Kinetic theory for neuronal networks with fast and slow excitatory conductances driven by the same spike train

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We present a kinetic theory for all-to-all coupled networks of identical, linear, integrate-and-fire, excitatory point neurons in which a fast and a slow excitatory conductance are driven by the same spike train in the presence of synaptic failure. The maximal-entropy principle guides us in deriving a set of three $(1+1)$-dimensional kinetic moment equations from a Boltzmann-like equation describing the evolution of the one-neuron probability density function. We explain the emergence of correlation terms in the kinetic moment and Boltzmann-like equations as a consequence of simultaneous activation of both the fast and slow excitatory conductances and furnish numerical evidence for their importance in correctly describing the coarse-grained dynamics of the underlying neuronal network.

PACS number(s): 87.19.L−, 05.20.Dd, 84.35.+i

I. INTRODUCTION

Attempts to understand the enormous complexity of neuronal processing that takes place in the mammalian brain, supported by the ever-increasing computational power used in the modeling of the brain, have given rise to greatly increased sophistication in mathematical and computational modeling of realistic neuronal networks [1–7]. Striking manifestations of spatiotemporal neuronal dynamics, such as patterns of spontaneous activity in the primary visual cortex (V1) [8,9] and motion illusions [10], which take place on length scales of several millimeters and involve millions of neurons, can now be computed using large-scale, coupled, point-neuron models [11,12]. The ability to describe still more complicated neuronal interactions in yet larger portions of the brain, such as among multiple areas or layers of the visual cortex, may be significantly enhanced by appropriate coarse graining.

Coarse-grained neuronal network models can describe network firing rates using the average membrane potential alone [13–25], or they can also take into account its fluctuations [26–29]. The latter models are applicable to networks in which neuronal firing occurs solely due to membrane potential fluctuations while the average membrane potential stays below the firing threshold [30–36], as well as to those that operate in the mean-driven regime in which the slaving potential that drives the neurons to fire is consistently above the firing threshold. A particularly fruitful use of coarse-grained models is in combination with point-neuron models, forming so-called embedded networks [37]. Such models are especially appropriate for describing neuronal dynamics in the brain because of the many regular feature maps in the laminar structure of the cerebral cortex. The primary visual cortex alone has a number of neuronal preference maps, such as for orientation or spatial frequency, laid out in regular or irregular patterns [38–44]. Certain subpopulations which contain sufficiently many neurons, but are small enough that their response properties can be treated as constant across the subpopulation, may be replaced by coarse-grained patches, while other subpopulations may be represented by point neu-

rons embedded in this coarse-grained background.

In the simplest case of all-to-all coupled neuronal networks, the initial step is to use a nonequilibrium statistical physics framework and develop a Boltzmann-type kinetic equation for the network probability density function of the voltage and various conductances [26–29,45–57]. Since this is a partial differential equation in three or more dimensions, it is advantageous to further project the dynamics to one dimension and obtain a reduced kinetic theory in terms of the voltage alone. For purely excitatory networks, as well as networks with both excitatory and inhibitory neurons and both simple and complex cells, such a theory was developed in [28,29]. It achieves dimension reduction by means of a novel moment closure, which was shown to follow from the maximum-entropy principle [58]. Efficient numerical methods for solving the resulting set of kinetic equations were developed in [59].

The predominant excitatory neurotransmitter in the central nervous systems of vertebrates is glutamate, which binds to a number of different types of post-synaptic receptors [60]. Two main classes of glutamate-binding receptors are the AMPA and NMDA receptors. Activation of the AMPA receptors gives rise to fast post-synaptic conductance dynamics with decay times of about 3–8 ms, while the activation of the NMDA receptors gives rise to slow conductance dynamics with decay times of about 60–200 ms, respectively [61–64]. AMPA and NMDA receptors are frequently colocalized, such as in the rat visual cortex [65] and hippocampus [63,66] or in the superficial layers of cat V1 [67], and may thus respond to the same spikes. This colocalization of receptors with different time constants motivates the present study. We will examine its theoretical description in terms of a kinetic theory and investigate its dynamical consequences.

From the viewpoint of kinetic theory, an important aspect of neuronal networks with conductances activated by fast- and slow-acting receptors, colocalized on the same synapses, is the nature of the statistical correlations arising due to the two types of conductances being driven by (parts of) the same network spike train. Therefore, in this paper, we develop a kinetic theory for purely excitatory neuronal net-

works of this type. For simplicity, we derive this kinetic theory for a linear, conductance-driven, all-to-all-coupled, integrate-and-fire (IF) network of identical excitatory point neurons that incorporates synaptic failure [68–73]. Once we find an appropriate set of conductance variables, which are driven by disjoint spike trains, we can derive the kinetic equation as in [29] and use the maximum-entropy principle of [58] to suggest the appropriate closure that will achieve a reduction of independent variables to time and voltage alone. However, this closure is more general than that of [58] insofar as it involves using the dynamics of the conductance (co)variances computed from a set of ordinary differential equations. Adding inhibitory neurons and space dependence of the neuronal connections to the kinetic description developed in this paper is a straightforward application of the results in [28,29,58].

The paper is organized as follows. In Sec. II, we describe the equations for a linear IF excitatory neuronal network with a fast and slow conductance. In Sec. III, we introduce a set of conductance-variable changes such that the resulting conductances are driven by disjoint spike trains. In Sec. IV, we present the Boltzmann-like kinetic equation that describes statistically the dynamics of the membrane potential and these new conductance variables, develop a diffusion approximation for it, and recast it in terms of the voltage and the fast and slow conductances alone. In Sec. V, we impose the boundary conditions for the kinetic equation obtained in Sec. IV in terms of the voltage and conductance variables and describe how the resulting problem becomes nonlinear due to the simultaneous presence of the firing rate as a self-consistency parameter in the equation and the boundary conditions. In Sec. VI, we find an equivalent statistical description of the network dynamics in terms of an infinite hierarchy of equations for the conditional conductance moments, in which the independent variables are the time and membrane potential alone. In Sec. VII we describe the maximum-entropy principle which we use to guide us in discovering an appropriate closure for the infinite hierarchy of equations from Sec. VI. In Sec. VIII, we discuss the dynamics of the conductance moments and (co)variances used in the closure and also their role in determining the validity of the conductance boundary conditions imposed in Sec. V. In Sec. IX we postulate the closure and derive three closed kinetic equations for the voltage probability density and the first conditional conductance moments as functions of time and membrane potential. We also derive the boundary conditions for these equations. In Sec. X we consider the limit in which the decay rate of the fast conductance becomes infinitely fast and the additional limit in which the decay rate of the slow conductance becomes infinitely slow. In Sec. XI, we present conclusions and discuss the agreement of our kinetic theory with direct, full numerical simulations of the corresponding IF model.

II. INTEGRATE-AND-FIRE NEURONAL NETWORK WITH FAST AND SLOW EXCITATORY CONDUCTANCES

The kinetic theory we develop in this paper describes statistically the dynamics exhibited by linear, IF networks composed of excitatory point neurons with two types of post-synaptic conductances: one mediated by a fast and another by a slow receptor channel. In a network of N identical, excitatory point neurons, the membrane potential of the ith neuron is governed by the equation

$$\frac{d}{dt}V_i = -\left(\frac{V_i - \varepsilon_r}{\tau}\right) - G_i(t)\left(\frac{V_i - \varepsilon_E}{\tau}\right), \qquad (1)$$

where τ is the leakage time constant, ε_r is the reset potential, ε_E is the excitatory reversal potential, and $G_i(t)$ is the neuron's total conductance. The voltage V_i evolves according to Eq. (1) as long as it stays below the firing threshold V_T. When V_i reaches V_T, the neuron fires a spike and V_i is reset to the value ε_r. In the absence of a refractory period, the dynamics of V_i then immediately becomes governed by Eq. (1) again.

The total conductance $G_i(t)$ of the ith neuron in the network (1) is expressed as the sum

$$G_i(t) = \lambda G_i^A(t) + (1-\lambda)G_i^N(t)$$
$$= \lambda G_i^f(t) + \lambda G_i^{(1)}(t) + (1-\lambda)G_i^{(2)}(t), \qquad (2a)$$

in which

$$G_i^A(t) = G_i^f(t) + G_i^{(1)}(t) \quad \text{and} \quad G_i^N(t) = G_i^{(2)}(t) \qquad (2b)$$

are the fast and slow conductances, respectively. The conductances $G_i^{(1)}(t)$ and $G_i^{(2)}(t)$ arise from the spikes mediated by the synaptic coupling among pairs of neurons within the network, while $G_i^f(t)$ is the conductance driven by the external stimuli. The parameter λ denotes the percentage of fast receptor contribution to the total conductance $G_i(t)$ [74–76].

If the coupling for the network (1) is assumed to be all-to-all, the conductances in (2b) can be modeled by the equations

$$\sigma_1 \frac{d}{dt}G_i^f = -G_i^f + f\sum_\mu \delta(t - t_{i\mu}), \qquad (3a)$$

$$\sigma_1 \frac{d}{dt}G_i^{(1)} = -G_i^{(1)} + \frac{\bar{S}}{Np}\sum_{k\neq i}\sum_l p_{kl}^{(1)}\delta(t - t_{kl}), \qquad (3b)$$

$$\sigma_2 \frac{d}{dt}G_i^{(2)} = -G_i^{(2)} + \frac{\bar{S}}{Np}\sum_{k\neq i}\sum_l p_{kl}^{(2)}\delta(t - t_{kl}), \qquad (3c)$$

where we have assumed that the rising time scales of the conductances are infinitely fast. In Eqs. (3a)–(3c), $\delta(\cdots)$ is the Dirac delta function, σ_1 and σ_2 are the time constants of the fast and slow synapses, f is the synaptic strength of the external inputs, and $\bar{S}$ is the network synaptic strength. The δ functions on the right-hand sides of (3a)–(3c) describe the spike trains arriving at the neuron in question. In particular, the time $t_{i\mu}$ is that of the μth external input spike delivered to the ith neuron and t_{kl} is the lth spike time of the kth neuron in network. Note that the network neuron spikes $\{t_{kl}\}$ are common to $G_i^{(1)}$ and $G_i^{(2)}$ due to the all-to-all nature of the network couplings.

The coefficients $p_{kl}^{(1)}$ and $p_{kl}^{(2)}$ in Eqs. (3b) and (3c) model the stochastic nature of the synaptic release [68–73]. Each

$p_{kl}^{(i)}$, $i=1,2$, is taken to be an independent Bernoulli-distributed stochastic variable upon receiving a spike at the time t_{kl}; i.e., $p_{kl}^{(i)}=1$ with probability p and 0 with probability $1-p$, where p is the synaptic release probability. The stochastic nature of the synaptic release will play an important role in the next two sections in helping us determine the appropriate conductance variables, which are driven by disjoint spike trains and can be used in deriving the correct Boltzmann-like kinetic equation. Moreover, synaptic noise often appears to be the dominant noise source in neuronal network dynamics [77–79]. Other types of neuronal noise, such as thermal [78] and channel noise [79,80], can also be incorporated in the kinetic theory developed here or the kinetic theory with only fast excitatory conductances, developed in [28,29,58].

In the remainder of the paper, we assume that the train of the external input spiking times $t_{i\mu}$ is a realization of a Poisson process with rate $\nu_0(t)$. While it need not be true that the spike times of an individual neuron, t_{ki} with a fixed i, are Poisson distributed, all the network spiking times t_{kl} can be considered as Poisson distributed with the rate $Nm(t)$ when the number of neurons, N, in the network is sufficiently large, the firing rate per neuron is small, and each neuronal firing event is independent of all the others [81]. This Poisson approximation for the spike trains arriving at each neuron in the network is used in deriving the kinetic equation. The division of the spiking terms in Eqs. (3b) and (3c) by the number of neurons, N, provides for a well-defined network coupling in the large-network limit $N\rightarrow\infty$.

III. CONDUCTANCES DRIVEN BY DISJOINT SPIKE TRAINS

The fact that two different sets of conductances with distinct time constants are driven by spikes belonging to the same spike train prevents us from being able to derive a kinetic representation of the neuronal network in the present case by using a straightforward generalization of the results in [28,29,58]. Therefore we must take advantage of the stochastic nature of the synaptic release and first introduce a set of conductance variables which are all driven by disjoint spike trains. We find this set in two steps.

As a first step, we introduce four auxiliary conductance variables $X_i^{(1)}$, $X_i^{(2)}$, $Y_i^{(1)}$, and $Y_i^{(2)}$, which obey the dynamics

$$\sigma_1 \frac{d}{dt}X_i^{(1)} = -X_i^{(1)} + \frac{\bar{S}}{Np}\sum_{k\neq i}\sum_l p_{kl}^{(1)}p_{kl}^{(2)}\delta(t-t_{kl}), \quad (4a)$$

$$\sigma_1 \frac{d}{dt}X_i^{(2)} = -X_i^{(2)} + \frac{\bar{S}}{Np}\sum_{k\neq i}\sum_l p_{kl}^{(1)}(1-p_{kl}^{(2)})\delta(t-t_{kl}), \quad (4b)$$

$$\sigma_2 \frac{d}{dt}Y_i^{(1)} = -Y_i^{(1)} + \frac{\bar{S}}{Np}\sum_{k\neq i}\sum_l p_{kl}^{(1)}p_{kl}^{(2)}\delta(t-t_{kl}), \quad (4c)$$

$$\sigma_2 \frac{d}{dt}Y_i^{(2)} = -Y_i^{(2)} + \frac{\bar{S}}{Np}\sum_{k\neq i}\sum_l p_{kl}^{(2)}(1-p_{kl}^{(1)})\delta(t-t_{kl}). \quad (4d)$$

We have chosen these variables so that the dynamics of $X_i^{(1)}$ and $Y_i^{(1)}$ is driven by the synaptic release on both the fast and slow receptors simultaneously, $X_i^{(2)}$ is driven by the release on the fast receptors without release on the slow receptors, and $Y_i^{(2)}$ is driven by the release on the slow receptors without release on the fast receptors.

By adding the pairs of Eqs. (4a), (4b) and (4c), (4d), respectively, we find that $G_i^{(1)}=X_i^{(1)}+X_i^{(2)}$ and $G_i^{(2)}=Y_i^{(1)}+Y_i^{(2)}$ satisfy Eqs. (3b) and (3c). From Eqs. (4a) and (4c), we likewise compute that the conductance $A_i=\sigma_1 X_i^{(1)}+\sigma_2 Y_i^{(1)}$ is driven by the synaptic release on both the fast and slow receptors simultaneously, while $B_i=\sigma_1 X_i^{(1)}-\sigma_2 Y_i^{(1)}$ receives no synaptic driving at all. From Eqs. (1), (3a), (4b), and (4d), we thus finally collect a set of equations in which all the conductance variables have been chosen so that they are driven by disjoint spike trains. This set is

$$\frac{d}{dt}V_i = -\left(\frac{V_i-\varepsilon_r}{\tau}\right) - G_i(t)\left(\frac{V_i-\varepsilon_E}{\tau}\right), \quad (5a)$$

$$\sigma_1 \frac{d}{dt}G_i^f = -G_i^f + f\sum_{\mu}\delta(t-t_{i\mu}), \quad (5b)$$

$$\frac{d}{dt}A_i = -\frac{1}{\sigma_+}A_i - \frac{1}{\sigma_-}B_i + \frac{2\bar{S}}{Np}\sum_{k\neq i}\sum_l p_{kl}^{(1)}p_{kl}^{(2)}\delta(t-t_{kl}), \quad (5c)$$

$$\frac{d}{dt}B_i = -\frac{1}{\sigma_+}B_i - \frac{1}{\sigma_-}A_i, \quad (5d)$$

$$\sigma_1 \frac{d}{dt}X_i^{(2)} = -X_i^{(2)} + \frac{\bar{S}}{Np}\sum_{k\neq i}\sum_l p_{kl}^{(1)}(1-p_{kl}^{(2)})\delta(t-t_{kl}), \quad (5e)$$

$$\sigma_2 \frac{d}{dt}Y_i^{(2)} = -Y_i^{(2)} + \frac{\bar{S}}{Np}\sum_{k\neq i}\sum_l p_{kl}^{(2)}(1-p_{kl}^{(1)})\delta(t-t_{kl}), \quad (5f)$$

with the total conductance G_i given by

$$G_i(t) = \lambda G_i^f(t) + \lambda_+ A_i + \lambda_- B_i + \lambda X_i^{(2)} + (1-\lambda)Y_i^{(2)}. \quad (5g)$$

In Eqs. (5a)–(5g), the constants $\sigma_\pm$ and $\lambda_\pm$ are

$$\sigma_+ = \frac{2\sigma_1\sigma_2}{\sigma_2+\sigma_1}, \quad \sigma_- = \frac{2\sigma_1\sigma_2}{\sigma_2-\sigma_1} \quad (6)$$

and

$$\lambda_+ = \frac{1}{2}\left(\frac{\lambda}{\sigma_1} + \frac{1-\lambda}{\sigma_2}\right), \quad \lambda_- = \frac{1}{2}\left(\frac{\lambda}{\sigma_1} - \frac{1-\lambda}{\sigma_2}\right), \qquad (7)$$

respectively. In other words, the conductances G_i^f, A_i, $X_i^{(2)}$, and $Y_i^{(2)}$ in Eqs. (5a)–(5g) jump in a mutually exclusive fashion in that no two of them can jump as the result of the same spike.

In what is to follow, we still treat the spike trains that drive the conductance variables G_i^f, A_i, $X_i^{(2)}$, and $Y_i^{(2)}$ in Eqs. (5a)–(5g) as Poisson for the same reason as explained at the end of Sec. II.

IV. KINETIC EQUATION

To arrive at a statistical description of the neuronal network dynamics, we begin by considering the probability density

$$\rho \equiv \rho(v, g_f, \eta, \zeta, x_2, y_2, t)$$
$$= \mathbb{E}\left[\frac{1}{N}\sum_i \delta(v - V_i(t))\delta(g_f - G_i^f(t))\delta(\eta - A_i(t))\right.$$
$$\left.\times \delta(\zeta - B_i(t))\delta(x_2 - X_i^{(2)}(t))\delta(y_2 - Y_i^{(2)}(t))\right] \qquad (8)$$

for the voltage and the conductance variables in Eqs. (5a)–(5g). Here $\mathbb{E}$ represents the expectation over all possible realizations of the Poisson spike trains and initial conditions. An argument nearly identical to that presented in Appendix B of [29] shows that the evolution of the probability density $\rho(v, g_f, \eta, \zeta, x_2, y_2)$ for the voltages and conductances evolving according to Eqs. (5a)–(5g) is described by the kinetic equation

$$\frac{\partial \rho}{\partial t} = \frac{\partial}{\partial v}\left\{\left[\left(\frac{v-\varepsilon_r}{\tau}\right) + [\lambda g_f + \lambda_+ \eta + \lambda_- \zeta + \lambda x_2 + (1-\lambda)y_2]\left(\frac{v-\varepsilon_E}{\tau}\right)\right]\rho\right\} + \frac{\partial}{\partial g_f}\left[\frac{g_f}{\sigma_1}\rho\right] + \nu_0(t)\left[\rho\left(v, g_f - \frac{f}{\sigma_1}, \eta, \zeta, x_2, y_2\right)\right.$$
$$\left. - \rho(v, g_f, \eta, \zeta, x_2, y_2)\right] + \frac{\partial}{\partial \eta}\left[\left(\frac{1}{\sigma_+}\eta + \frac{1}{\sigma_-}\zeta\right)\rho\right] + m(t)p^2N\left[\rho\left(v, g_f, \eta - \frac{2\bar{S}}{Np}, \zeta, x_2, y_2\right) - \rho(v, g_f, \eta, \zeta, x_2, y_2)\right]$$
$$+ \frac{\partial}{\partial \zeta}\left[\left(\frac{1}{\sigma_+}\zeta + \frac{1}{\sigma_-}\eta\right)\rho\right] + \frac{\partial}{\partial x_2}\left[\frac{x_2}{\sigma_1}\rho\right] + m(t)p(1-p)N\left[\rho\left(v, g_f, \eta, \zeta, x_2 - \frac{\bar{S}}{Np\sigma_1}, y_2\right) - \rho(v, g_f, \eta, \zeta, x_2, y_2)\right] + \frac{\partial}{\partial y_2}\left[\frac{y_2}{\sigma_2}\rho\right]$$
$$+ m(t)p(1-p)N\left[\rho\left(v, g_f, \eta, \zeta, x_2, y_2 - \frac{\bar{S}}{Np\sigma_2}\right) - \rho(v, g_f, \eta, \zeta, x_2, y_2)\right]. \qquad (9)$$

Here, $\nu_0(t)$ is the Poisson spiking rate of the external input and $m(t)$ is the network firing rate normalized by the number of neurons, N. This normalization is used to prevent $m(t)$ from increasing without bounds in the large-N limit. Equivalently, the firing rate $m(t)$ is the population-averaged firing rate per neuron in the network.

We here give a brief, intuitive description of the derivation process leading from the dynamical equations (5a)–(5g) to the kinetic equation (9). To this end, we consider the dynamics of a neuron in the time interval $(t, t+\Delta t)$ and analyze the conditional expectations for the values of the voltage $V_i(t+\Delta t)$ and conductances $G_i^f(t+\Delta t)$, $A_i(t+\Delta t)$, $B_i(t+\Delta t)$, $X_i^{(2)}(t+\Delta t)$, and $Y_i^{(2)}(t+\Delta t)$ at time $t+\Delta t$, given their values $V_i(t)$, $G_i^f(t)$, $A_i(t)$, $B_i(t)$, $X_i^{(2)}(t)$, and $Y_i^{(2)}(t)$ at time t. If the time increment Δt is chosen to be sufficiently small, at most one spike can arrive at this neuron with nonzero probability during the interval $(t, t+\Delta t)$. Five different, mutually exclusive events can take place during this time-interval. The first event is that either no spike arrives at the neuron or else a spike arrives, but activates none of the conductances because of synaptic failure. This event occurs with probability $[1-\nu_0(t)\Delta t][1-p^2m(t)N\Delta t][1-p(1-p)m(t)N\Delta t]^2 + O(\Delta t^2)$ $=1-[\nu_0(t)+(2p-p^2)m(t)N]\Delta t + O(\Delta t^2)$. The neuron's

dynamics is then governed by the smooth (streaming) terms in Eqs. (5a)–(5g). The other four events consist of an external input or network spike arriving and activating one of the conductances G_i^f, A_i, $X_i^{(2)}$, or $Y_i^{(2)}$, with the respective probabilities $\nu_0(t)\Delta t + O(\Delta t^2)$, $p^2m(t)N\Delta t + O(\Delta t^2)$, and $p(1-p)m(t)N\Delta t + O(\Delta t^2)$ for the last two possible events. Due to our variable choice, no two of these conductances can be activated simultaneously. The corresponding conductance jumps are f/σ_1, $2\bar{S}/Np$, $\bar{S}/\sigma_1 Np$, and $\bar{S}/\sigma_2 Np$, respectively. This argument lets us compute the single-neuron conditional probability density function at time $t+\Delta t$. We then average over all possible values of $V_i(t)$, $G_i^f(t)$, $A_i(t)$, $B_i(t)$, $X_i^{(2)}(t)$, and $Y_i^{(2)}(t)$, as well as all neurons, initial conditions, and possible spike trains. This leads to the right-hand side of the kinetic equation (9) being the coefficient multiplying Δt in the Δt expansion of the density $\rho(v, g_f, \eta, \zeta, x_2, y_2, t+\Delta t)$, which implies (9). The details of the calculation are similar to those given in Appendix B of [29].

Assuming the conductance jump values f/σ_1, $\bar{S}/Np$, $\bar{S}/Np\sigma_1$, and $\bar{S}/Np\sigma_2$ to be small, we Taylor-expand the difference terms in (9) and thus obtain the diffusion approximation to the kinetic equation (9), given by

$$\frac{\partial}{\partial t}\rho = \frac{\partial}{\partial v}\left\{\left[\left(\frac{v-\varepsilon_r}{\tau}\right)+[\lambda g_f+\lambda_+\eta+\lambda_-\zeta+\lambda x_2+(1-\lambda)y_2]\left(\frac{v-\varepsilon_E}{\tau}\right)\right]\rho\right\}+\frac{\partial}{\partial g_f}\left\{\left[\frac{1}{\sigma_1}(g_f-\bar{g})\right]\rho\right\}+\frac{\sigma_f^2}{\sigma_1^2}\frac{\partial^2\rho}{\partial g_f^2}$$

$$+\frac{\partial}{\partial\eta}\left\{\left[\frac{1}{\sigma_+}(\eta-\bar\eta)+\frac{1}{\sigma_-}\zeta\right]\rho\right\}+4p^2\bar\sigma^2\frac{\partial^2\rho}{\partial\eta^2}+\frac{\partial}{\partial\zeta}\left\{\left(\frac{1}{\sigma_+}\zeta+\frac{1}{\sigma_-}\eta\right)\rho\right\}+\frac{\partial}{\partial x_2}\left\{\left[\frac{1}{\sigma_1}(x_2-\bar{x}_2)\right]\rho\right\}+p(1-p)\frac{\bar\sigma^2}{\sigma_1^2}\frac{\partial^2\rho}{\partial x_2^2}$$

$$+\frac{\partial}{\partial y_2}\left\{\left[\frac{1}{\sigma_2}(y_2-\bar{y}_2)\right]\rho\right\}+p(1-p)\frac{\bar\sigma^2}{\sigma_2^2}\frac{\partial^2\rho}{\partial y_2^2}. \tag{10}$$

In this equation the (time-dependent) coefficients are

$$\bar{g}(t)=f\nu_0(t),\quad \sigma_f^2(t)=\frac{1}{2}f^2\nu_0(t),$$

$$\bar\eta(t)=2\sigma_+p\bar{S}m(t),\quad \bar\sigma^2(t)=\frac{\bar{S}^2}{2Np^2}m(t),$$

$$\bar{x}_2(t)=\bar{y}_2(t)=(1-p)\bar{S}m(t), \tag{11}$$

with $\sigma_\pm$ and $\lambda_\pm$ as defined in (6) and (7), respectively.

We now reverse the conductance variable changes performed in Sec. III, used to derive Eqs. (5a)–(5g), in order to derive a kinetic equation (in the diffusion approximation) for the time evolution of the probability density function involving only the voltage v and the fast and slow conductances g_A and g_N, respectively: $\rho\equiv\rho(v,g_A,g_N)$. This kinetic equation is

$$\frac{\partial}{\partial t}\rho=\frac{\partial}{\partial v}\left\{\left[\left(\frac{v-\varepsilon_r}{\tau}\right)+[\lambda g_A+(1-\lambda)g_N]\left(\frac{v-\varepsilon_E}{\tau}\right)\right]\rho\right\}$$

$$+\frac{1}{\sigma_1}\frac{\partial}{\partial g_A}\{[g_A-\bar{g}_A(t)]\rho\}+\frac{1}{\sigma_2}\frac{\partial}{\partial g_N}\{[g_N-\bar{g}_N(t)]\rho\}$$

$$+\frac{\sigma_A^2}{\sigma_1^2}\frac{\partial^2\rho}{\partial g_A^2}+\frac{2p\sigma_0^2}{\sigma_1\sigma_2}\frac{\partial^2\rho}{\partial g_A\,\partial g_N}+\frac{\sigma_0^2}{\sigma_2^2}\frac{\partial^2\rho}{\partial g_N^2}, \tag{12}$$

with

$$\bar{g}_A(t)=f\nu_0(t)+\bar{S}m(t),\quad \bar{g}_N(t)=\bar{S}m(t),$$

$$\sigma_A^2(t)=\frac{1}{2}f^2\nu_0(t)+\sigma_0^2(t),\quad \sigma_0^2(t)=\frac{\bar{S}^2}{2Np}m(t). \tag{13}$$

Note that the cross-derivative term in the last line of the kinetic equation (12) is due to the correlation between the jumps in fast and slow conductances G^A and G^N when both synaptic releases occur with probability p^2. Had we treated the spike trains in Eqs. (3b) and (3c) as if they were distinct, this cross term would be missing.

V. BOUNDARY CONDITIONS IN TERMS OF VOLTAGE AND CONDUCTANCES

The first term in Eq. (12) is the derivative of the probability flux in the voltage direction:

$$J_V(v,g_A,g_N,t)=-\left[\left(\frac{v-\varepsilon_r}{\tau}\right)+[\lambda g_A+(1-\lambda)g_N]\right.$$

$$\left.\times\left(\frac{v-\varepsilon_E}{\tau}\right)\right]\rho(v,g_A,g_N,t). \tag{14}$$

Since we have assumed that the neurons in the network (1) and (3a)–(3c) have no refractory period, a neuron's voltage is reset to ε_r as soon as it crosses the threshold value V_T, before any change to the neuron's conductance can occur. This implies the voltage-flux boundary condition

$$J_V(V_T,g_A,g_N,t)=J_V(\varepsilon_r,g_A,g_N,t). \tag{15}$$

With the conductance boundary conditions, we must proceed a bit more cautiously. Specifically, in the IF system (1) and (3a)–(3c), the spike-induced jumps in the conductances are positive. In conjunction with the form of Eqs. (3a)–(3c), this fact implies that a neuron's conductances G_i^A and G_i^N must always be positive and that there cannot be any conductance flux across the boundary of the first quadrant in the (G_i^A,G_i^N) conductance plane in either direction. One would therefore expect the probability density $\rho(v,g_A,g_n,t)$ to be nonzero only when $g_A>0$ and $g_N>0$ as a result of the natural conductance dynamics, and not as a result of any boundary conditions.

The approximation leading from the difference equation (9) to the diffusion equation (10), however, replaces the conductance jumps by a transport and a diffusion term, and one should expect that this combination of terms may imply some, at least local, downward conductance flux even across the half-rays $g_A=0$, $g_N>0$ and $g_N=0$, $g_A>0$. Therefore, a no-flux boundary condition across these two half-rays would have to be enforced, essentially artificially, as part of the diffusion approximation. In addition, due to the cross-derivative term in Eq. (12), the individual conductance fluxes cannot be defined uniquely in the (g_A,g_N) conductance variables, but only in the transformed conductance variables in which the second-order-derivative terms in (12) become diagonalized. Employing such a transformation, taking the dot product of the flux vector with the appropriate normal, and then transforming that expression back in the (g_A,g_N) conductance variables would make the already somewhat artificial no-flux boundary conditions also extremely unwieldy to compute.

Alternatively, in Eq. (12), we allow for the probability density $\rho(v,g_A,g_N,t)$ to be a non-negative function everywhere and take instead the smallness of $\rho(v,g_A,g_N,t)$ for

$g_A \leq 0$ or $g_N \leq 0$ as part of the diffusion approximation; its loss may limit the temporal validity range of this approximation. The boundary conditions that we assume for the conductances in the solution of Eq. (12) are thus simply that no neuron have infinitely large or small conductances—that is,

$$\rho(v, g_A \rightarrow \pm\infty, g_N, t) \rightarrow 0,$$

$$\rho(v, g_A, g_N \rightarrow \pm\infty, t) \rightarrow 0, \qquad (16)$$

sufficiently rapidly, together with all its derivatives.

As a parenthetical remark, we should point out that, technically, the adoption of the approximate boundary conditions (16) is also advantageous in eliminating unwanted boundary terms from the conductance-moment equations to be derived in Secs. VI and VIII, and thus significantly simplifying the resulting reduced kinetic theory. In Sec. VIII we will also present a conductance-moment-based validity criterion for the approximation made in adopting the conditions (16).

The population-averaged firing rate per neuron, $m(t)$, is the total voltage flux (14) across the firing threshold V_T that includes all values of the conductances and is thus given by the integral

$$m(t) = \int \int_{-\infty}^{\infty} J_V(V_T, g_A, g_N, t) dg_A dg_N. \qquad (17)$$

Note that this firing rate feeds into the definitions (13) for the parameters in the kinetic equation (12).

Equation (12), boundary conditions (15) and (16), and the expression for the firing rate, Eq. (17), which reenters Eq. (12) as a self-consistency parameter via Eqs. (13), provide a complete statistical description (in the diffusion approximation) of the dynamics taking place in the neuronal network (1) and (3a)–(3c). The simultaneous occurrence of the firing rate $m(t)$ in both Eq. (12) and the integral (17) of the voltage boundary condition makes this description highly nonlinear. Solving a nonlinear problem involving a partial differential equation in four dimensions is a formidable task, and it is therefore important to reduce the dimensionality of the problem to 2 by eliminating the explicit dependence on the conductances from the description. We describe this reduction process in the subsequent sections.

VI. HIERARCHY OF MOMENTS

In this section, we derive a description of the dynamics in terms of functions of voltage alone. In other words, we seek to describe the evolution of the voltage probability density

$$\varrho(v, t) = \int \int_{-\infty}^{\infty} \rho(v, g_A, g_N, t) dg_A dg_N \qquad (18)$$

and the conditional moments

$$\mu_{r,s}(v) = \int \int_{-\infty}^{\infty} g_A^r g_N^s \rho(g_A, g_N|v) dg_A dg_N, \qquad (19)$$

where the conditional density $\rho(g_A, g_N|v)$ is defined by the equation

$$\rho(v, g_A, g_N, t) = \varrho(v, t)\rho(g_A, g_N, t|v). \qquad (20)$$

We derive a hierarchy of equations for the conditional moments (19), for which we will subsequently devise an approximate closure via the maximal entropy principle. For clarity of exposition, we rename

$$\mu_A(v) \equiv \mu_{1,0}(v), \quad \mu_N(v) \equiv \mu_{0,1}(v), \qquad (21a)$$

$$\mu_A^{(2)}(v) \equiv \mu_{2,0}(v), \quad \mu_N^{(2)}(v) \equiv \mu_{0,2}(v), \quad \mu_{AN}^{(2)}(v) \equiv \mu_{1,1}(v). \qquad (21b)$$

In order to obtain the equations that describe the dynamics of the conditional moments (19), we begin by, for any given function $f(v, g_A, g_N, t)$, using Eq. (12) to derive an equation for the evolution of this function's projection onto the v space alone. We multiply (12) by $f(v, g_A, g_N, t)$ and integrate over the conductance variables. Integrating by parts and taking into account the boundary conditions (16) stating that ρ must vanish together with all its derivatives at $g_A \rightarrow \pm\infty$ and $g_N \rightarrow \pm\infty$, faster than any power of g_A or g_N, we thus arrive at the equation

$$\frac{\partial}{\partial t} \int \int_{-\infty}^{\infty} f\rho \, dg_A dg_N + \frac{\partial}{\partial v} \int \int_{-\infty}^{\infty} f J_V \, dg_A dg_N$$

$$= \int \int_{-\infty}^{\infty} \frac{\partial f}{\partial t} \rho \, dg_A dg_N + \int \int_{-\infty}^{\infty} \frac{\partial f}{\partial v} J_V \, dg_A dg_N$$

$$- \int \int_{-\infty}^{\infty} \frac{(g - \bar{g}_A)}{\sigma_1} \frac{\partial f}{\partial g_A} \rho \, dg_A dg_N$$

$$- \int \int_{-\infty}^{\infty} \frac{(g - \bar{g}_N)}{\sigma_2} \frac{\partial f}{\partial g_N} \rho \, dg_A dg_N$$

$$+ \int \int_{-\infty}^{\infty} \frac{\sigma_A^2}{\sigma_1^2} \frac{\partial^2 f}{\partial g_A^2} \rho \, dg_A dg_N$$

$$+ \int \int_{-\infty}^{\infty} \frac{2p\sigma_0^2}{\sigma_1 \sigma_2} \frac{\partial^2 f}{\partial g_A \, \partial g_N} \rho \, dg_A dg_N$$

$$+ \int \int_{-\infty}^{\infty} \frac{\sigma_0^2}{\sigma_2^2} \frac{\partial^2 f}{\partial g_N^2} \rho \, dg_A dg_N. \qquad (22)$$

Letting $f = g_A^r g_N^s$ in (22), with $r, s = 0, 1, 2, \ldots$, and using (14), we now derive a set of equations for the moments

$$\int \int_{-\infty}^{\infty} g_A^r g_N^s \rho(v, g_A, g_N) dg_A dg_N = \varrho(v)\mu_{r,s}(v). \qquad (23)$$

These equations read

$$\frac{\partial}{\partial t}\varrho - \frac{\partial}{\partial v}\left\{\left[\left(\frac{v - \varepsilon_r}{\tau}\right) + \left(\frac{v - \varepsilon_E}{\tau}\right)[\lambda\mu_A + (1-\lambda)\mu_N]\right]\varrho\right\} = 0, \qquad (24a)$$

$$\frac{\partial}{\partial t}(\varrho\mu_A) - \frac{\partial}{\partial v}\left\{\left[\left(\frac{v-\varepsilon_r}{\tau}\right)\mu_A + \left(\frac{v-\varepsilon_E}{\tau}\right)[\lambda\mu_A^{(2)}\right.\right.$$
$$\left.\left.+ (1-\lambda)\mu_{AN}^{(2)}]\right]\varrho\right\} = -\frac{1}{\sigma_1}(\mu_A - \bar{g}_A)\varrho, \qquad (24b)$$

$$\frac{\partial}{\partial t}(\varrho\mu_N) - \frac{\partial}{\partial v}\left\{\left[\left(\frac{v-\varepsilon_r}{\tau}\right)\mu_N + \left(\frac{v-\varepsilon_E}{\tau}\right)[\lambda\mu_{AN}^{(2)}\right.\right.$$
$$\left.\left.+ (1-\lambda)\mu_N^{(2)}]\right]\varrho\right\} = -\frac{1}{\sigma_2}(\mu_N - \bar{g}_N)\varrho, \qquad (24c)$$

and, for $r+s \geq 2$,

$$\frac{\partial}{\partial t}(\varrho\mu_{r,s}) - \frac{\partial}{\partial v}\left\{\left[\left(\frac{v-\varepsilon_r}{\tau}\right)\mu_{r,s} + \left(\frac{v-\varepsilon_E}{\tau}\right)[\lambda\mu_{r+1,s}\right.\right.$$
$$\left.\left.+ (1-\lambda)\mu_{r,s+1}]\right]\varrho\right\} = \left[-\frac{r}{\sigma_1}(\mu_{r,s} - \bar{g}_A\mu_{r-1,s})\right.$$
$$-\frac{s}{\sigma_2}(\mu_{r,s} - \bar{g}_N\mu_{r,s-1}) + \frac{\sigma_A^2}{\sigma_1^2}r(r-1)\mu_{r-2,s}$$
$$\left.+ \frac{2p\sigma_0^2}{\sigma_1\sigma_2}rs\mu_{r-1,s-1} + \frac{\sigma_0^2}{\sigma_2^2}s(s-1)\mu_{r,s-2}\right]\varrho, \qquad (24d)$$

where two zero subscripts in any of the moments should be interpreted as making this moment unity and a negative subscript as making it zero. Equations (24a)–(24d) indeed form an infinite hierarchy, which needs to be closed at a finite order if we are to simplify the problem by eliminating the dependence on the conductances.

Noting the form of the voltage-derivative terms in (22) and using the voltage boundary condition (15) and the flux definition (14), we find the boundary conditions

$$\left[\left(\frac{V_T-\varepsilon_r}{\tau}\right)\mu_{r,s}(V_T) + \left(\frac{V_T-\varepsilon_E}{\tau}\right)[\lambda\mu_{r+1,s}(V_T)\right.$$
$$+ (1-\lambda)\mu_{r,s+1}(V_T)]\left.\right]\varrho(V_T) - \left(\frac{\varepsilon_r-\varepsilon_E}{\tau}\right)[\lambda\mu_{r+1,s}(\varepsilon_r)$$
$$+ (1-\lambda)\mu_{r,s+1}(\varepsilon_r)]\varrho(\varepsilon_r) = 0. \qquad (25)$$

VII. MAXIMUM-ENTROPY PRINCIPLE

When the Poisson rate ν_0 of the external input is independent of time, Eq. (12) possesses an invariant Gaussian solution $\rho_0(g_A, g_N)$ given by the formula

$$\rho_0(g_A, g_N) = \frac{\sqrt{\det M}}{\pi}e^{-(g-\bar{g})\cdot M(g-\bar{g})}, \qquad (26)$$

where

$$M = \begin{pmatrix} \alpha & \beta \\ \beta & \gamma \end{pmatrix}, \quad g = \begin{pmatrix} g_A \\ g_N \end{pmatrix}, \quad \bar{g} = \begin{pmatrix} \bar{g}_A(t) \\ \bar{g}_N(t) \end{pmatrix}, \qquad (27)$$

$$\alpha = \frac{\sigma_1(\sigma_1+\sigma_2)^2}{2D}, \quad \beta = \frac{p\sigma_1\sigma_2(\sigma_1+\sigma_2)}{D}, \qquad (28a)$$

$$\gamma = \frac{\sigma_A^2}{\sigma_0^2}\frac{\sigma_2(\sigma_1+\sigma_2)^2}{2D} \qquad (28b)$$

and

$$D = \sigma_A^2(\sigma_1+\sigma_2)^2 - 4p^2\sigma_0^2\sigma_1\sigma_2. \qquad (28c)$$

From (13), we see that $\sigma_A^2 > \sigma_0^2$, and since $0 < p \leq 1$, it is clear that $D > 0$. We also calculate that $\det M = \alpha\gamma - \beta^2 = \sigma_1\sigma_2(\sigma_1+\sigma_2)^2/4D\sigma_0^2 > 0$, where the inequality holds because all the factors are positive. The inequalities $\det M > 0$ and $\alpha > 0$, which follow from (28a)–(28c), imply that the matrix M is positive definite. The solution (26) is normalized to unity over the (g_A, g_N) space; its normalization over the (v, g_A, g_N) space would be $V_T - \varepsilon_r$.

Using the equilibrium solution $\rho_0(g_A, g_N)$ in (26), we now formulate the maximal entropy principle, which will guide us in determining the correct closure conditions for the hierarchy (24a)–(24d). According to this principle, we seek the density function $\hat{\rho}(v, g_A, g_N, t)$ which maximizes the entropy

$$S[\rho, \rho_0](v,t) = -\int\int_{-\infty}^{\infty}\ln\frac{\rho(v, g_A, g_N, t)}{\rho_0(g_A, g_N)}\rho(v, g_A, g_N, t)dg_A dg_N, \qquad (29)$$

subject to three constraints: (18), and also (23) with $r=1$ and $s=0$, and (23) with $r=0$ and $s=1$, which are

$$\int\int_{-\infty}^{\infty}g_A\rho(v, g_A, g_N)dg_A dg_N = \varrho(v)\mu_A(v),$$

$$\int\int_{-\infty}^{\infty}g_N\rho(v, g_A, g_N)dg_A dg_N = \varrho(v)\mu_N(v). \qquad (30)$$

Applying Lagrange multipliers to maximizing the entropy (29) under the constraints (18) and (30), we find for the maximizing density function $\hat{\rho}(v, g_A, g_N)$ to have the form

$$\hat{\rho}(v, g_A, g_N) = \rho_0(g_A, g_N)\exp[a_0(v) + a_A(v)g_A + a_N(v)g_N], \qquad (31)$$

where the multipliers $a_0(v)$, $a_A(v)$, and $a_N(v)$ are to be determined. Solving the constraints (18) and (30), we find

$$\hat{\rho}(v, g_A, g_N, t) = \frac{\sqrt{\det M}}{\pi}\varrho(v)e^{-(g-\mu)\cdot M(g-\mu)}, \qquad (32)$$

where $\mu = (\mu_A(v), \mu_N(v))^T$ is the vector of the first conditional moments, defined by (21a), (21b), and (19).

To find the relations between the first and second conditional moments of the probability density function $\hat{\rho}(v, g_A, g_N, t)$ in (32), which maximizes the entropy (29) under the constraints (18) and (30), we first put

$$x = g_A - \mu_A(v), \quad y = g_N - \mu_N(v). \qquad (33)$$

We then use the definition of the matrix M in (27) to rewrite the normalization of the function (26) in the form

$$\int \int_{-\infty}^{\infty} e^{-(\alpha x^2 + 2\beta xy + \gamma y^2)} dx\, dy = \frac{\pi}{\sqrt{\alpha\gamma - \beta^2}},$$

which we differentiate upon α, β, and γ, respectively, and from (32) obtain the expressions for the second moments of the conductances x and y in (33) with respect to the maximizing density $\hat{\rho}(v, g_A, g_N, t)$. Using (23) and (28a)–(28c), for the (co)variances

$$\Sigma_A^2(v) \equiv \mu_A^{(2)}(v) - [\mu_A(v)]^2,$$

$$C_{AN}(v) \equiv \mu_{AN}^{(2)}(v) - \mu_A(v)\mu_N(v),$$

$$\Sigma_N^2(v) \equiv \mu_N^{(2)}(v) - [\mu_N(v)]^2, \qquad (34)$$

we thus obtain the relations

$$\Sigma_A^2(v) = \frac{\gamma}{2(\alpha\gamma - \beta^2)} = \frac{\sigma_A^2}{\sigma_1},$$

$$C_{AN}(v) = -\frac{\beta}{(\alpha\gamma - \beta^2)} = \frac{2p\sigma_0^2}{\sigma_1 + \sigma_2},$$

$$\Sigma_N^2(v) = \frac{\alpha}{2(\alpha\gamma - \beta^2)} = \frac{\sigma_0^2}{\sigma_2}. \qquad (35)$$

Equations (34) and (35) furnish the expressions for the second-order conditional moments in term of the first-order conditional moments and amount to closure conditions based on the maximum-entropy principle. With the aid of these closure conditions we can close the hierarchy (24a)–(24d) at first order when the external-input and network firing rates are constant in time.

VIII. DYNAMICS OF CONDUCTANCE MOMENTS

More generally we seek the closure in terms of the moments

$$\langle g_A^r g_N^s \rangle = \int_{\varepsilon_r}^{V_T} \int \int_{-\infty}^{\infty} g_A^r g_N^s \rho(v, g_A, g_N) dv\, dg_A dg_N$$

$$= \int_{\varepsilon_r}^{V_T} \varrho(v)\mu_{r,s}(v) dv, \qquad (36)$$

with $0 \le r \le 2$, $0 \le s \le 2$, and $1 \le r+s \le 2$. These moments are the averages of the conditional moments $\mu_A(v)$ through $\mu_N^{(2)}(v)$ in (21a) and (21b) over the voltage distribution $\varrho(v)$. Integrating (24a)–(24d) over the voltage interval $\varepsilon_r < v < V_T$ and using the boundary conditions (25), we find for these moments the ordinary differential equations

$$\frac{d}{dt}\langle g_A \rangle = -\frac{1}{\sigma_1}[\langle g_A \rangle - \bar{g}_A(t)], \qquad (37a)$$

$$\frac{d}{dt}\langle g_N \rangle = -\frac{1}{\sigma_2}[\langle g_N \rangle - \bar{g}_N(t)], \qquad (37b)$$

$$\frac{d}{dt}\langle g_A^2 \rangle = -\frac{2}{\sigma_1}[\langle g_A^2 \rangle - \langle g_A \rangle \bar{g}_A(t)] + \frac{2\sigma_A^2}{\sigma_1^2}, \qquad (37c)$$

$$\frac{d}{dt}\langle g_A g_N \rangle = -\left(\frac{1}{\sigma_1} + \frac{1}{\sigma_2}\right)\langle g_A g_N \rangle + \frac{1}{\sigma_1}\langle g_N \rangle \bar{g}_A(t)$$
$$+ \frac{1}{\sigma_2}\langle g_A \rangle \bar{g}_N(t) + \frac{2p\sigma_0^2}{\sigma_1\sigma_2}, \qquad (37d)$$

$$\frac{d}{dt}\langle g_N^2 \rangle = -\frac{2}{\sigma_2}[\langle g_N^2 \rangle - \langle g_N \rangle \bar{g}_N(t)] + \frac{2\sigma_0^2}{\sigma_2^2}. \qquad (37e)$$

The initial conditions for these equations can be computed from the initial probability density $\rho(v, g_A, g_N, t=0)$ or its marginal counterpart over the conductances alone.

For the (co)variances

$$\sigma_g^2(t) = \langle g_A^2 \rangle - \langle g_A \rangle^2,$$

$$c_{AN}(t) = \langle g_A g_N \rangle - \langle g_A \rangle\langle g_N \rangle,$$

$$\sigma_N^2(t) = \langle g_N^2 \rangle - \langle g_N \rangle^2, \qquad (38)$$

Eqs. (37a)–(37e) yield the equations

$$\frac{d}{dt}\sigma_g^2 = -\frac{2}{\sigma_1}\sigma_g^2 + \frac{2\sigma_A^2}{\sigma_1^2}, \qquad (39a)$$

$$\frac{d}{dt}c_{AN} = -\left(\frac{1}{\sigma_1} + \frac{1}{\sigma_2}\right)c_{AN} + \frac{2p\sigma_0^2}{\sigma_1\sigma_2}, \qquad (39b)$$

$$\frac{d}{dt}\sigma_N^2 = -\frac{2}{\sigma_2}\sigma_N^2 + \frac{2\sigma_0^2}{\sigma_2^2}. \qquad (39c)$$

Note that when the parameters σ_A^2 and σ_0^2 do not depend on time, Eqs. (39a)–(39c) have the unique attracting equilibrium points

$$\sigma_g^2 = \frac{\sigma_A^2}{\sigma_1}, \quad c_{AN} = \frac{2p\sigma_0^2}{\sigma_1 + \sigma_2}, \quad \sigma_N^2 = \frac{\sigma_0^2}{\sigma_2}, \qquad (40)$$

whose values are identical to the respective right-hand sides of the maximal-entropy relations (35). This observation casts the (co)variances (38) even in the time-dependent case as suitable candidates for replacing the right-hand sides of (35) in a general second-order closure scheme, which we will postulate in the next section.

We need to stress, however, that even if we were to solve the moment equations (37a)–(37e) (and their higher-order counterparts) explicitly, we would not obtain an explicit solution to the moment problem for the density $\rho(v, g_A, g_N)$. This is because Eqs. (37a)–(37e), and so also their solutions, depend on the as-yet-unknown firing rate $m(t)$. How to find this rate will be explained in the next section.

Here, we discuss another important aspect of the conductance moment dynamics—namely, their significance in the validity of the diffusion approximation leading to Eq. (12) and the boundary conditions (16). As pointed out in Sec. V, the probability density function $\rho(v, g_A, g_N)$ must be negligibly small in the region outside the first quadrant $g_A > 0$, $g_N > 0$, in order for this approximation to hold. [This smallness can, for example, be expressed in terms of the integral of $\rho(v, g_A, g_N)$ over that region and the voltage being small.] It

is clear that the necessary condition for this smallness is that the ratio of the variances, $\sigma_g^2(t)$ and $\sigma_N^2(t)$, versus the first moments, $\langle g_A \rangle$ and $\langle g_N \rangle$, as computed from Eqs. (39a), (39c), (37a), and (37b), respectively, must be small. If this is not the case, the diffusion approximation (12), as well as the reduction to the voltage dependence alone discussed in the next section, may become invalid.

IX. CLOSURE AND REDUCED KINETIC MOMENT EQUATIONS

In this section, we postulate a second-order closure for the hierarchy (24a)–(24d) of equations for the moments (19) based on the discussion of the previous two sections. First, using Eq. (24a), we rewrite Eqs. (24b) and (24c) in such a way that the second moments $\mu_A^{(2)}(v)$, $\mu_{AN}^{(2)}(v)$, and $\mu_N^{(2)}(v)$ in them are expressed in terms of the first moments $\mu_A(v)$ and $\mu_N(v)$ and the (co)variances $\Sigma_A^2(v)$, $C_{AN}(v)$, and $\Sigma_A^2(v)$ via Eqs. (34).

In view of the discussion presented in the preceding two sections, for the closure in the general case, we consider it natural to postulate

$$\Sigma_A^2(v) \equiv \sigma_g^2(t), \quad \Sigma_N^2(v) \equiv \sigma_N^2(t),$$

$$C_{AN}(v) \equiv c_{AN}(t), \tag{41}$$

where the (co)variances $\Sigma_A^2(v)$, $C_{AN}(v)$, and $\Sigma_N^2(v)$ are defined as in (34) and $\sigma_g^2(t)$, $c_{AN}(t)$, and $\sigma_N^2(t)$ are computed from Eqs. (39a)–(39c) with the appropriate initial conditions, as discussed after listing Eqs. (37a)–(37e).

Since the (co)variances $\sigma_g^2(t)$, $c_{AN}(t)$, and $\sigma_N^2(t)$ no longer depend on the voltage v, Eqs. (24a)–(24c) for the voltage probability density function $\varrho(v)$ and the first conditional moments $\mu_A(v)$ and $\mu_N(v)$ under the closure assumption (41) simplify to become

$$\frac{\partial}{\partial t}\varrho(v) = \frac{\partial}{\partial v}\left\{\left[\left(\frac{v-\varepsilon_r}{\tau}\right) + [\lambda\mu_A(v) + (1-\lambda)\mu_N(v)]\right.\right.$$
$$\left.\left.\times\left(\frac{v-\varepsilon_E}{\tau}\right)\right]\varrho(v)\right\}, \tag{42a}$$

$$\frac{\partial}{\partial t}\mu_A(v) = -\frac{1}{\sigma_1}(\mu_A(v) - \bar{g}_A) + \left\{\left(\frac{v-\varepsilon_r}{\tau}\right)\right.$$
$$+ [\lambda\mu_A(v) + (1-\lambda)\mu_N(v)]\left(\frac{v-\varepsilon_E}{\tau}\right)\left.\right\}\frac{\partial}{\partial v}\mu_A(v)$$
$$+ [\lambda\sigma_g^2(t) + (1-\lambda)c_{AN}(t)]$$
$$\times\frac{1}{\varrho(v)}\frac{\partial}{\partial v}\left[\left(\frac{v-\varepsilon_E}{\tau}\right)\varrho(v)\right], \tag{42b}$$

$$\frac{\partial}{\partial t}\mu_N(v) = -\frac{1}{\sigma_2}(\mu_N(v) - \bar{g}_N) + \left\{\left(\frac{v-\varepsilon_r}{\tau}\right)\right.$$
$$+ [\lambda\mu_A(v) + (1-\lambda)\mu_N(v)]\left(\frac{v-\varepsilon_E}{\tau}\right)\left.\right\}\frac{\partial}{\partial v}\mu_N(v)$$
$$+ [\lambda c_{AN}(t) + (1-\lambda)\sigma_N^2(t)]$$

$$\times\frac{1}{\varrho(v)}\frac{\partial}{\partial v}\left[\left(\frac{v-\varepsilon_E}{\tau}\right)\varrho(v)\right]. \tag{42c}$$

Equations (42a)–(42c) provide the desired reduced kinetic description of moments, and are the main result of this paper.

Equation (42a) is clearly in conservation form, with the corresponding voltage probability flux

$$\mathcal{J}_V(v,t) = -\left[\left(\frac{v-\varepsilon_r}{\tau}\right) + [\lambda\mu_A(v) + (1-\lambda)\mu_N(v)]\right.$$
$$\left.\times\left(\frac{v-\varepsilon_E}{\tau}\right)\right]\varrho(v) = \int\int_{-\infty}^{\infty} J_V(v,g_A,g_N,t)dg_Adg_N, \tag{43}$$

where $J_V(v,g_A,g_N,t)$ is the probability flux (14) in the voltage direction for the original kinetic equation (12). The second equality in (43) is obtained from the definitions (14), (21a), and (21b) and Eq. (23), just as in the derivation of Eq. (25). From (14) and the definition (17) of the population-averaged firing rate per neuron, $m(t)$, we now immediately see that this firing rate can be expressed as the voltage flux through the firing threshold:

$$m(t) = \mathcal{J}_V(V_T,t). \tag{44}$$

We now proceed to derive the boundary conditions for the reduced equations (42a)–(42c). First, from the definition of the voltage probability flux (43) and the voltage boundary condition (15), we immmediately derive the equation

$$\mathcal{J}_V(V_T,t) = \mathcal{J}_V(\varepsilon_r,t), \tag{45}$$

which is also the first equation of Eqs. (25) and further gives the boundary condition

$$\{(V_T - \varepsilon_r) + [\lambda\mu_A(V_T) + (1-\lambda)\mu_N(V_T)](V_T - \varepsilon_E)\}\varrho(V_T)$$
$$= [\lambda\mu_A(\varepsilon_r) + (1-\lambda)\mu_N(\varepsilon_r)](\varepsilon_r - \varepsilon_E)\varrho(\varepsilon_r). \tag{46a}$$

Under the closure (41), using the (co)variance definitions (34), and the voltage flux probability definition (43), the boundary condition (45), and the firing rate expression (44), we can transform Eqs. (25) for $r=1$, $s=0$ and $r=0$, $s=1$, respectively, into the equations

$$\tau m(t)[\mu_A(V_T) - \mu_A(\varepsilon_r)] = [\lambda\sigma_g^2(t) + (1-\lambda)c_{AN}(t)]$$
$$\times[(V_T - \varepsilon_E)\varrho(V_T)$$
$$- (\varepsilon_r - \varepsilon_E)\varrho(\varepsilon_r)], \tag{46b}$$

$$\tau m(t)[\mu_N(V_T) - \mu_N(\varepsilon_r)] = [\lambda c_{AN}(t) + (1-\lambda)\sigma_N^2(t)]$$
$$\times[(V_T - \varepsilon_E)\varrho(V_T)$$
$$- (\varepsilon_r - \varepsilon_E)\varrho(\varepsilon_r)]. \tag{46c}$$

Equations (46a)–(46c) provide the physiological boundary conditions for the kinetic moment equations (42a)–(42c).

In passing, let us remark that, due to the definitions (34), (36), and (38), the closure (41) implies the moment relations

$$\int_{\varepsilon_r}^{V_T}\varrho(v)\mu_A^2(v)dv = \left(\int_{\varepsilon_r}^{V_T}\varrho(v)\mu_A(v)dv\right)^2,$$

$$\int_{\varepsilon_r}^{V_T} \varrho(v) \mu_A(v) \mu_N(v) dv = \int_{\varepsilon_r}^{V_T} \varrho(v) \mu_A(v) dv$$

$$\times \int_{\varepsilon_r}^{V_T} \varrho(v) \mu_N(v) dv,$$

$$\int_{\varepsilon_r}^{V_T} \varrho(v) \mu_N^2(v) dv = \left(\int_{\varepsilon_r}^{V_T} \varrho(v) \mu_N(v) dv \right)^2.$$

Recapping the results of this section, the reduced statistical description for the voltage dynamics alone is furnished by Eqs. (42a)–(42c), the boundary conditions (46a)–(46c), the ordinary differential equations (39a)–(39c), the firing rate definition (44), the parameter definitions (13), and the initial conductance distribution or its linear and quadratic moments. This problem is highly nonlinear because of the nonlinear moment equations (42b) and (42c) and boundary condition (46a) and because the firing rate $m(t)$ enters the governing equations as well as the boundary conditions as a self-consistency parameter.

X. DISTINGUISHED LIMITS

A. Instantaneous fast-conductance time scale

In the limit of the instantaneous fast conductance time scale—i.e., when $\sigma_1 \to 0$—regardless of whether the forcing terms $\sigma_A^2(t)$ and $\sigma_0^2(t)$ depend on time or not, the solutions $\sigma_g^2(t)$ and $c_{AN}(t)$ of Eqs. (39a) and (39b) relax on the $O(\sigma_1)$ time scale to their respective forcing terms, so that

$$\sigma_g^2(t) \to \frac{\sigma_A^2(t)}{\sigma_1},$$

$$c_{AN}(t) \to \frac{2p\sigma_0^2(t)}{\sigma_2} = \frac{\bar{S}^2}{N\sigma_2} m(t). \tag{47}$$

The limits (47) imply that $\sigma_1 \sigma_g^2(t) \to \sigma_A^2(t)$ and $\sigma_1 c_{AN}(t) \to 0$, and thus Eq. (42b) becomes

$$\mu_A(v) = \bar{g}_A(t) + \frac{\lambda \sigma_A^2(t)}{\varrho(v)} \frac{\partial}{\partial v} \left[\left(\frac{v - \varepsilon_E}{\tau} \right) \varrho(v) \right]. \tag{48}$$

In other words, the conditional moment $\mu_A(v)$ relaxes on the $O(\sigma_1)$ time scale to being slaved to the dynamics of $\varrho(v)$ and $\mu_N(v)$.

In the limit of the instantaneous fast conductance time scale, as $\sigma_1 \to 0$, we thus only have two equations governing the moments $\varrho(v)$ and $\mu_N(v)$,

$$\frac{\partial}{\partial t} \varrho(v) = \frac{\partial}{\partial v} \left\{ \left[\left(\frac{v - \varepsilon_r}{\tau} \right) + [\lambda \mu_A(v) + (1 - \lambda) \mu_N(v)] \right. \right.$$

$$\left. \left. \times \left(\frac{v - \varepsilon_E}{\tau} \right) \right] \varrho(v) \right\}, \tag{49a}$$

$$\frac{\partial}{\partial t} \mu_N(v) = -\frac{1}{\sigma_2} [\mu_N(v) - \bar{g}_N(t)] + \left\{ \left(\frac{v - \varepsilon_r}{\tau} \right) \right.$$

$$+ [\lambda \mu_A(v) + (1 - \lambda) \mu_N(v)] \left(\frac{v - \varepsilon_E}{\tau} \right) \left. \right\} \frac{\partial}{\partial v} \mu_N(v)$$

$$+ [\lambda c_{AN}(t) + (1 - \lambda) \sigma_N^2(t)]$$

$$\times \frac{1}{\varrho(v)} \frac{\partial}{\partial v} \left[\left(\frac{v - \varepsilon_E}{\tau} \right) \varrho(v) \right], \tag{49b}$$

while $\mu_A(v)$ is expressed by the relation (48). Here, the time-dependent coefficients $\bar{g}_A(t)$, $\bar{g}_N(t)$, and $\sigma_A^2(t)$ can be found in (13) and $c_{AN}(t)$ is computed in (47). Note that all these quantities can now be computed from the external-input and network firing rates $\nu_0(t)$ and $m(t)$ alone, without having to solve any additional differential equation. Only the coefficient $\sigma_N^2(t)$ is still computed from the ordinary differential equation (39c), with $\sigma_0^2(t)$ again given in terms of the firing rate $m(t)$ in (13). The closure (41), in the limit $\sigma_1 \to 0$, effectively becomes

$$\sigma_1 \Sigma_A^2(v) = \sigma_A^2(t), \quad \Sigma_N^2(v) = \sigma_N^2(t),$$

$$C_{AN}(v) = \frac{2p\sigma_0^2(t)}{\sigma_2}. \tag{50}$$

Due to relation (48), Eq. (49b) is now second-order in the voltage v.

Recall that the terms in (49a) and (49b) multiplied by $c_{AN}(t)$ originate from the correlation effects due to the spikes that are common to both the fast and slow receptors. In a steady state, using (40) and taking the limit $\sigma_1 \to 0$, we have $c_{AN} \to 2p\sigma_N^2$—i.e., a rather strong correlation effect if the synaptic failure is low.

Because of (47), as $\sigma_1 \to 0$, the boundary condition (46b) simplifies to become

$$(V_T - \varepsilon_E) \varrho(V_T) = (\varepsilon_r - \varepsilon_E) \varrho(\varepsilon_r), \tag{51a}$$

and therefore the condition (46c) also simplifies to become

$$\mu_N(V_T) = \mu_N(\varepsilon_r). \tag{51b}$$

Using the boundary conditions (51a) and (51b) and relation (48), we can finally simplify the boundary condition (46a) to become

$$\tau(V_T - \varepsilon_r) \varrho(V_T) + \lambda^2 \sigma_A^2(t)(V_T - \varepsilon_E) \frac{\partial \varrho}{\partial v}(V_T)$$

$$= \lambda^2 \sigma_A^2(t)(\varepsilon_r - \varepsilon_E) \frac{\partial \varrho}{\partial v}(\varepsilon_r). \tag{51c}$$

Note that these boundary conditions are now linear in ϱ and μ_N, but still contain the firing rate through the parameter $\sigma_A^2(t)$.

To summarize, in the $\sigma_1 \to 0$ limit, the simplified description of the problem is achieved by Eqs. (49a) and (49b), relation (48), the boundary conditions (51a)–(51c), the single ordinary differential equation (39c), the firing rate definition

(44), the parameter definitions (13), and the initial conductance distribution or its initial moments $\langle g_N \rangle(0)$ and $\langle g_N^2 \rangle(0)$.

B. Instantaneous fast-conductance and infinite slow-conductance time scales

If, in addition to $\sigma_1 \to 0$, we now also consider the limit $\sigma_2 \to \infty$—i.e., if we consider the dynamics over the time scales with $\sigma_1 \ll t \ll \sigma_2$—we find

$$c_{AN}(t) = \frac{\overline{S}^2}{N\sigma_2} m(t) \to 0 \tag{52}$$

from (47), as well as $d\sigma_N^2/dt=0$ from (39c). It is therefore clear that

$$\sigma_N^2(t) = \sigma_N^2(0), \tag{53}$$

where $\sigma_N^2(0)=\langle g_N^2 \rangle(0)-\langle g_N \rangle^2(0)$ and $\langle g_N^2 \rangle(0)$ and $\langle g_N \rangle(0)$ are computed from their definitions in (36) with the integrals taken against the initial probability density $\rho(v,g_A,g_N,t=0)$ or its conductance-dependent marginals. Using (52) and (53), we conclude that Eqs. (49a) and (49b) then reduce yet further to

$$\frac{\partial}{\partial t}\varrho(v) = \frac{\partial}{\partial v}\left\{ \left[\left(\frac{v-\varepsilon_r}{\tau} \right) + [\lambda\mu_A(v) + (1-\lambda)\mu_N(v)] \right. \right.$$
$$\left. \left. \times \left(\frac{v-\varepsilon_E}{\tau} \right) \right] \varrho(v) \right\}, \tag{54a}$$

$$\frac{\partial}{\partial t}\mu_N(v) = \left\{ \left(\frac{v-\varepsilon_r}{\tau} \right) + [\lambda\mu_A(v) + (1-\lambda)\mu_N(v)] \right.$$
$$\left. \times \left(\frac{v-\varepsilon_E}{\tau} \right) \right\} \frac{\partial}{\partial v}\mu_N(v)$$
$$+ \frac{(1-\lambda)\sigma_N^2(0)}{\varrho(v)} \frac{\partial}{\partial v}\left[\left(\frac{v-\varepsilon_E}{\tau} \right)\varrho(v) \right], \tag{54b}$$

with $\mu_A(v)$ again expressed by (48). Because of (52), the correlation term disappears from Eq. (54b). The closure (41), in the limit $\sigma_1 \to 0$ and $\sigma_2 \to \infty$, effectively becomes

$$\sigma_1\Sigma_A^2(v) = \sigma_A^2(t), \quad \Sigma_N^2(v) = \sigma_N^2(0),$$

$$C_{AN}(v) = 0. \tag{55}$$

The complete description of the problem in this limit is achieved using the same ingredients as in the previous section, except that Eq. (54b) replaces Eq. (49b) and that the variance $\sigma_N^2(0)$ does not evolve, so there is no need to solve any of the ordinary differential equations (39a)–(39c).

XI. DISCUSSION

A comparison among a full simulation of IF neuronal network ensembles corresponding to different realizations of the Poisson inputs, and two corresponding numerical solutions of kinetic moment equations—one including and the other
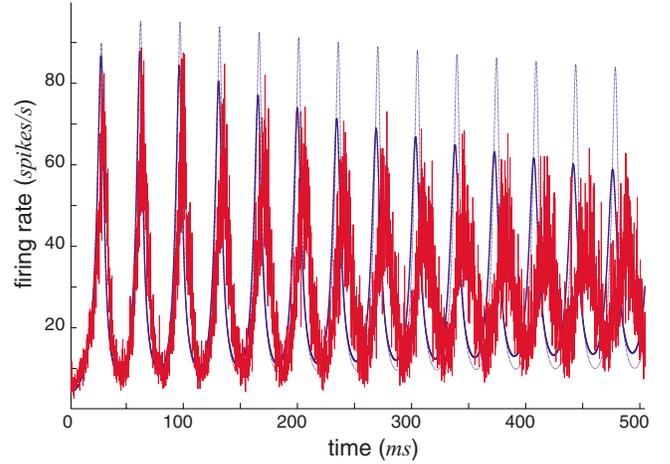

FIG. 1. (Color online) Accuracy of the kinetic theory for a network of neurons with fast and slow conductances driven by the same spike train: The time evolution of the population-averaged firing rate. Gray (red online): simulation of the IF neuronal network described in the text, averaged over 1024 ensembles. Dark line (blue online): numerical solution of the kinetic moment equations (42a)–(42c). Light line (blue online): numerical solution of the kinetic moment equations (42a)–(42c), without the correlation terms—i.e., with $c_{AN}(t)=0$. A step stimulus is turned on at $t=0$ with $N=20$, $\tau=20$, $\varepsilon_r=0$, $\varepsilon_E=4.67$, $V_T=1$, $\lambda=0.5$, $\sigma_1=0.005$, $\sigma_2=0.01$, $f_A=0.05$, $\nu_A=11$, $f_N=0.13$, $\nu_N=0.13$, $p=1$, and $\overline{S}=0.857$.

excluding the correlations $c_{AN}(t)$—is presented in Fig. 1. The results are depicted in gray (red online), thick, and fine (blue online) lines, respectively. The IF neuronal network simulated here is a straightforward generalization of Eqs. (1) and (3a)–(3c), which includes external drive for the slow conductances G_i^N with the Poisson rate ν_N and strength f_N in addition to the drive for the fast conductances G_i^A with the Poisson rate ν_A and strength f_A. The kinetic moment equations are the corresponding generalizations of (42a)–(42c).

It is apparent that the curve representing the results of the kinetic theory with the correlations included faithfully tracks the temporal decay of the firing rate oscillations computed using the IF network. On the other hand, the kinetic theory that does not take the correlations into account dramatically overestimates the amplitude of the firing rate and thus underestimates the decay rate of its oscillations.

The results depicted in Fig. 1 convincingly illustrate how important it is to include explicitly in the kinetic theory the assumption that both the fast and slow conductances are driven by the same spike train. The correlation terms appearing as the consequence in the kinetic moment equations render an accurate statistical picture of the corresponding IF network dynamics.

Finally, let us remark that developing a kinetic theory for more realistic neuronal networks, for instance, with neurons containing dendritic and somatic compartments and a voltage-dependent time course of the slow conductance mimicking the true NMDA conductance [82–84], would proceed along the same lines as those employed in the current paper.

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