{\gamma_1^2} \frac{1}{r_s^2 \tau_1 C} \right. \right.
\]

\[
-3 \left( \frac{K \omega}{r_s} \right)^2 + \cdots \right].
\]

This gives the peak frequency

\[
\omega_{pf} \approx \left[ \frac{2r_s C/g_1 + K}{3K} \right]^{1/4} \sqrt{\gamma_1 \tau_1 C}.
\]
Therefore, apart from a numerical factor, the peak modulation of the 
spike rate coincides with the resonant subthreshold frequency \( \sqrt{g_1/\tau_1 C} \). In the limit considered here, the spike rate resonance is, however, 
broaden than the subthreshold one. As shown by Eq. (75), its width is 
comparable to \( \omega_{pr} \), while the subthreshold resonance peak is much 
sharper with a width \( \sim \tau_1 \). The phase of \( \hat{r} \) can be similarly 
analyzed. In the frequency range \( 1/\tau_1 \ll \omega \ll r_c/K \), the expansion of \( \hat{r} \) reads

\[
\hat{r}(\omega) = \frac{1}{C(\theta-V_r)} \left[ 1 + i \frac{K g_1}{\tau_c} \left( \frac{1}{\omega - \omega C g_1} + \cdots \right) \right].
\]  

(77)

So, the phase of \( \hat{r} \) decreases monotonically in this frequency 
range and vanishes at the resonant subthreshold frequency \( \omega_p \sim \sqrt{g_1/\tau_1 C} \). The maximum of the phase stands at a lower 
frequency, which is only determined, for \( \tau_1 \to +\infty \), by the 
prefactor of \( \hat{r}_{IF} \) in Eq. (73). In the low frequency range \( \omega \sim 1/\tau_1 \), the phase of \( \hat{r}_{IF} \) coincides with the phase of \( [1 + i \omega \tau_1]/[1 + i \omega \tau_1 + g_1 \hat{r}_{IF}(\omega = 0)] \). Its maximum stands at

\[
\omega = [1 + g_1 \hat{r}_{IF}(\omega = 0)]^{1/2} = \left[ 1 + \frac{g_1 K}{C r_c} \right]^{1/2}. 
\]  

(78)

The opposite case when the subthreshold frequency \( \omega_p \) is 
larger than the characteristic frequency \( r_c/K \) can be analyzed in 
similar way. For \( \omega \sim \omega_p \), the firing modulation can be 
approximately written as [Eq. (62)]

\[
\hat{r} = \frac{e^{-i\pi/4}}{C(\theta-V_r)} \sqrt{\frac{r_c}{\omega K} \left[ 1 + i \omega \tau_1 \right]} \left[ 1 + i \omega \tau_1 - g_1 / C \omega \right]. 
\]  

(79)

It is maximal at the resonant subthreshold frequency. This is also 
the frequency where the phase of \( \hat{r}(\omega) \) vanishes. The phase maximum stands at the smaller frequency \( \omega_p / \sqrt{3} \).

**B. The general two-variable case**

It is conceptually not more difficult to analyze the general 
two-variable GIF model case than the previous \( g = 0 \) case. We 
restrict ourselves to \( g > 0 \) so that the model is stable 
when \( \tau_1 \geq \tau \) (i.e., so that \( \alpha = \tau_1 g/C > 1 \) in this limit). The 
computation, however, involves more complicated functions and 
less explicit expressions. Instead of simply repeating the 
previous analysis, here the appropriate generalized 
expressions are obtained from a direct expansion of the Fokker-
Planck equation (44) in the large \( \tau_1 \) limit. We find it conven-
tient to introduce \( \sigma = \sqrt{\Delta C g} \), which measures the 
amplitude of the fluctuations in voltage units, the time con-
stant \( \tau = C g \), and the conductance ratio \( \gamma = g_1 / g \). With 
these notations, the limit considered is that of large \( \beta = \tau g_1 / C \) at fixed \( \sigma \) and \( \gamma \).

**1. Steady firing rate**

With a steady noisy injected current [i.e., \( I_{nc}(t) = 0 \)], the 
membrane potential distribution obeys the time-independent 
version of the Fokker-Planck equation (44). Anticipating that 
\( \omega \) does not fluctuate in the limit \( \beta \to +\infty \), we introduce the 
new variable \( \tilde{w} \) with

\[
\tilde{w} = \bar{w} + z \sigma \beta^a, 
\]  

(80)

where the constant value \( \bar{w} \) and the power \( a < 0 \) remain to be 
determined. With this new variable, the steady-state prob-
ability distribution \( P_s \) obeys

\[
\partial_t \left[ (g v + g_1 \bar{w} - I_0) P_s \right] + \frac{\sigma^2}{2 \beta} \partial_z \partial_z \partial_t \left[ \sigma^2 \right] (\bar{w} - v) P_s \\
= -g_1 \left[ \sigma \beta^a \bar{w} \partial_z P_s + \sigma^{-1} \beta^{-a-1} \partial_z \left[ (\bar{w} - v) P_s \right] \right] \\
+ \frac{1}{\beta} \partial_z \bar{w} P_s. 
\]  

(81)

The first two subdominant terms on the rhs of Eq. (81) are of 
same order when \( \beta^a \sim \beta^{-a-1} \), i.e., for \( a = -1/2 \) that we 
choose. In order to simplify further expressions, we find it 
convenient to also replace \( v \) by the dimensionless variable \( y \) 
with

\[
y = \frac{g v + g_1 \bar{w} - I_0}{g \sigma}. 
\]  

(82)

In these notations, the time-independent Fokker-Planck equation 
finally reads

\[
\frac{1}{2} \partial_y^2 P_s + \partial_y (y P_s) = -
\gamma \left[ \frac{1}{\sigma} \frac{\partial P_s}{\partial y} \right] + \frac{1}{\beta} \partial_z (z P_s), 
\]  

(83)

where \( \gamma = g_1 / g \) and we have defined \( \tilde{w} = [(g + g_1) \bar{w} \\
- I_0] / (g \sigma) \). With variables \( y \) and \( z \), the boundary condi-
tions are imposed at the threshold \( y_\theta \) and at the reset potential \( y_r \),

\[
y_\theta = \frac{1}{g \sigma} (g \theta + g_1 \bar{w} - I_0), \quad y_r = \frac{1}{g \sigma} (g V_r + g_1 \bar{w} - I_0). 
\]  

(84)

The boundary conditions read

\[
P(y_\theta, z) = P(y_\theta, z) = 0, \\
\frac{1}{2} \partial_y \left[ (y_\theta, z) \right] = -r(z), 
\]  

(85)

where the square brackets denotes the discontinuity of the 
bracketed quantity \( \{ f(y) \} \). The firing-rate is equal to the 
total rate of threshold crossing.
With the new variables and the normalization of \( P \) chosen as 
\[
\int_{-\infty}^{\gamma_{\theta}} dy \int_{-\infty}^{+\infty} dz P(y,z) = 1,
\]
it reads
\[
r = \frac{1}{\tau} \int_{-\infty}^{+\infty} dz \, r(z).
\]  \( \tag{86} \)

When \( \beta \) is large, the solution to Eq. (83) can be obtained by series expansion,
\[
P_s(y,z) = P_0(y,z) + \beta^{-1/2} P_1 (y,z) + \beta^{-1} P_2 (y,z) + \cdots,
\]
\[
r_s(z) = r_0(z) + \beta^{-1/2} r_1(z) + \beta^{-1} r_2(z) + \cdots.
\]  \( \tag{87} \)

The zeroth-order solution is obtained by neglecting the rhs of Eq. (83),
\[
P_0(y,z) = 2 r_0(z) Q_0(y),
\]  \( \tag{88} \)
\[
Q_0(y) = e^{-y^2} \int_{\gamma_{\theta}}^{y_{\theta}} e^{u^2} \Theta(u-y) \, du,
\]  \( \tag{89} \)
where \( \Theta \) is the usual Heaviside function, \( \Theta(u) = 1 \) for \( x \geq 0 \) and \( 0 \) otherwise. It is identical to the steady-state probability distribution for the usual leaky integrate-and-fire model (see, e.g., Ref. [17]) except that the prefactor \( r_0(z) \) is a function of the supplementary variable \( z \) instead of a constant and remains to be obtained as well as the bounds \( y_{\theta} \) and \( y_r \) that depend on the unknown \( \bar{w} \) [see Eqs. (80) and (84)]. These unknowns are determined by solvability conditions on higher-order equations.

The first-order correction \( P_1(y,z) \) obeys
\[
\frac{1}{2} \frac{\partial^2 P_1}{\partial y^2} + \frac{\partial}{\partial y} (y P_1) = -\gamma \left[ \frac{\partial P_0}{\partial y} + (\gamma - y) \frac{\partial P_0}{\partial z} \right].
\]  \( \tag{90} \)

The integral over \( y \) on the lhs of Eq. (90) from \( y = -\infty \) to \( y = y_{\theta} \) is seen to vanish after using boundary conditions (85). Therefore, this needs to be also true for the rhs of Eq. (90) if the equation is to be solvable. That is,
\[
\int_{-\infty}^{y_{\theta}} dy \left( \frac{\partial}{\partial y} (\gamma - y) Q_0(y) \right) = 0.
\]  \( \tag{91} \)

This solvability condition determines \( \bar{w} \) (and, therefore, \( y_{\theta}, y_r \) and \( \tilde{y} \)). It is equivalent to the previous self-consistent equation (51), which was obtained on a more intuitive basis.

Once \( \bar{w} \) is determined, the normalization condition gives the steady-state rate to lowest order in \( 1/\beta \),
\[
\frac{1}{r_0 \tau} = 2 \int_{-\infty}^{y_{\theta}} dy \int_{-\infty}^{+\infty} du e^{-u^2} \frac{\exp(2y_{\theta} u) - \exp(2y, u)}{u}
\]  \( \tag{92} \)

When condition (91) is satisfied, Eq. (90) can be solved without difficulty. As can be seen from the rhs of Eq. (90) and explicitly given in the Appendix, the resulting \( P_1(y,z) \) is obtained as a linear combination of \( r_0'(z) \) and \( z r_0(z) \) multiplied by determined functions of \( y \). The solvability condition on \( P_1 \) at second order, analogous to Eq. (91), imposes that \( r_0'(z) \) is proportional to \( z r_0(z) \) and shows that \( r_0(z) \) is a Gaussian. The explicit expression of \( \langle z^2 \rangle \) as well as the first nontrivial correction to \( r_0 \) are determined in the Appendix [see Eqs. (A28)–(A30)]. A comparison between direct numerical simulation results and the perturbative estimates of the steady-state rate is provided in Fig. 8. The large \( \tau_1 \) result (92) is seen to describe quite accurately the numerical results already for \( \tau_1 / \tau = 5 \).

2. Spike rate modulation: Direct linearization

In order to obtain the instantaneous spike rate modulation induced by a small oscillatory current \( (I_{osc}(t) = 1/2 \exp(i \omega t) + c.c.) \), we consider the direct linearization of the time-dependent Fokker-Planck equation (44) around the steady-state distribution.

In variables \( y, z \), Eq. (44) reads
\[
-\tau \partial y P + \frac{1}{2} \frac{\partial^2 P}{\partial y^2} + \frac{\partial}{\partial y} (y P) = -\gamma \left[ \frac{\partial P_0}{\partial y} + (\gamma - y) \frac{\partial P_0}{\partial z} \right]
\]  \( \tag{93} \)
\[
= -\gamma \left( \frac{1}{\sqrt{\beta}} \left( \frac{\partial P}{\partial y} + (\gamma - y) \frac{\partial P}{\partial z} \right) + \frac{1}{\beta} \frac{\partial (zP)}{\partial z} \right)
\]
\[
+ \frac{I_{osc}(t)}{g \sigma} \partial y P,
\]
with boundary conditions (85) [with a time-dependent \( r(z, t) \)]. \( P(y, z, t) \) and \( r(z, t) \) are sought in the form \( P(y, z, t) = P^s(y, z) + (2g \sigma)^{-1} \left[ \widetilde{P}(y, z) \exp(i \omega t) + c.c. \right] \), \( r(z, t) = r_s(z) + (2g \sigma)^{-1} \left[ \widetilde{r}(z, \omega) \exp(i \omega t) + c.c. \right] \). The firing rate [Eq. (86)] and its modulation are obtained by integration over \( z \) (and division by \( \tau \)) and are written as
\[ r(t) = r_s + (2g\sigma)^{-1}[\dot{I}(\omega) \exp(i\omega t) + \text{c.c.}], \]  
(94)

Note that the normalization of the current in this section makes the normalization of \( \dot{r}(\omega) \) differ by a factor \( g\sigma \) from the normalization in Eq. (9). Modulation \( \dot{P} \) obeys at lowest order in \( 1/\sqrt{\beta} \),
\[-i\tau\omega\dot{P}_0 + \frac{1}{2}\partial^2 \dot{\hat{P}}_0 + \frac{\partial}{\partial y}(y\dot{P}_0) = \partial_y \dot{P}_0. \]
(95)

At this order, the \( z \) dependence of \( \dot{P}_0 \) factors out and it can be written as
\[ \dot{P}_0 = 2r_0(z)\dot{Q}_0^{IF}, \]
(96)
where \( \dot{Q}_0^{IF} \) is identical to the response of a classic IF neuron under oscillatory drive. The function \( \dot{Q}_0^{IF} \) can be written [17,25] as a linear combination of a particular solution to Eq. (95) plus two independent solutions \( \phi_1 \) and \( \phi_2 \) of the allied homogeneous equation. The particular solution of Eq. (95), \( \partial_y Q_0^{IF}[1 + i\omega\tau] \), is obtained by differentiating the steady-state equation to lowest order [i.e., Eq. (83) with rhs equal to zero] with respect to \( y \). Introducing Kummer’s function \( M(a,b,x) \) [32], functions \( \phi_1(y) \) and \( \phi_2(y) \) can be taken as independent linear combinations of the confluent hypergeometric functions \( M[(1-i\omega\tau)/2,1/2,-y^2] \) and \( yM[1-i\omega\tau/2,3/2,-y^2] \). It is convenient to choose \( \phi_2(y) \) proportional to the combination that has a fast decrease at \( y = -\infty \),
\[ \phi_2(y) = \frac{1}{\Gamma\left[\frac{1+i\omega\tau}{2}\right]} M\left[\frac{1-i\omega\tau}{2},\frac{1}{2},-y^2\right] + \frac{2y}{\Gamma\left[\frac{1+i\omega\tau}{2}\right]} M\left[\frac{1-i\omega\tau}{2},\frac{3}{2},-y^2\right]. \]
(79)

This gives the zeroth-order estimate of \( \dot{r}(\omega) \) [Eq. (94)],
\[ \dot{Q}_0^{IF}(y) = \frac{1}{1+i\omega\tau} \frac{dQ_0}{dy} + \frac{\dot{\alpha}_0\phi_2(y)}{\partial_y\phi_1(y)} + \frac{\dot{\gamma}_0\phi_2(y)}{\partial_y\phi_2(y)}, \quad y < y_r, \]
(98)
\[ \dot{Q}_0^{IF}(y) = \frac{1}{1+i\omega\tau} \frac{dQ_0}{dy} + \frac{\dot{\alpha}_0\phi_2(y)}{\partial_y\phi_1(y)} + \frac{\dot{\gamma}_0\phi_2(y)}{\partial_y\phi_2(y)}, \quad y > y_r. \]

The three boundary conditions (85) determine the three unknown coefficients \( \dot{\alpha}_0(\phi), \dot{\beta}_0(\omega), \) and \( \dot{\gamma}_0(\phi) \) and give the firing-rate modulation
\[ \dot{r}_0^{IF}(\omega) = \frac{r_0}{1+i\omega\tau} \frac{\int_0^{\gamma_r} dy \dot{Q}_0^{IF}(\omega)}{1+i\omega\tau} \cdot \]
(99)

Again, we have added the superscript IF to emphasize that the rate modulation (99) is identical to the result for a classic IF model with an injected current \( I_0 = g_s \tilde{w} \). For further use below, we also note that integration of Eq. (95) over \( y \) provides the identity
\[ Y(\omega) = 2\tau_0 \int_{-\infty}^{\gamma_r} dy Q_0^{IF}(\omega) \frac{1 - (y_{\theta} - y_{\gamma})^2}{1 + i\omega\tau}, \]
(100)
where function \( Y(\omega) \) is defined by the first equality.

The obtained firing-rate modulation \( \dot{r}_0^{IF}(\omega) \) is plotted and compared to the results of a direct numerical simulation of the GIF model in Fig. 9.

The agreement is rather good at high frequency but does not capture the resonance at low frequency. Moreover, as for the previous zero-leak case, the zero frequency limit of Eq. (99) does not correspond to the result obtained by varying the injected current in the steady-state rate (92). That is,
\[ \dot{r}_0^{IF}(\omega = 0) = 2\tau_0 \int_{-\infty}^{\gamma_r} e^{-u^2} du \int_{-\infty}^{\gamma_r} e^{-u^2} du \cdot \]
(101)

This differs from the expected formula for very slow oscillations, which should be given by the adiabatic oscillations of the steady-state rate. Namely, from Eq. (92) one obtains
\[ \lim_{\omega \to 0} \dot{r}_0^{IF}(\omega) = g_s \frac{d r_0}{d I_0} \frac{d \tilde{w}}{d I_0} \left[ 1 - g_s \frac{d \tilde{w}}{d I_0} \right], \]
(102)
where \( \tilde{w} \) is determined by Eq. (91) and depends on \( I_0 \) because \( y_{\theta} \) and \( y_{\gamma} \) do. As before, the two formulas differ because the variation of \( \tilde{w} \) due to the injected current is overlooked in the direct linearization. The approach should therefore be refined at low frequency as shown in the following section.

3. Spike rate modulation: The low frequency regime

In the low frequency regime, the terms coming from time differentiation become small and comparable to the terms of first order in \( 1/\sqrt{\beta} \). Thus, the perturbation series has to be reordered.

The adiabatic result at \( \omega = 0 \) lead us to anticipate that, for a slow oscillating current \( I_{osc}(t) = 1/2 [\tilde{w}\exp(i\omega t) + \text{c.c.}] \), \( \tilde{w} \) is peaked around a time-dependent oscillating value. This suggests a change of variables from \( w \) to \( z \) with
Again, the solution to (104) is sought of the form $P(y,z,t) = P_0(y,z) + (2g\sigma)^{-1} [\hat{\mathcal{P}}(y,z) \exp(i\omega t) + \text{c.c.}].$ For low frequencies $\omega < 1/\sqrt{\beta \tau}$ (or smaller), the linear probability modulation obeys to lowest order in $1/\sqrt{\beta}$,

$$
\frac{1}{2} \frac{\partial^2 \hat{P}_0}{\partial y^2} + \frac{\partial}{\partial y} (\hat{y}\hat{P}_0) = (1 - g\hat{w}_1) \partial_y P_0.
$$

Equation (105) only differs from the previously solved Eq. (95), in that it is evaluated at $\omega = 0$ and that the rhs of the two equations differ by a constant proportionality factor. Therefore, one has

$$
\hat{P}_0 = 2r_0(z) [1 - g\hat{w}_1] Q_{0F}^0(y; \omega = 0),
$$

with

$$
Q_{0F}^0(y; \omega = 0) = - \frac{\partial Q_0}{\partial y} + \frac{r_{0F}^0(0 = 0)}{r_0} Q_0(y) + \exp(-y^2)
$$

$$
\times \left[ -\exp\left(y_0^2\right) + (\theta(y_0^2) + \exp(y_0^2) - 1) \right],
$$

where $r_0$ and $\hat{r}_0(\omega = 0)$ are given by Eqs. (92) and (101). Formula (108) can be obtained by taking the limit $\omega \to 0$ of general expression (98) or more simply by directly solving Eq. (95) with $\omega = 0$. In this case, the normalization condition to the solution of the homogeneous equation can be obtained by imposing the condition

$$
\int_{-\infty}^{y_0} dy \hat{Q}_{0F}^0(y) = 0,
$$

which directly follows from Eq. (95) for $\omega \neq 0$.

The unknown constant $\hat{w}_1$ is determined by a solvability condition at next order. The $1/\sqrt{\beta}$ correction $\hat{P}_1$ to $\hat{P}_0$ obeys

$$
\frac{1}{2} \frac{\partial^2 \hat{P}_1}{\partial y^2} + \frac{\partial}{\partial y} (\hat{y}\hat{P}_0) = - \gamma \frac{\partial P_0}{\partial y} + (v - \gamma \hat{w}_1 P_0)
$$

$$
\times g\hat{w}_1 \hat{P}_0 + i\omega \tau \hat{P}_0.
$$

The solvability condition, obtained by integrating Eq. (110) over $y$ together with Eq. (106) and (109), reads

$$
\int_{-\infty}^{y_0} dy \{ \gamma (v - \gamma y) \hat{P}_0 + (1 + i\omega \tau) g\hat{w}_1 \hat{P}_0 \} = 0.
$$

With the previous expressions (106) and (108), Eq. (111) is found to be equivalent to the following self-consistent equation for $\hat{w}_1$:

$$
\hat{w}_1 = \gamma \frac{(1 - g\hat{w}_1 P_0)}{(1 + i\omega \tau) 2\tau_0} \int_{-\infty}^{y_0} dy Q_{0F}^0(y; \omega = 0).
$$
In Eq. \( r^* \) leads to the alternative formula:

\[ \hat{r}^* = \gamma Y(0) / (1 + i\omega \tau_1 + \gamma Y(0)). \]

where

\[ Y(0) = 1 - (y_{\theta} - y_{r}) \tau_{r}^{II} (\omega = 0) \]

and \( \tau_{r}^{II} (\omega = 0) \) is given explicitly in Eq. (101). The firing-rate modulation in the low frequency regime is given by Eqs. (107) and (113):

\[ \hat{r}_0(\omega) = \frac{1 + i\omega \tau_1}{1 + i\omega \tau_1 + \gamma Y(0)} \tau_{r}^{II} (\omega = 0). \]

An expression that interpolates between the low and high frequency regimes is simply

\[ \hat{r}_0(\omega) = \frac{1 + i\omega \tau_1}{1 + i\omega \tau_1 + \gamma Y(0)} \tau_{r}^{II} (\omega). \]

A slightly different interpolating expression was proposed in Sec. IV A 2. It is obtained by keeping the \(-i\omega P_0\tau\) term in Eq. (105). This simply replaces \( \hat{Q}_0^{II}(y; \omega = 0) \) by \( \hat{Q}_0^{II}(y; \omega) \) in each step from Eq. (105) to Eq. (116) and it leads to the alternative formula:

\[ \hat{r}_0^{c}(\omega) = \frac{1 + i\omega \tau_1}{1 + i\omega \tau_1 + \gamma Y(\omega)} \tau_{r}^{II} (\omega). \]

with \( Y(\omega) \) defined by Eq. (100) and \( \tau_{r}^{II}(w) \) given by Eq. (99).

The analytical formulas are compared to results of direct numerical simulations in Figs. 9 and 10. For these parameter values, the two formulas of Eq. (116) and (117) are numerically very close and describe quite well the numerical results.

C. Unmasking of the subthreshold resonance by noise

In high noise conditions, the firing-rate resonance curve is peaked around the subthreshold frequency as seen in Figs. 7(C) and 9. The corresponding resonance curves in low noise conditions with the same average firing-rate (obtained by increasing the injected current \( I_0 \)) are shown in Figs. 7(A) and 10. They display a strong resonance peak at the firing-rate frequency and peaks of lower amplitude at its harmonics, attenuated but recognizable features of the firing-rate resonance curves in the deterministic limit (compare with Fig. 5). Figures 9 and 10 also show that the GIF response \( \hat{r}_0(\omega) \) at low frequencies can be either smaller than the leaky IF response \( \hat{r}_0^{IF}(\omega) \) (hence creation of a peak around subthreshold frequency, see Fig. 9) or higher than the leaky IF response (hence a trough around subthreshold frequency, see inset in Fig. 10). The condition that determines whether a peak or a trough is present can be obtained from Eq. (117). A peak is found for \( Y(0) > 0 \), while a trough is found for \( Y(0) < 0 \). Alternatively, this condition can be obtained from the slope of the \( f-I \) curve, since \( Y(0) \) is linearly related to \( \tau_{r}^{IF} (\omega = 0) \). For a slope larger than \( \int f/C(\theta - V_0) \), a peak is obtained in the firing-rate response, and a trough otherwise. Note that \( \int f/C(\theta - V_0) \) is the slope that is obtained in the high firing-rate limit in the absence of a refractory period. Thus, the qualitative behavior of the firing-rate response at low frequency can be obtained by an inspection of the \( f-I \) curves shown in Fig. 8. For low noise levels, the slope is small at low firing-rates (hence a peak at subthreshold frequency), then increases above its asymptotic value (hence a trough at subthreshold frequency), and then decreases towards its asymptotic value (the trough becomes less and less pronounced as firing-rates increase). For high noise levels, the slope is always smaller than its asymptotic value, which means that a peak at subthreshold frequency is always present, but the peak should vanish at very large rates.

For the parameter values of Figs. 9 and 10, the peak of the firing-rate resonance curve is plotted in Fig. 11 as a function of the noise intensity. This clearly illustrates the peak shift from the firing-rate frequency to the subthreshold preferred frequency with increasing noise. Thus, noise helps to uncover a resonant peak at the subthreshold preferred frequency in the firing-rate response. In some sense, this might be considered as a form of stochastic resonance [19]. However, this phenomenon is very different from previously discussed stochastic resonance phenomena in neurons (see, e.g., Ref. [27]). These studies considered the spectrum of the interspike interval distribution (ISI) of a neuron subjected to a noisy sinusoidal current as the quantity of interest. What was shown in a variety of models, including the leaky integrate-and-fire neuron, is that the signal-to-noise ratio (SNR) of the transmitted frequency exhibits a peak at some positive noise level. Here, we have considered a very different quantity, the linear response of the instantaneous firing-rate. This measure is more appropriate in the context of the transmission of an oscillatory signal at the network level. It is also one of the main quantities that determines whether a network is asynchronous or not (see, e.g., Ref. [17]). The behavior of this measure is quite different from the SNR of the ISI distribu-
tion. In the suprathreshold firing regime, noise decreases the relative size of the resonant peak at the firing frequency, in both IF and GIF neurons, in a monotonic way. In the subthreshold firing regime, noise enhances in a monotonic way the relative size of the resonant peak at the subthreshold preferred frequency, if the firing rate is kept constant as noise is varied. This behavior occurs in GIF neurons with subthreshold resonance, but not in IF neurons that have no subthreshold preferred frequency.

V. CONCLUSIONS AND PERSPECTIVES

In this paper, a generalized integrate-and-fire model has been studied in order to shed light on the relation between subthreshold resonance and firing-rate modulation.

It had been shown in a previous study [12] using both the GIF model and conductance-based modeling that a sufficiently large amount of noise was necessary for the subthreshold resonance to be able to create a firing-rate resonance. The present study provides a detailed analysis of this phenomenon for the two-variable GIF model. For noiseless and weak noise inputs, the results of Secs. II and IV show that the firing-rate modulation is strongest at the firing-rate frequency (and its harmonics) and that there is a trough in the response at frequencies around the subthreshold frequency. Contrary to this, for sufficiently noisy inputs, the results of Sec. IV show that the resonance of the firing-rate stands around the subthreshold frequency and the perturbative results describe well the numerical data. In the present paper, we have illustrated in Figs. 5, 7, 9, and 10 the situation in which the background firing rate is larger than the subthreshold preferred frequency. The two variable resonant GIF neurons are type II and their minimal firing rate in the absence of noise cannot be much smaller than the subthreshold resonant frequency. Hence, the situation in which the firing rate is smaller than the subthreshold frequency can be achieved, in practice, only with noise and, in this regime, the firing-rate amplifies preferentially inputs at the subthreshold resonant frequency [12].

As regards the mathematical treatment of the two-variable GIF model, the main results have been obtained perturbatively in the limit where the supplementary variable is slow as compared to the membrane potential dynamics. It is worth emphasizing that this is relevant for the description of many real cells. From the multiple cell types that exhibit resonance in the nervous system, most show resonance at frequencies of a few Hertz. Neurons in the inferior olive [28,29] and in the thalamus [30,31] show resonance at about 4 Hz. Pyramidal cells in the neocortex can show resonance at 1–2 Hz at hyperpolarized levels [5] or 5–20 Hz at more depolarized levels [6]. Finally, pyramidal cells in the hippocampus also show resonance at low frequencies in the θ band (2–7 Hz, [7,8]). Such frequencies can be obtained with a time constant of the “activation variable” w around τw ~ 100 ms. It is interesting to note that for such values of τw, the small τw/τ1 expansion gives a very good approximation of the reduced model behavior (see Figs. 9 and 10). The reduced model itself often gives a very good approximation of the behavior of more realistic conductance-based cells [12].

Other approximate treatments can probably be developed to describe different parameter regimes. Several cells show resonance at higher frequencies. For instance, interneurons of the hippocampus show resonance in the γ band (30–50 Hz, [8]). Such frequencies are obtained with smaller time constants τ1 and hence the small τ1/τ1 expansion gives less accurate results. However, the difference between simulations and analytical data seem to be accounted well by a frequency-independent multiplicative factor. It thus seems that no qualitatively new phenomenon arises from the higher-order terms, at least in the range of the values of τ1 investigated here (10–200 ms). Obtaining the exact solution of the problem would nevertheless be interesting but appears rather difficult.

The main features observed in simulations of more realistic models [12] are similar to those obtained with the GIF model and can thus be described by the present analysis. Several simplifying assumptions made in the formulation of the GIF model should, however, be noted. The most obvious ones are that the GIF model subthreshold properties are independent of the membrane potential and that spike-generating dynamics is absent. Numerical results using conductance-based models [12] show that the basic phenomenon is independent of these simplifications. It could nonetheless be worthwhile to try and develop a direct analysis of these more realistic models.

A second set of simplifications pertains not to the neuron dynamics itself but to the modeling of its inputs. It has been chosen here for simplicity to consider a white noise current source. While this could be studied in an experiment in isolated cells or in a slice, this certainly greatly simplifies synaptic inputs in at least two important respects. They are better modeled as conductance modifications and, furthermore, noise is colored on the time scale of the synaptic dynamics [33]. It is known that the replacement of white noise by
colored noise can modify the response of neurons at high frequency [25]. Again, the numerical results of Ref. [12] indicate that the qualitative phenomenon is preserved in this more complicated case, but a more quantitative analysis might be worth pursuing.

It is certainly of great interest to understand how the properties of individual cells affect the collective properties of networks of cells. The present study may help in two ways to make progress in this direction. First, at a purely numerical level, the IF neuron has proven very useful as the simplest spiking neuron model and it has been widely used as the elementary component of large network simulations. The GIF neuron should provide the appropriate substitute and permit the incorporation of key features of the subthreshold element of large network simulations. The GIF neuron should provide the appropriate substitute and permit the incorporation of key features of the subthreshold elementary component of large network simulations. The spiking neuron model and it has been widely used as the

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APPENDIX: FIRST CORRECTION TO THE FIRING RATE IN THE LARGE $\tau_1$ EXPANSION

The formalism of Sec. IV B can be used to obtain higher-order corrections to the lowest-order results given in the main text in a systematic way. This is illustrated here by deriving the first correction to the steady firing-rate both for the zero-leak case and for the general $g \neq 0$ case. The zero-leak case is treated separately because much more explicit expressions can be obtained. This also serves to illustrate a method of calculation that avoids the explicit computation of the probability distribution by focusing on its moments.

1. The zero-leak case and the moment method

The aim is to calculate the first higher-order correction to the firing-rate for the simple case of $g = 0$. The regime of interest is that for which $\beta$ is large and, therefore, the corrections will be sought in the form of a series of inverse powers of $\sqrt{\beta}$. The time-independent Fokker-Planck equation (44) for this case is

$$0 = \frac{\Delta}{2 C^2} \frac{\partial^2 P}{\partial v^2} + \frac{1}{C} \frac{\partial}{\partial v} \left[ (g_1 w - I_0) P \right] + \frac{1}{\tau_1} \frac{\partial}{\partial w} \left[ (w - v) P \right].$$

The substitutions $v = \bar{w} + x \sqrt{\Delta/C g_1}$ and $w = \bar{w} + z \beta^{-1/2} \sqrt{\Delta/C g_1}$ are made, yielding the reduced-variable Fokker-Planck equation:

$$0 = \frac{1}{2} \frac{\partial^2 P}{\partial x^2} + \frac{\zeta}{2} \frac{\partial P}{\partial x} + \frac{1}{\sqrt{\beta}} \left( \frac{\partial P}{\partial x} - x \frac{\partial P}{\partial z} \right) + \frac{1}{\beta} \frac{\partial}{\partial z} (z P),$$

(A1)

with $\zeta$ defined by

$$\zeta = 2 \sqrt{\frac{C}{\Delta g_1}} (g_1 \bar{w} - I_0).$$

Note that in this section, the normalization of $z$ is different by a factor of $\sqrt{g/g_1}$ from that chosen in the rest of this paper (which is not compatible with $g = 0$).

The first correction to the firing-rate can be conveniently obtained by taking various moments of Eq. (A1). To this end, multiplying by a factor $x^m z^n$ and integrating over the space of the $x$ and $z$ variables gives

$$\rho(z^n)(x_0^m - x_m^m) + m(m - 1)(x_m^{m-2} z^n) = m \zeta (x_m^{m-1} z^n)$$

$$+ \frac{2m}{\sqrt{\beta}} (x_m^{m-1} z^{n+1}) = \frac{2n}{\sqrt{\beta}} (x_m^{m+1} z^{n-1}) + \frac{2n}{\beta} (x_m^{m} z^n),$$

(A2)

where the following definitions have been used:

$$\langle A \rangle = \int_{-\infty}^{\infty} dz \int_{-\infty}^{x_0} dx A P,$$

$$\rho(z^n) = \int_{-\infty}^{\infty} dz z^n \frac{\partial P}{\partial x} \ 	ext{with} \ p = \rho(1),$$

$$x_0 = \sqrt{\frac{C g_1}{\Delta}} (\theta - \bar{w}) \ \text{and} \ x_r = \sqrt{\frac{C g_1}{\Delta}} (V_r - \bar{w}).$$

(A3)

Putting $m = 0$ in Eq. (A2) gives

$$\langle x z^{n-1} \rangle = \frac{1}{\sqrt{\beta}} (z^n) \ 	ext{for} \ n \geq 1.$$  \ (A4)

This equation (with $n = 1$) states that, to leading order, $\langle x \rangle \sim 1/\sqrt{\beta}$. For $n = 0$, with $m = 1$ and $m = 2$, Eq. (A2) becomes

$$\langle x_0 - x \rangle \rho = \zeta + \frac{2}{\sqrt{\beta}} (z),$$

(A5)
respectively. On substituting for \( \rho \), these two equations give to zero order

\[
\zeta = -\frac{2}{(x_0 + x_r)}. \tag{A7}
\]

Using the definitions of \( \zeta \), \( x_0 \), and \( x_r \), Eq. (A7) gives a quadratic equation for \( \bar{w} \). The root that is consistent with the normalization condition on the probability density can be shown to be \( \bar{w} = \langle v \rangle \) [Eq. (52)]. As expected, this zero-order result is equivalent to the self-consistent replacement: \( w \rightarrow \langle v \rangle \). The choice is made to enforce relation (A7) to all orders (this can be taken as a definition of shift \( \bar{w} \)).

From the moment equation with \( m = 1 \) and \( n = 0 \), constant \( \rho \) (which is related to the firing-rate) is given by

\[
\rho = \frac{\zeta}{x_0 - x_r} \left( 1 + \frac{2}{\sqrt{\beta}} \langle z \rangle \right).
\]

It remains only to obtain \( \langle z \rangle \) to leading order. This can be achieved by using the moment equation (A2) with \( m = 1 \) and \( m = 2 \):

\[
\rho(z^n)(x_0 - x_r) = \zeta(z^n) + \frac{2}{\sqrt{\beta}} \langle z^{n+1} \rangle
\]

\[
- \frac{2n}{\sqrt{\beta}} \langle x z^{n-1} \rangle + \frac{2n}{\beta} \langle x z^n \rangle, \tag{A8}
\]

\[
\rho(z^n)(x_0^2 - x_r^2) + 2 \langle z^n \rangle = 2 \zeta(xz^n) + \frac{4}{\sqrt{\beta}} \langle xz^{n+1} \rangle
\]

\[
- \frac{2n}{\sqrt{\beta}} \langle x^2 z^{n-1} \rangle + \frac{2n}{\beta} \langle x^2 z^n \rangle. \tag{A9}
\]

On multiplying Eq. (A8) by 2 and Eq. (A9) by \( \zeta \) and adding them to eliminate \( \rho(z^n) \) using Eq. (A7), the following is obtained:

\[
n \zeta(x^3 z^{n-1}) + 2n \langle x^2 z^{n-1} \rangle = 2 + \zeta^2 + 2n \langle z^{n+1} \rangle
\]

\[
+ \frac{2 \zeta}{\sqrt{\beta}} \langle z^{n+2} \rangle + \frac{n \zeta}{\sqrt{\beta}} \langle x z^n \rangle, \tag{A10}
\]

where relation (A4) has also been used. With \( n = 0 \), this equation yields

\[
\langle z \rangle = -\frac{1}{\sqrt{\beta}} \left( 2 + \zeta^2 \right). \tag{A11}
\]

and with \( n = 1 \),

\[
\left( 2 + \zeta^2 + \frac{2}{\beta} \right) \langle z^2 \rangle = \zeta(x^3) + 2 \langle x^2 \rangle - \frac{2 \zeta}{\sqrt{\beta}} \langle z^3 \rangle - \frac{\zeta}{\sqrt{\beta}} \langle x z^2 \rangle. \tag{A12}
\]

The last result implies that, to zero order,

\[
\langle z^2 \rangle_0 = \frac{(\zeta(x^3)_0 + 2 \langle x^2 \rangle_0)}{(2 + \zeta^2)}. \tag{A13}
\]

The zero-order forms of Eq. (A2) with \( m = 1, 2, 3, 4 \) and \( n = 0 \) can be used to obtain \( \langle x^2 \rangle_0 \) and \( \langle x^3 \rangle_0 \):

\[
\langle x^2 \rangle_0 = \frac{1}{3} \frac{x_0^2 - x_r^2}{x_0 - x_r} = \frac{1}{3} (x_0^2 + x_0 x_r + x_r^2)
\]

\[
\langle x^3 \rangle_0 = \frac{1}{4} \frac{x_0^4 - x_r^4}{x_0 - x_r} + \frac{1}{\beta} \frac{z_0^3 - x_r^3}{x_0 - x_r} = -\frac{1}{4} (x_0 + x_r)^3.
\]

Combining these results and noting the relation between \( \rho \) and the firing-rate \( r = -g_1 p / 2 C \) gives

\[
r = r_0 \left( 1 - \frac{1}{\beta} \frac{4 \langle z^2 \rangle_0}{(2 + \zeta^2)} \right) = r_0 \left( 1 - \frac{4}{\beta} \frac{(\zeta(x^3)_0 + 2 \langle x^2 \rangle_0)}{(2 + \zeta^2)^2} \right) \tag{A14}
\]

as the order \( 1/\beta \) correction to the firing-rate. The zero-order firing-rate \( r_0 = g_1 / \{ C(x_0^2 - x_r^2) \} \) is equivalent to the result given in Eq. (53).

2. The first-order correction in the general case

The starting point is the Fokker-Planck equation (83). Inserting the series expansion, Eq. (92), in Eq. (83), gives the successive orders in \( P \),

\[
LP_0 = 0, \tag{A15}
\]

\[
LP_1 = -\gamma \left( z \frac{\partial P_0}{\partial y} + (\bar{y} - y) \frac{\partial P_0}{\partial z} \right), \tag{A16}
\]

\[
LP_2 = -\gamma \left( z \frac{\partial P_1}{\partial y} + (\bar{y} - y) \frac{\partial P_1}{\partial z} + \frac{\partial}{\partial z} \langle z P_0 \rangle \right), \tag{A17}
\]

\[
LP_3 = -\gamma \left( z \frac{\partial P_2}{\partial y} + (\bar{y} - y) \frac{\partial P_2}{\partial z} + \frac{\partial}{\partial z} \langle z P_1 \rangle \right), \tag{A18}
\]

where the linear operator \( L \) is defined by

\[
LP = \frac{1}{2} \frac{\partial^2 P}{\partial y^2} + \frac{\partial}{\partial y} (y P). \tag{A19}
\]

We note that functions \( P \), must be even (odd) in \( z \) for even (odd) orders \( i \). This implies that the corrections to the firing rate at odd orders are zero, since the firing rate is obtained by integrating \( P \) over \( z \) at \( y = \bar{y}_0 \) [Eq. (46)].

The solution to equation (A15) that satisfies the boundary conditions is given by Eq. (89),

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\[ P_0(y,z) = 2 r_0(z) Q_0(y), \quad (A20) \]
\[ Q_0(y) = e^{-y^2} \int_{y}^{+\infty} e^{u^2} \Theta(u-y_r) du, \quad (A21) \]
\[ r_0 \tau = \int_{-\infty}^{+\infty} r_0(z) dz = \left( 2 \int_{-\infty}^{+\infty} Q_0(y) dy \right)^{-1}, \quad (A22) \]

where \( r_0(z) \) is determined by a solvability condition [see Eq. (A28) below] for the second-order Eq. (A17).

The solution to Eq. (A16) that satisfies the boundary conditions is
\[ P_1(y,z) = 2 r_1(z) Q_0(y) + 4 \gamma [z r_0(z) J Q_0(y)] \]
\[ - r_1'(z) J K Q_0(y), \quad (A23) \]
where \( J \) and \( K \) are operators defined by
\[ J f(x) = \exp(-x^2) \int_{x}^{+\infty} \exp(u^2) f(u) du, \quad (A24) \]
\[ K f(x) = \int_{-\infty}^{x} (u-y) f(u) du, \quad (A25) \]

and \( r_1(z) \) is defined by Eq. (87) and is determined by a solvability condition on the third-order Eq. (A18) [Eq. (A33) below].

The solution to Eq. (A16) that satisfies the boundary conditions is
\[ P_2(y,z) = 2 r_2(z) Q_0(y) + 4 \gamma [z r_0(z) J Q_0(y)] \]
\[ - r_2'(z) J K Q_0(y) + [z r_0(z)]' J J Q_0(y) \]
\[ + 8 \gamma \{z^2 r_0(z) J^2 Q_0(y) - z r_0'(z) J K Q_0(y) \}
\[ - [z r_0(z)]' J K Q_0(y) \} + 8 \gamma^2 r_0'' J K J K Q_0(y), \quad (A26) \]

where
\[ I f(x) = \int_{-\infty}^{x} f(u) du \quad (A27) \]

and an additional condition must be imposed on \( r_0(z) \) to satisfy the boundary conditions:
\[ 4 \gamma K JK Q_0(y_\theta) \frac{\partial^2 r_0}{\partial z^2} + \left( \frac{1}{r_0 \tau} - 4 \gamma K J Q_0(y_\theta) \right) \frac{\partial}{\partial z} (z r_0) = 0. \quad (A28) \]

This condition gives \( r_0(z) \):
\[ r_0(z) = \frac{r_0 \tau}{\sqrt{2 \pi (z^2)_0}} \exp \left( - \frac{z^2}{2 (z^2)_0} \right), \quad (A29) \]

The solution \( r_1(z) \) is equal to \( r_0(z) \) times a polynomial in \( z \) containing only terms in \( z^3 \) and \( z \). The first moment is directly obtained by integrating Eq. (A33) twice over \( z \),
\[ \int_{-\infty}^{+\infty} dz z r_1(z) = (z^3)_0 \left( 2 \gamma \left( \frac{4 \gamma K J^2 Q_0 - 2 I J K Q_0}{1 - 4 \gamma K J Q_0} \right) \right. \]
\[ + \left. \frac{2 \gamma K J^2 Q_0 - I J K Q_0}{K J K Q_0} \right|_{y=y_\theta}, \quad (A34) \]


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