# Effect of interacting second- and third-order stimulus-dependent correlations on population-coding asymmetries

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Spike correlations among neurons are widely encountered in the brain. Although models accounting for pairwise interactions have proved able to capture some of the most important features of population activity at the level of the retina, the evidence shows that pairwise neuronal correlation analysis does not resolve cooperative population dynamics by itself. By means of a series expansion for short time scales of the mutual information conveyed by a population of neurons, the information transmission can be broken down into firing rate and correlational components. In a proposed extension of this framework, we investigate the information components considering both second- and higher-order correlations. We show that the existence of a mixed stimulus-dependent correlation term defines a new scenario for the interplay between pairwise and higher-than-pairwise interactions in noise and signal correlations that would lead either to redundancy or synergy in the information-theoretic sense.

## I. INTRODUCTION

Contemporary experiments in neuroscience have challenged the question of whether the information conveyed by the activity of an ensemble of neurons is determined solely by the number of action potentials fired by each cell independently or correlations present in such spike trains also play a key role in information transmission [1–11]. In this sense, finding suitable models for capturing the statistical structure of firing patterns distributed across several neurons provides a challenge and a prerequisite for understanding population codes. Recently, pairwise models have proven their worth in analyzing retinal ganglion cells [12,13]. Nevertheless, these studies have raised the question of the relevance of higher-order correlations (HOCs) in binarized spike trains, since pairwise models fail to completely explain the variability in activity patterns at a more general level [14–21]: Even just triplet correlations have been implied to deeply impact on information processing in a small population of neurons [22].

Indeed, neurophysiological research has shown that pairwise models fail to explain the responses of spatially localized triplets of cells [16–18,23] when describing the activity of large neuronal populations responding to natural stimuli [18]. Deviations from the pairwise-maximum-entropy (PME) model indicate that HOCs have to be taken into account for modeling the population statistics [24–27]. Thus, the intricacy of the neurophysiological data highlights the need to develop a theoretical framework accounting for the statistical complexity of synchronous activity patterns. Pattern probabilities for the so-called dichotomized Gaussian (DG) model [23–27] were estimated using the cumulative distribution of multivariate Gaussians showing high-precision fitting of the experimental data, therefore evidencing that HOCs are required to properly account for cortical dynamics.

Neurophysiologically speaking, single neurons are considered to make small and understandable contributions to animal behavior [12]. However, most behaviors involve large numbers of neurons, thousands or even millions. The human brain has approximately $86 \times 10^9$ neurons [28], and as these neurons may be connected to other neurons via as many as $10^{15}$ synaptic connections, the ways that information might be transmitted among them are extremely complex. These neurons are often organized into layers or regions, such that nearby neurons have similar response properties. If the information from different cells were independent, it would consequently increase linearly with the number of cells in the population. If that is not the case, then two regimes are possible. On the one hand, if many cells in the sample carry similar information, then the code is said to be redundant, since information of the whole population would be overestimated if the cells are taken to be independent [29]. On the other hand, some information arises only by taking into account interactions (or simultaneous responses) of different neurons, for example, information only available from the relative timing of firing. This code is said to be synergistic, and more information is available in the population than one would obtain by the sum of the information gathered from each neuron alone. It is important, therefore, to gain a deeper understanding about correlations across neurons in the brain and their impact on population coding, that is, the modalities with which correlations contribute to neuronal information transmission, rather than just a quantification of the total information transmitted by the population [30]. A valid measure to assess the role of correlations in the neural code is to evaluate whether information is encoded synergistically, redundantly, or independently [11,31–41].

The information-theoretic series expansion formalism was introduced in [3,4,42,43]. It allows us to separately quantify the information available if each cell were to convey information independently from the deviations that arise from synergy and redundancy effects, considering up to pairwise spike correlations across neurons. These nonlinear effects result from different contributions that can be summed up as redundant contributions due to similarities in the mean response profiles of different cells, either a redundant or a synergistic stimulus-independent correlation term or a synergistic stimulus-dependent correlational contribution [11,33,41].

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The series expansion approach is based on the assumption that information is transmitted in poststimulus time windows that are short compared to typical interspike intervals, so that the average number of emitted spikes per stimulus presentation is low [3,4,42]. In this paper, we present an extension of this approach up to third-order contributions and propose a general dependency for any order. We obtain an exact analytical expression that allows us to estimate a correction for the stimulus-dependent correlational component of the mutual information (MI) within the series expansion approach. That is, when neuronal correlations on spike trains are considered, for instance, a three-neuron system, there is a limitation in only analyzing pairwise interactions. Two types of external input can generate triplewise and pairwise correlations, with identical cross- and autocorrelation analysis in both cases [14–19,44]. In other words, pairwise input network connectivity could generate HOCs that would be indistinguishable from those generated by triplewise input network connectivity. It would not be possible to distinguish, in such scenario, the two distinct neuronal population activities even through a cross- and autocorrelation analysis, and the differences between these two configurations are not captured by mere pairwise correlations. It is HOCs that determine whether coincident spikes of two neurons are also coincident with the spikes of the third neuron [14–19,44]. Pairwise correlations are not therefore enough to provide reliable descriptions of neural systems in general [14–19].

Furthermore, we show that the existence of a mixed stimulus-dependent correlation term (of the MI expansion) defines a new scenario when analyzing HOCs. At third-order level it takes into account possible "chance" [45] triplets of spikes that may have arisen from second-order correlations and could contribute to either under- or overestimation of the total information. Coding can thus be synergistic or redundant, depending on the value of a mixed stimulus-dependent correlation term. We perform a nonhomogenous Poisson computational modeling considering a von Mises distribution of stimuli across different neurons, showing how the existence of the mixed stimulus-dependent correlation term can modify information. We also evaluate this formalism using pairwise and triplewise input correlation values considering a spiking network. The current approach defines a new scenario when analyzing HOCs, putting in evidence the limitations of only considering pairwise neuronal correlations on spike trains and reshaping the "achievable regions" of synergy/redundancy when investigating a small population of neurons.

## II. BREAKDOWN OF INFORMATION INTO CODING MECHANISMS

As formulated in [42], we consider a time period of short duration during which the activity of $N$ cells is observed. The neuronal population response to the stimulus in this poststimulus time window is denoted by a vector $\mathbf{r}$, each element $r_1, \ldots, r_N$ of the vector describing the response of an individual cell. Each different stimulus is denoted as $s$, and the stimuli considered are purely abstract; the formalism detailed in this paper is applicable to a wide variety of experimental paradigms. The response of each cell can be described in a number of ways depending on the questions to be addressed.

For example, in a spike count code, $r_i$ would simply be the spike count of cell $i$ measured in the poststimulus time window on a given trial with the stimulus $s$ present. Conversely, in this paper, we will describe the response by the firing rate, i.e., the spike count divided by the poststimulus time window and denote it by $r_i(s)$ to explicitly state stimulus dependency. Alternatively, if we were interested in a spike timing code, the response $r_i$ would be a sequence of spike arrival times $\{t_j^i\}$, where $t_j^i$ denotes the time of the $j$th spike emitted by the $i$th neuron in a given trial, as used in [3,4]. The equations derived are valid for any choice of neuronal code $\mathbf{r}$, including spike timing codes with the appropriate notation.

For a given choice of code, following [46], we can write the mutual information transmitted by the population response about the whole set of stimuli $\{s\}$ as

$$I = \left\langle \sum_{\mathbf{r} \in \{r\}} P(\mathbf{r}|s) \log_2 \left[ \frac{P(\mathbf{r}|s)}{P(\mathbf{r})} \right] \right\rangle_s, \qquad (1)$$

where $\{r\}$ denotes the response space. The angular brackets indicate the average over different stimuli, $\langle A(s) \rangle_s \equiv \sum_{s \in \{s\}} P(s)A(s)$, $P(s)$ being the probability that the stimulus $s$ is present. $P(\mathbf{r}|s)$ is the probability of observing a particular response $\mathbf{r}$ conditional to stimulus $s$, and $P(\mathbf{r}) = \langle P(\mathbf{r}|s) \rangle_s$ is its average across all stimulus presentations. The probability $P(\mathbf{r}|s)$ can be determined experimentally by repeating each stimulus in exactly the same way on many trials, while recording the neuronal responses. Mutual information quantifies how well an ideal observer of neuronal responses can discriminate between all the different stimuli, based on a single trial. In Eq. (1) the summation is over all possible population responses. Equation (1), as expressed in [30], quantifies the total information transmitted by the activity of a neuronal population. However, it tells us nothing about the specific contribution of cross-neuronal correlations to the total transmitted information or whether cross correlations make the code redundant or synergistic.

Hence, to exactly describe the impact of correlation on information, it is necessary to define a response-related correlation measure. This measure is usually denoted as $\gamma(\mathbf{r}|s)$, and it quantifies how much higher the probability that neurons emit a response is than that expected in the uncorrelated case, normalized to the probability of the event with firing rates expected in the uncorrelated case [3,30,40,42]. It is referred to as "noise correlation" in previous literature [3,30,40,42], as it measures correlations in the response variability upon repeated trials of the same stimulus. Positive values indicate correlation and negative values indicate anticorrelation [42].

Another important coefficient for describing population coding that quantifies similarity in the stimulus modulation of responses of individual cells is the "signal similarity" coefficient or "signal correlation" $\nu(\mathbf{r})$ [3,30,40,42]. That is, it conveys correlations in the mean responses of the neurons across the set of stimuli. It is different from zero if signals coming from individual neurons are either positively correlated or negatively correlated. Both measures can vary from $-1$ to $\infty$, with 0 indicating lack of correlation. Further information on these correlation coefficients is detailed in Appendix A.

By considering these quantities, it is possible to write the total information in components, each reflecting the

contribution of a different coding mechanism, as in [30,42].

$$I(\mathbf{r}; \{s\}) = I_{\text{lin}} + I_{\text{sig-sim}} + I_{\text{cor-ind}} + I_{\text{cor-dep}}. \quad (2)$$

Each component is specified in Appendix B. The mutual information is exactly equal to the split of information within the exact information breakdown approach as in [30]. It is important to note that these components have the same meaning in both the exact information breakdown and the series expansion approximation when considering the different order contributions [3,42]. Moreover, notice that by using the exact information breakdown formalism [30], we are not in control of which correlation order dominates the spike train data.

By means of this breakdown, it is possible to separate the additive contribution to information from the contribution of neurons as independent units. Positive, negative, or null contributions from mechanisms would arise from considering the neurons as units of a population. Synergy (positive addition) then would be evidence of a population code among interacting cells and redundancy (negative contribution) would result in a less-than-additive combination of information [33,47]. The first term of the information breakdown $I_{\text{lin}}$ is the information obtained if each cell were to convey independent information, i.e., no redundancy or synergy is considered. The total information transmitted by the population is the linear sum of the information conveyed by each individual cell [3,11,30,41,42]. The second term, $I_{\text{sig-sim}}$, takes into account the redundancy that could arise even in the absence of cross correlation, when there are similarities in the distribution across stimuli of stimulus-conditional response probabilities of individual cells. This term is always less than or equal to zero, so it cannot lead to synergy [3,11,30,41,42].

If the population responses are statistically independent, these are the only nonzero contributions to the information breakdown. In this sense, the sum of $I_{\text{lin}}$ and $I_{\text{sig-sim}}$ quantifies how much information can be obtained from the neurons evaluated individually, without any reference to the simultaneous activity of other neurons.

The next two terms in the information breakdown are correlational-dependent components: a stimulus-dependent component $I_{\text{cor-dep}}$ and a stimulus-independent component $I_{\text{cor-ind}}$. Hence, they express any further effects that cross-cell correlations might have beyond those accounted for by individual cell properties. In that regard, the sum of the two correlational terms $I_{\text{cor-ind}}$ and $I_{\text{cor-dep}}$ quantifies the amount of information truly available from the correlated activity of the whole population [3,11,30,41,42].

It can be proved by means of basic information theory inequalities that the stimulus-dependent correlational component ($I_{\text{cor-dep}}$) is non-negative, and it is zero if and only if, for any given response $\mathbf{r}$, the correlation strength $\gamma(\mathbf{r}|s)$ is stimulus independent. Therefore, this term measures how well stimuli identity is "tagged" by differences in trial-to-trial spike correlations across the stimuli [30]. $I_{\text{cor-dep}}$ is nonzero only if the correlation strength $\gamma(\mathbf{r}|s)$ is different from zero for some response $\mathbf{r}$ or stimulus $s$.

For a given response $\mathbf{r}$, the stimulus-independent correlational component ($I_{\text{cor-ind}}$) is positive (synergistic) when signal similarity and cross correlation have the opposite sign and

negative (redundant) otherwise. That is, even if not stimulus-modulated, cross correlations can still affect the neuronal code through an interaction between cross-cell correlation and signal similarity [48,49]. Furthermore, as opposed to $I_{\text{cor-dep}}$, $I_{\text{cor-ind}}$ does not vanish if $\gamma(\mathbf{r}|s)$ or $\nu(\mathbf{r})$ is not equal to zero.

## III. HIGHER-ORDER CORRELATIONS IN THE SHORT TIME EXPANSION

To evaluate how order-specific interactions affect the total information coding of a neuronal population, it is necessary to rely on the series expansion approach [3,4,42]. Let us assume first that spikes are not locked with infinite precision. Given these conditions, individual firing probabilities scale with the time duration $t$ as [3,4,42]

$$P(r_i|r_j, r_k, \ldots, r_n; s) \sim t, \quad (3)$$

and using the chain rule

$$\begin{aligned} P(r_i, \ldots, r_n; s) &= P(r_i|r_j, \ldots, r_n; s) P(r_j|r_k, \ldots, r_n; s) \\ &\times P(r_k|\ldots, r_n; s) \cdots P(r_n; s), \quad (4) \end{aligned}$$

the probability of having $n$ spikes fired is the product of the conditional probabilities of each fire due to the presence of other firings in the pattern. Then, as each of the terms is proportional to $t$, the probability of having $n$ firings scales as [3,4,42]

$$P(r_i, r_j, r_k, \ldots, r_n; s) \sim t^n. \quad (5)$$

As a proposed extension of the series expansion of [3,4,42], we can write the probability of having three neurons (labeled as $i$, $j$, and $k$) firing as

$$P(r_i, r_j, r_k; s) = \overline{r}_i(s)\overline{r}_j(s)\overline{r}_k(s)t^3[1 + \gamma_{ijk}(s)] + O(t^4), \quad (6)$$

where

$$\gamma_{ijk}(s) = \frac{\overline{r_i(s)r_j(s)r_k(s)}}{\overline{r}_i(s)\overline{r}_j(s)\overline{r}_k(s)} - 1 \quad (7)$$

denotes the triplewise noise correlation. Similarly, triplewise signal correlation is given by

$$\nu_{ijk} = \frac{\langle \overline{r}_i(s)\overline{r}_j(s)\overline{r}_k(s)\rangle_s}{\langle \overline{r}_i(s)\rangle_s \langle \overline{r}_j(s)\rangle_s \langle \overline{r}_k(s)\rangle_s} - 1. \quad (8)$$

Given these definitions, the following additional assumptions are made to be able to compute the series expansion: first, that the mutual information is analytic in time and, second, that different trials are random realizations of the same process. The validity of these and previous assumptions has been examined elsewhere [3,4,42]. Then the mutual information can be expanded as a series of the poststimulus time window as

$$I = I_0 + tI_1 + \frac{t^2}{2}I_2 + \frac{t^3}{6}I_3 + \cdots, \quad (9)$$

where $I_1$ is the instantaneous information rate and $I_i$, with $i \geqslant 2$, is the $i$th derivative of information. We insert the different-order response probabilities into the sum over responses in Eq. (1), contained in the sequence of spikes. For each term in the sum over responses, we use the power expansion of the logarithm as in [42]. We then gather together

all the terms in the sum which have the same power in $t$, and using equation Eq. (9), one obtains the expressions of the information derivatives. The first- and second-order terms can be found in [42], where they are separated into coding components in the same manner as was later done in [30].

The first order of the expansion (and also the first term of the information breakdown) corresponds to $I_{\text{lin}}$; i.e., no redundancy or synergy is considered. The second order is decomposed in the following components (noted by the subindex 2 to distinguish them from higher-order ones) (as in [30]): $I_{\text{sig-sim},2}$, which takes into account the redundancy that can arise even in the absence of cross correlation, and the two correlational terms, $I_{\text{cor-ind},2}$ and $I_{\text{cor-dep},2}$, which measure the amount of information truly available from the pairwise correlated activity of the whole population. We refer to Appendix C for further details of these terms.

It is interesting to note that the decomposition of this short time limit expansion up to the second order is exactly analogous to the one previously detailed in the exact breakdown of neuronal population information into coding components when just considering pairwise interactions. The latter can be simply derived from the second-order series expansion by appropriately replacing the second-order noise and signal correlations [3] with the exact ones [30] and the instantaneous rates with the single-cell response probabilities (i.e., the probability of each cell response considered independently of the other cells). Despite this analogy, only the first- and second-order moments of the response probability distributions are considered in the approximated second-order series expansion equations, and the approximation can be improved by successively inserting higher-order terms.

However, if the expansion is continued up to higher orders, an extra component must be considered, which is related to the stimulus-dependent correlational component. By extending this approach to take into account contributions made by third-order interactions, we obtain the components $I_{\text{sig-sim},3}$, $I_{\text{cor-ind},3}$, and $I_{\text{cor-dep},3}$, as expected. We also obtain an additional term that reflects the possibility of "mistagging" a stimulus with triplewise statistics when it actually corresponded to the coincident spiking of three neurons that may arise by chance from pairwise correlations [45], which we denote as $I_{\text{cor-ch},3}$.

Thus, at third order, the nonlinear contribution is $I_3 = I_{\text{sig-sim},3} + I_{\text{cor-ind},3} + I_{\text{cor-dep},3} + I_{\text{cor-ch},3}$. The signal similarity contribution is

$$I_{\text{sig-sim},3} = \frac{1}{6 \ln 2} \sum_{i,j,k=1}^{N} \langle \overline{r}_i(s) \rangle_s \langle \overline{r}_j(s) \rangle_s \langle \overline{r}_k(s) \rangle_s$$
$$\times \left[ \nu_{ijk} + (1 + \nu_{ijk}) \ln \left( \frac{1}{1 + \nu_{ijk}} \right) \right]. \quad (10)$$

The total amount of information attributable to third-order correlated activity on the overall neural coding is given by the stimulus-independent contribution

$$I_{\text{cor-ind},3} = \frac{1}{6 \ln 2} \sum_{i,j,k=1}^{N} \langle \overline{r}_i(s) \overline{r}_j(s) \overline{r}_k(s) \gamma_{ijk}(s) \rangle_s \ln \left( \frac{1}{1 + \nu_{ijk}} \right)$$
$$\quad (11)$$

and the stimulus-dependent correlation component

$$I_{\text{cor-dep},3} = \frac{1}{6 \ln 2} \sum_{i,j,k=1}^{N} \langle \overline{r}_i(s) \overline{r}_j(s) \overline{r}_k(s) [1 + \gamma_{ijk}(s)]$$
$$\times \ln \left\{ \frac{\langle \overline{r}_i(s') \overline{r}_j(s') \overline{r}_k(s') \rangle_{s'} [1 + \gamma_{ijk}(s)]}{\langle \overline{r}_i(s') \overline{r}_j(s') \overline{r}_k(s') [1 + \gamma_{ijk}(s')] \rangle_{s'}} \right\} \Big\rangle_s. \quad (12)$$

The extra term reads as

$$I_{\text{cor-ch},3} = -\frac{1}{2 \ln 2} \sum_{i,j,k=1}^{N} \langle \overline{r}_i(s) \overline{r}_j(s) \overline{r}_k(s) [1 + \gamma_{ijk}(s)]$$
$$\times \ln \left\{ \frac{\overline{r}_i(s) \overline{r}_j(s) \, [1 + \gamma_{ij}(s)]}{\langle \overline{r}_i(s') \overline{r}_j(s') [1 + \gamma_{ij}(s')] \rangle_{s'}} \right\} \Big\rangle_s. \quad (13)$$

This $I_{\text{cor-ch},3}$ component can be consistently found when higher-than-pairwise interactions are considered, and it depends on lower-order noise correlations. We refer to Appendix C for details of the calculations of the third-order terms. By extending the definitions for spike probabilities and correlations for the higher-order components (see also Appendix C $n$th-order calculations), we can further infer the dependency of this extra term in the general case of the $n$th order, when $n > 2$. The $n$th-order $I_{\text{cor-ch}}$ component from the series expansion, which we present here just for the sake of completeness, can be written as

$$I_{\text{cor-ch},n} = -\frac{1}{n! \ln 2} \sum_{i_1,\ldots,i_n=1}^{N} \langle \overline{r}_{i_1}(s) \cdots \overline{r}_{i_n}(s)$$
$$\times \left[ 1 + \gamma_{i_1,\ldots,i_n}(s) \right] \sum_{m=2}^{n-1} \binom{n}{m}$$
$$\times \ln \left\{ \frac{\overline{r}_{i_1}(s) \cdots \overline{r}_{i_m}(s) [1 + \gamma_{i_1,\ldots,i_m}(s)]}{\langle \overline{r}_{i_1}(s') \cdots \overline{r}_{i_m}(s') [1 + \gamma_{i_1,\ldots,i_m}(s')] \rangle_{s'}} \right\} \Big\rangle_s,$$
$$\quad (14)$$

where $\gamma_{i_1,\ldots,i_m}$ is the $m$th-order noise correlation coefficient. We refer to Appendix C for further details of the information series expansion and explanations of how the previous equations were obtained.

In the following, we discuss the meaning of the term $I_{\text{cor-ch},3}$ when just pairwise correlations are specified. Let us consider the case of three neurons with four different scenarios. Figure 1(a) illustrates the case in which the three neurons do not share common inputs, but there might still be coincidences between spikes across pairs of neurons (marked in yellow/light gray). In Fig. 1(b), just two neurons share common inputs, and thus there exists pairwise correlation (marked in red/dark gray). Note that in this case, there could be coincidences between spikes among triplets of neurons as two neurons are correlated and the third one correlates by chance to this pair. Figure 1(c) depicts the case in which all three neurons share pairwise inputs, and coincidence triplets are more likely to be produced than in Fig. 1(b). Finally, Fig. 1(d) illustrates the case in which the neurons share pairwise and triplewise inputs, respectively denoted in red (dark gray) and green (dashed gray line). Nevertheless, pairwise and triplewise correlations might appear by chance. Thus, the
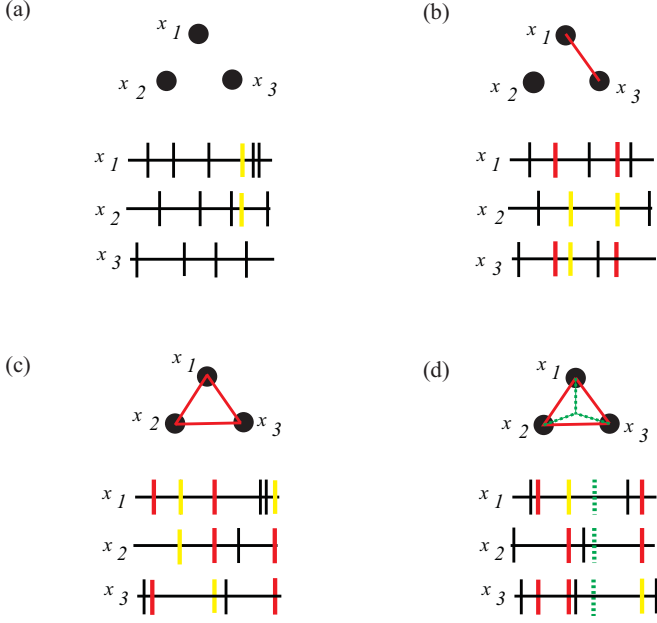
FIG. 1. Scheme of three interacting neurons. (a)–(d) Four characteristic cases described in the text. Note that pairwise and triplewise inputs are represented in red (dark gray) and green (dashed gray line), respectively. Correlations by chance are marked in yellow (light gray).

apparent differences between these two populations are not captured by mere pairwise correlations and even if we were just considering the case in which a population of neurons has just pairwise, common inputs, there might also be triplewise correlations by chance, as previously conveyed. If such were the case, we would need the term $I_{\text{cor-ch},3}$, which quantifies the amount of information provided by mixture of real pairwise and triplewise correlations by chance. Next we discuss how accounting for the $I_{\text{cor-ch},3}$ term in the series expansion can change the synergy or redundancy scenario when considering a population of neurons.

## IV. SYNERGISTIC AND REDUNDANT CODING IN HIGHER-ORDER TERMS

To further study how HOCs may contribute to information processing in the brain, we need to evaluate how the $I_{\text{cor-ch},3}$ component in each higher-order term shapes coding when considering that neurons are interacting with each other in a population. As already explained in [42], the series expansion shows that overall correlations in the distribution of mean responses alone, i.e., signal correlations, can only lead to redundancy. To achieve a synergistic coding of information, correlations in the variability of the responses (or noise correlations) are needed. It can be proved that even when the latter are independent of the stimuli, it is still possible to have synergy by taking into consideration the sign of the Shannon redundancy (obtained from Eq. (1) by subtracting the information conveyed by the population from the sum of that carried by each single cell [42]).

When correlations are taken to be independent of the chosen stimulus, i.e., $\gamma(\mathbf{r}|s) = \gamma(\mathbf{r})$, it is possible to quantitatively derive the values of $\gamma$ and $\nu$ for which the system is redundant or synergistic. That is, in the following paragraphs

we define a measure $I_{SRL}$ that allows us to define the different scenarios of redundancy or synergy when considering third-order contributions.

We consider a triplet of neurons, in which the noise correlation is taken to be stimulus independent, i.e., $\gamma_{123}(s) = \gamma_{123}$. In this framework, it is possible to analytically calculate the curves $(\gamma_{123}, \nu_{123})$ for which the mutual information changes signs. To this end, let us consider first $I_3 = 0$, as it constitutes the value for which third-order contributions change from synergistic to redundant and vice versa ($I_3 > 0$ contribute synergistically and $I_3 < 0$ redundantly, respectively). Thus, in this first case ($I_3 = 0$),

$$
\begin{aligned}
0 = \langle \bar{r}_1(s)\rangle_s \langle \bar{r}_2(s)\rangle_s \langle \bar{r}_3(s)\rangle_s \Bigg[ &\nu_{123} + (1+\nu_{123}) \\
&\times \ln\left(\frac{1}{1+\nu_{123}}\right) \Bigg] + \langle \bar{r}_1(s)\bar{r}_2(s)\bar{r}_3(s)\rangle_s \gamma_{123} \\
&\times \ln\left(\frac{1}{1+\nu_{123}}\right) + 0 + \Bigg\langle \bar{r}_1(s)\bar{r}_2(s)\bar{r}_3(s) \\
&\times [1 + \gamma_{123}] \ln\Bigg[ \frac{\bar{r}_1(s)\bar{r}_2(s)}{\langle \bar{r}_1(s')\bar{r}_2(s')\rangle_{s'}} \frac{\bar{r}_1(s)\bar{r}_3(s)}{\langle \bar{r}_1(s')\bar{r}_3(s')\rangle_{s'}} \\
&\times \frac{\bar{r}_2(s)\bar{r}_3(s)}{\langle \bar{r}_2(s')\bar{r}_3(s')\rangle_{s'}} \Bigg] \Bigg\rangle_s.
\end{aligned}
\tag{15}
$$

As expected, when correlations are taken to be independent of the chosen stimulus, $I_{\text{cor-dep},3}$ becomes zero under this assumption. However, the other terms remain relevant (see Sec. II). After some algebra,

$$
\gamma_{123} = \frac{\frac{\nu_{123}}{1+\nu_{123}} - [\ln(1+\nu_{123}) + f(\bar{\mathbf{r}})]}{[\ln(1+\nu_{123}) + f(\bar{\mathbf{r}})]},
\tag{16}
$$

where we define the function $f(\bar{\mathbf{r}})$ as

$$
\begin{aligned}
f(\bar{\mathbf{r}}) &= f(\bar{r}_1(s),\bar{r}_2(s),\bar{r}_3(s)). \\
&= \frac{1}{\langle \bar{r}_1(s)\bar{r}_2(s)\bar{r}_3(s)\rangle_s} \Bigg\langle \bar{r}_1(s)\bar{r}_2(s)\bar{r}_3(s) \\
&\quad \times \ln\Bigg[ \frac{\bar{r}_1(s)\bar{r}_2(s)}{\langle \bar{r}_1(s')\bar{r}_2(s')\rangle_{s'}} \frac{\bar{r}_1(s)\bar{r}_3(s)}{\langle \bar{r}_1(s')\bar{r}_3(s')\rangle_{s'}} \\
&\quad \times \frac{\bar{r}_2(s)\bar{r}_3(s)}{\langle \bar{r}_2(s')\bar{r}_3(s')\rangle_{s'}} \Bigg] \Bigg\rangle_s,
\end{aligned}
\tag{17}
$$

where $f(\bar{\mathbf{r}})$ is a normalized average of the product of the triplet of neuron's firing rates weighted on the natural logarithm of the product of the normalized pairwise firing rates [50]. Notice that if pairs of neurons do not code for the stimuli, then $f(\bar{\mathbf{r}})$ is null. Thus, we study in the following the sign of the third-order information components in the regions delimited by the curves determined by Eq. (16). Let us now consider the case $I_3 \neq 0$. If $I_3$ is positive, then its contribution is synergistic; otherwise, when $I_3$ is negative, it is redundant. We then estimate the synergy contribution of the triplets as $I_{SRL} = I - (I_{\text{lin}} + I_2)$, which is calculated as the total mutual information $I$ [Eq. (9)] minus the linear sum of the information conveyed by each individual cell ($I_{\text{lin}}$) and minus the pairwise contributions to the information $I_2$, considering just three neurons and imposing the constraint that all correlations are taken to be independent of the chosen stimulus. After some algebra, the synergy $I_{SRL}$
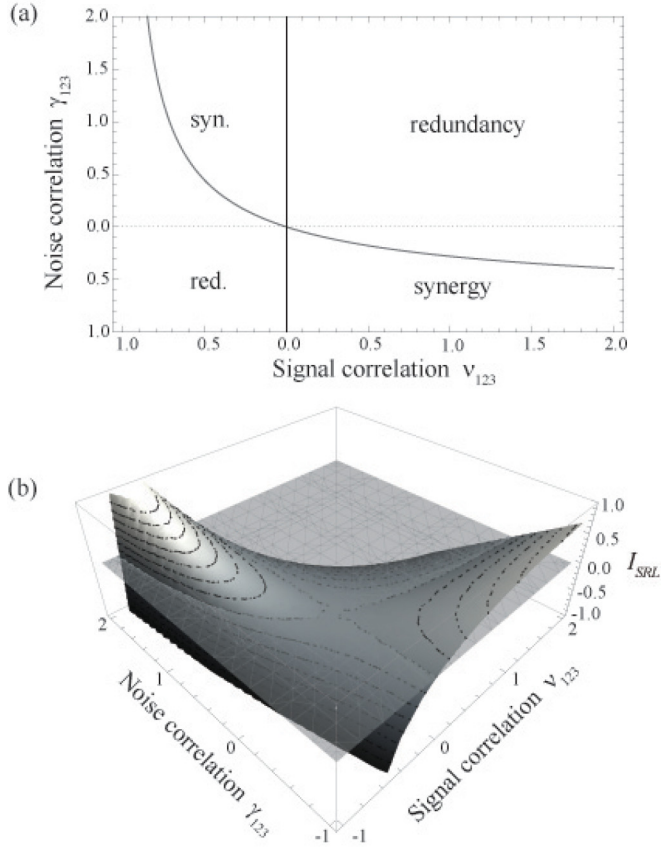
FIG. 2. $I_{SRL}$ (bits) versus triplewise noise correlation $\gamma_{123}$ versus triplewise signal correlation $\nu_{123}$. The consideration of a triplet of neurons, in which the noise correlation is taken to be stimulus independent, illustrates the range of possible dynamics when $f(\bar{\mathbf{r}})=0$ (or $I_{\text{cor-ch},3}=0$). (a) Regions with the positive values of $I_{SRL}$ that correspond to synergy and negative values that correspond to redundancy (taking the plane $\gamma_{123}$ versus $\nu_{123}$). (b) The 3D plot of $I_{SRL}$ versus $\gamma_{123}$ versus $\nu_{123}$ corresponding to the above plane. As expected, values above the zero axis indicate synergistic encoding, while values below zero indicate redundancy.

reads as

$$
\begin{aligned}
I_{SRL} = \langle \bar{r}_1(s) \rangle_s \langle \bar{r}_2(s) \rangle_s \langle \bar{r}_3(s) \rangle_s \{ \nu_{123} \\
- (1 + \nu_{123})(1 + \gamma_{123})[\ln(1 + \nu_{123}) \\
+ f(\bar{r}_1(s), \bar{r}_2(s), \bar{r}_3(s))] \}.
\end{aligned}
\tag{18}
$$

If $I_{SRL}$ is positive, then, as expected, the contribution of the triplets to the code is said to be synergistic; on the contrary, when $I_{SRL}$ is negative, it is redundant. If this quantity is zero, then the code is, at most, nonlinear at a pairwise level. Note in Eq. (18) that the factor outside the braces given by $\langle \bar{r}_1(s) \rangle_s \langle \bar{r}_2(s) \rangle_s \langle \bar{r}_3(s) \rangle_s$ is strictly positive as it depends exclusively on the mean firing rates of the neurons considered.

Figures 2 to 4 illustrate the different coding regimes for the third-order term in a three-cell example, when analyzing $I_{SRL}$ versus $\gamma_{123}$ versus $\nu_{123}$. When the $I_{\text{cor-ch},3}$ term is zero, then the analysis is the same as in [42] for the two-cell example when just considering pairwise correlations, and which corresponds to Figs. 2(a) and 2(b). That is to say, from the results shown in Figs 2(a) and 2(b) we have taken
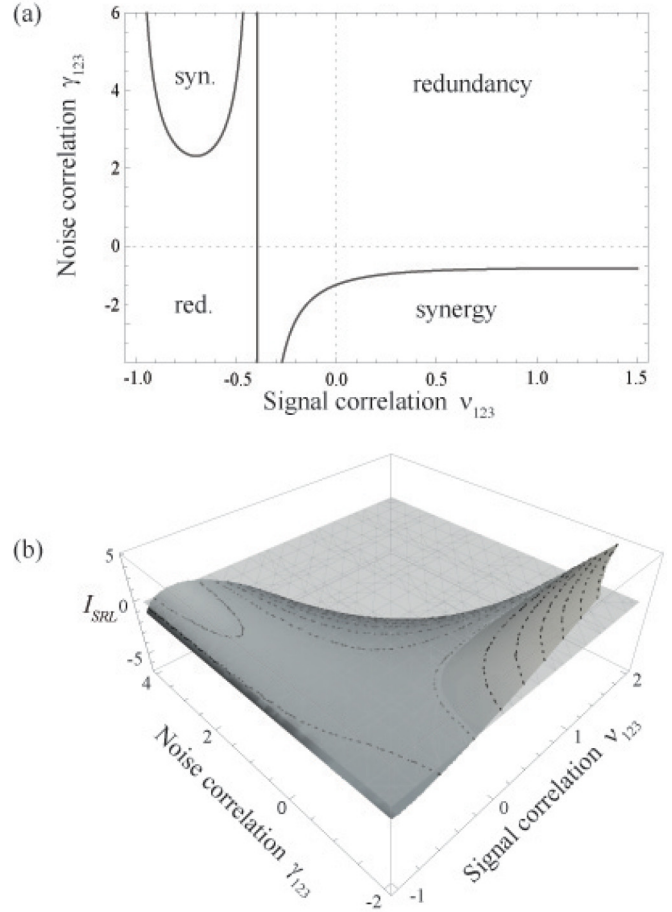


FIG. 3. $I_{SRL}$ (bits) versus triplewise noise correlation $\gamma_{123}$ versus triplewise signal correlation $\nu_{123}$. Same as in Figs. 2(a) and 2(b) but considering $f(\bar{\mathbf{r}}) > 0$ (then $I_{\text{cor-ch},3} \neq 0$).

$f(\bar{\mathbf{r}}) = 0$, and in this case when considering triplewise noise correlation $\gamma_{123}$ versus triplewise signal correlation $\nu_{123}$, the zones of redundancy and synergy are exactly the same as the one shown in the case of pure pairwise correlations [42]. Thus, in such a scenario, when $f(\bar{\mathbf{r}}) = 0$, the zones of synergy and redundancy are defined just by pairwise correlations as in [42]. If the mean responses of each neuron to the various stimuli are uncorrelated, $\nu_{123} = 0$, then (independently of the value of the noise correlation $\gamma_{123}$) the redundancy is exactly zero, as shown along the vertical axis line of Fig. 2(a) [see also the dashed line parallel to the $\gamma_{123}$ axis in Fig. 2(b)]. If the cells anticovary in their response profiles to stimuli, then, to obtain synergy, they must have a positive-valued noise correlation above the boundary established. On the contrary, if the cells do have positive signal correlation, then coincidences must be actively suppressed by a negative noise correlation stronger than the corresponding boundary value. When the signal and noise correlations have the same sign, one always obtains redundancy in the short time scale limit. Figure 2(b) shows, in addition to this, that the gradient of the amount of redundancy or synergy becomes steeper with respect to noise correlation as the signal correlation increases, in comparison to the lack of variability when the signal correlation is small regardless of the value of the noise correlation. When the
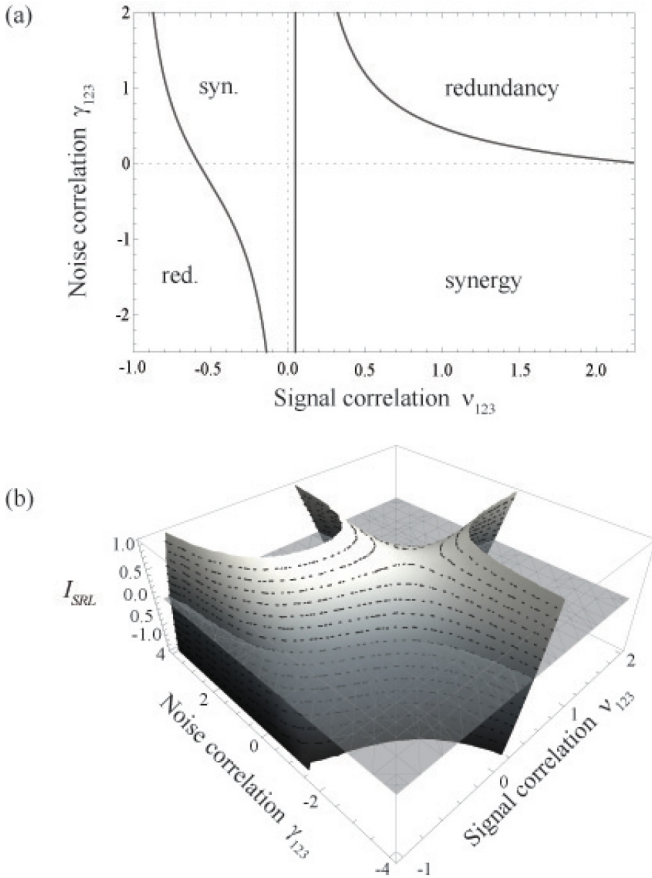
FIG. 4. $I_{SRL}$ (bits) versus triplewise noise correlation $\gamma_{123}$ versus triplewise signal correlation $\nu_{123}$. Same as in Figs. 2(a) and 2(b) but considering $f(\bar{\mathbf{r}}) < 0$ (then $I_{\text{cor-ch},3} \neq 0$).

neurons covary in the mean number of spikes they fire to each stimulus, all else being equal, we have a redundant situation. However, if there is enough anticorrelation in the noise, or vice versa there is anticorrelation in the signal and enough positive correlation in the noise, then the coding becomes synergistic.

However, when the $I_{\text{cor-ch},3}$ term is nonzero (either positive or negative), there is a substantial modification in the correlational dynamics. Analytically, we find that this change depends on the value of $f(\bar{\mathbf{r}})$, a function that solely depends on the average firing rates of the three neurons in question. Even when its value is small, it has great impact on the interplay of the noise and signal correlations. On the one hand, as can be seen in Figs. 3(a) and 3(b), when $f(\bar{\mathbf{r}})$ is positive, then the redundancy region is greatly increased for expected values of correlations. Still, it is possible to achieve synergy for positive signal correlation and negative noise correlation below a certain threshold. On the other hand, when $f(\bar{\mathbf{r}})$ is negative, as shown in Figs. 4(a) and 4(b), then small correlations of any sign lead to synergy, whereas it is possible to have a redundant code surpassing a threshold for signal and noise correlations of opposite signs. For both cases, the total amount of redundancy or synergy is much more sensitive to variation when both noise and signal correlations are high. It is important to remark that in both cases presented in Figs. 3, 4(a), and 4(b), when $f(\bar{\mathbf{r}}) \neq 0$ ($I_{\text{cor-ch},3} \neq 0$), triplewise correlations completely redefine the possible scenarios of synergy and redundancy.

There is evidence that cooperative computation characterizes neuronal interactions on various time and spatial scales [51–54]. Direct evidence shows that pairwise neuronal correlation analysis does not resolve such cooperative population dynamics [14–21,45,55]. We have shown the existence of a mixed stimulus-dependent correlation term that defines a new scenario when analyzing HOCs, putting in evidence the limitations of only considering pairwise neuronal correlation on spike trains in a three-neuron system. We used an extension of the MI series expansion for short time scales to explicitly estimate a mixed term between pairwise and triplewise stimulus-dependent correlations through $I_{\text{cor-ch},3}$, which greatly modifies the interplay between correlation in the noise and correlation in the signal that could lead to either redundancy or synergy depending on the firing rates averaged over trials and stimuli.

## V. VON MISES STIMULI AND INTEGRATE-AND-FIRE NETWORK

A stochastic process that generates a sequence of events, a spike train, for example, is said to be a Poisson process if the probability of an event occurring at any given time is independent of the immediately preceding event. Despite its obvious limitations, the Poisson process has proven to provide an extremely useful approximation of stochastic neuronal firing of a neuronal population when properly extended. The methodology we used to perform our computational modeling of a small populations of correlated neurons is similar to the one used in Ref. [56,57] and has been previously applied in [3,4,11,41,42]. In the following, we consider an inhomogeneous Poisson process, which produces variations in the firing rate. In order to do so, the probability $\{P(t_i)\}$ of having $N$ spikes at a time window $t_i$ (the index $i$ spans from 1 to $M$, so that $0 \leqslant t_1 \leqslant t_2 \leqslant \cdots \leqslant t_M \leqslant T$) is expressed as [3,4,11,41,56,57]

$$P(t_i) = \frac{[\Lambda_\theta(t_i)]^N}{N!} \exp{[-\Lambda_\theta(t_i)]}, \tag{19}$$

where $\Lambda_\theta$ at a given $t_i$ is built by incorporating the different stimulus conditions for a given time $t_i$, which is defined as

$$\Lambda_\theta(t_i) = [m + a \exp(b\{\cos[(\theta + \varphi) - \theta_{\text{pref}}] - 1\})]t_i. \tag{20}$$

That is, $\Lambda_\theta$ is the predicted function of the stimuli for a given time $t_i$. Note that the process is defined as nonhomogeneous since the average rate of arrivals is allowed to vary with time. For the computational model we chose values similar to the ones adopted in [58]: $m = 15$, which is an offset; $a = 1.3$ determines the height of the tuning curve; $b = 3$ determines the tuning bandwidth (quantified as the width of tuning halfway between the minimum and maximum evoked response); $\theta_{\text{pref}} = \frac{\pi}{4}$ is the preferred orientation; and $\theta$ is the stimulus orientation (spans from 0 to $2\pi$). The firing rate modulations across neurons are produced by taking a von Mises dependency [58] and by incorporating a phase shift in the stimulus dependency $\varphi = \frac{\pi}{10}$ between the different cells. In practice, this is made for each cell throughout the random numbers chosen from the Poisson distribution with parameter fed by $\Lambda(t_i)$ at the given time $t_i$. Thereafter, considering different trails, we build the probabilities of having

a particular response **r** conditional to stimulus $s = \theta$. This generates different inhomogeneous Poisson processes where the correlation across neurons them are generated by the different firing rate modulations as in [3,4,11,41]. The main idea behind this computational modeling is that nearby neurons share common inputs and have similar receptive fields (see, for instance, [11]). Thus, it can be assumed that the firing rate of each neuron approximately follows an inhomogeneous Poisson statistics, and by taking a phase shift in the stimulus dependency between each of the cells the rate modulations are generated. This has experimental support as it has been recently proved that the rate modulations can indeed increase correlations across neurons [59].

In the following we consider the case shown in Fig. 1(d) that illustrates the case in which three neurons share pairwise and triplewise inputs. We carried out the computational modeling described above with a set of two and three cells with inhomogeneous Poisson firing, in which spikes are not independent because of the rate modulation in their inputs as in [3,4,11,41,56,57]. We consider three ensembles of pairs of neurons given by the pairs $\{x_1, x_2\}$, $\{x_1, x_3\}$, and $\{x_1, x_3\}$, which have pairwise correlations due to rate modulations. This is carried out by properly truncating the response space of the ensemble $\{x_1, x_2, x_3\}$. Finally, we consider the triplewise correlations within $\{x_1, x_2, x_3\}$, which are three cells generated with inhomogeneous Poisson firing as described above. To compute the degree of synergy in the population for a range of time windows, we calculated a synergy index (which we call the synergy fraction [11]) as

$$\text{synergy fraction} = 1 - \frac{I_{\text{lin}}}{I}. \quad (21)$$

Values higher than 0 indicate synergistic coding, whereas values lower than 0 indicate redundancy. Note that as we pointed out in Sec. IV if $I_{\text{cor-ch},3} \neq 0$, there is a substantial modification in synergy and redundancy regions as triplewise correlations change the dynamics compared with the case in which just pure pairwise correlations are considered. Thus, triplewise correlations in such case may lead to either synergy or redundancy. Figure 5 shows the synergy fraction when considering the inhomogeneous Poisson simulation with three different cells as in Figs. 1(c) and 1(d), a time step of 1 ms, 1000 trials, and 100 different von Mises stimuli. In particular, Fig. 5(a) shows that as the time window is increased, the redundancy becomes larger when just pairwise correlations in the neuronal ensemble $\{x_1, x_2\}$, $\{x_2, x_3\}$, and $\{x_1, x_3\}$ are considered. In this Fig. 5(a) we estimate the synergy fraction when considering the kind of interaction shown in Fig. 1(c). However, this is not the case when the effect of triplewise correlations is also taken into account, as in Fig. 1(d). This is illustrated in Fig. 5(b), where the effect of adding third-order stimulus-dependent correlations increases the synergy fraction as the time window becomes larger. This can be explained by the fact that there is a significant amount of stimulus-independent correlations at third order, as shown in Fig. 5(c). This effect become more relevant as the time window increases. Notice from Fig. 5(c) that $I_{\text{cor-ch},3} \neq 0$, and thus when considering the interactions described in Fig. 1(d), triplewise correlations become relevant. As we discussed at the end of Sec. IV, the scenario of $I_{\text{cor-ch},3} \neq 0$ allows us to redefine
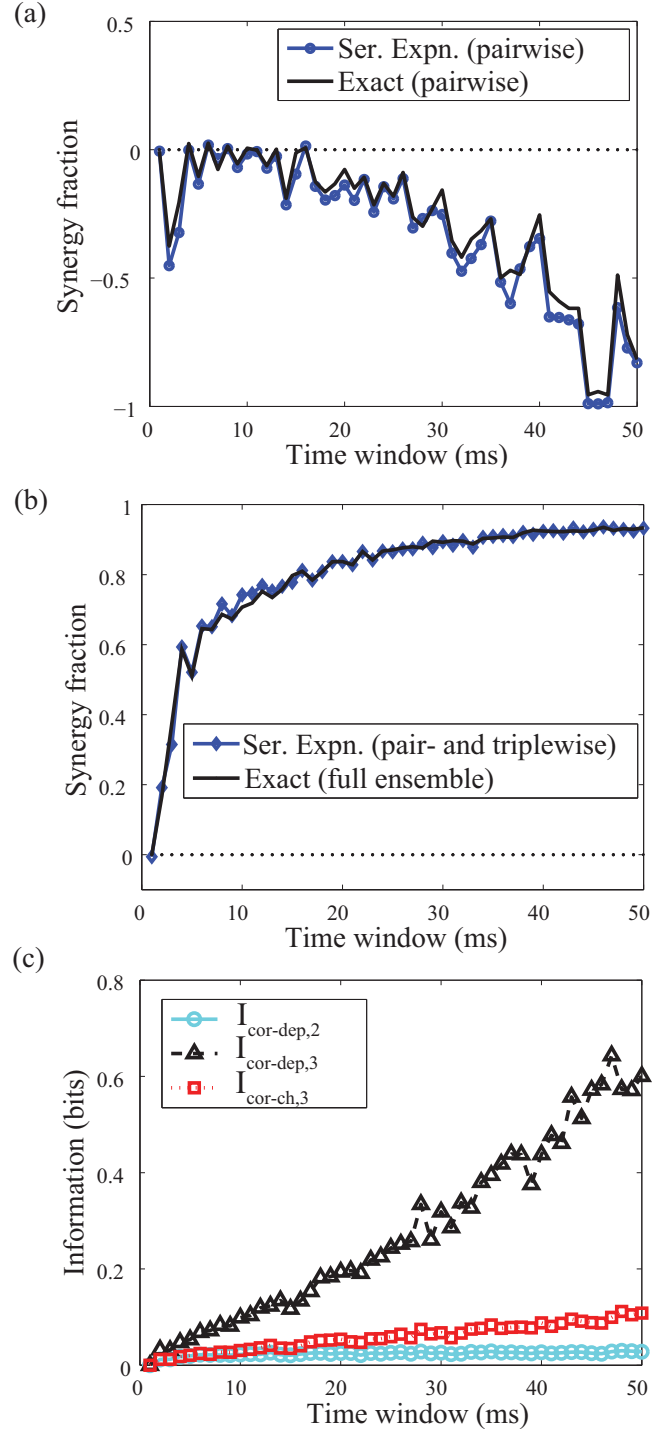


FIG. 5. (a) Synergy fraction when considering just pairwise correlations as in Fig. 1(c). The blue (gray) line shows the synergy fraction using the total mutual information $I$ obtained using the series expansion, while the black line shows the one obtained using the definition shown in Eq. (1). (b) Same as (a), but estimating the synergy fraction when triplewise correlation terms are also included as in Fig. 1(d). (c) Contributions of the stimulus-dependent correlation components.

the "achievable regions" of synergy and/or redundancy when compared with the case in which just pairwise correlations are taken into account.

In a biologically realistic neural network, it often takes multiple inputs for a neuron to be able to propagate a signal. A simple representation of this is to consider multiple input signals connecting one neuron to the next, increasing or decreasing the effect of single neuronal firing. This is achieved by adjusting the connection weights between each neuron and thus, in a computer simulation of a neural network, we can mimic neural dynamics through a methodology known as integrate-and-fire [60]. When the neuron membrane potential reaches its threshold, it fires a spike and the signal is transmitted to another neuron. Then, the propagated signal could induce a spike in this new neuron. If the neuron does not fire, its potential may be increased and when it receives another input within a relatively short time window, it will be more likely to reach the threshold and fire a spike.

To study the hypothesis of synergy and redundancy regimes when correlations are independent of the chosen stimulus, spike trains were simulated using a small, fully connected network of integrate-and-fire neurons. In this model, neurons were activated using brief initial random current inputs and could continuously exhibit self-sustained activity [60,61]. Despite its simplicity, the integrate-and-fire model with balanced excitation and inhibition can account for several aspects of the firing statistics observed in the responses of neurons across large regions of the cerebral cortex [60,61]. To test our theoretical framework, we performed simulations using the model previously explained to obtain numerical values for the different variables compatible with the assumptions and approximations made. It is important to point out that when the $I_{\text{cor-ch},3}$ term is nonzero (either positive or negative), there is a substantial modification in the correlational dynamics. This alteration depends on the value of $f(\bar{\mathbf{r}})$, which is a function of the firing rates of the three neurons in question. For a triplet of neurons taken from the population, a redundant contribution ($I_{SRL} < 0$) was obtained with $f(\bar{\mathbf{r}}) \approx 0.24$ and $\nu_{123} = 0.07$, with $\gamma_{123} = 0.000\,001$ close to zero. The interplay between correlation in the noise and correlation in the signal leads, in this case, to redundancy as in Figs. 3(a) and 3(b).

## VI. IZHIKEVICH SPIKING NETWORK

Neurons fire spikes when they are near a bifurcation from resting to spiking activity, and it is the delicate balance between noise, dynamic currents, and initial condition that determines the phase diagram of neural activity. While there is a huge number of possible ionic mechanisms of excitability and spike generation, there are just four bifurcation mechanisms that can result in such a transition. These bifurcations divide neurons into four categories: integrators or resonators, monostable or bistable [62]. Bifurcation methodologies [62] allow us to accurately reproduce the biophysical properties of Hodgkin-Huxley neuronal models by just taking a two-dimensional system of ordinary differential equations and four different parameters. This model is named "simple model of spiking neurons" [63], and the system of ordinary differential equations reads

$$\frac{dv}{dt} = 0.04v^2 + 5v + 140u + i_c, \tag{22}$$

$$\frac{du}{dt} = a(bv - u), \tag{23}$$

with the auxiliary after-spike resetting

$$\text{if } v \geqslant +30\,\text{mV}, \quad \text{then} \quad \begin{cases} v \leftarrow c, \\ u \leftarrow u + d, \end{cases} \tag{24}$$

where $v$ is the membrane potential of the neuron and $u$ is a membrane recovery variable, which accounts for the activation of $K_+$ ionic currents and inactivation of $Na_+$ ionic currents and gives negative feedback to $v$. Thus, we are just considering a two-dimensional system of ordinary differential equations of two variables $u$ and $v$, and all the known types of neurons can be reproduced by taking different values of the four parameters $a$, $b$, $c$, and $d$. After the spike reaches its apex at $+30$ mV (not to be confused with the firing threshold), the membrane voltage and the recovery variable are reset according to Eq. (24). The variable $i_c$ is a noisy thalamic current of the model [63–65].

Summing up, each neuron can be described by a simple spiking model that allows us to reproduce several of the most fundamental neurocomputational features of biological neurons [64]. Here we consider a network simulation model in which the number for interconnected neurons is a parameter under control, and each neuron can be interconnected randomly with two or more neurons [63–65]. The inhibitory inputs hyperpolarize the potential and move it away from the threshold. In contrast, excitatory inputs depolarize the membrane potential (i.e., they bring it closer to the threshold).

We consider a network simulation that takes into account cortical spiking neurons with axonal conduction delays and spike-timing-dependent plasticity as a Hebbian synaptic learning rule. The magnitude of the synaptic weight between presynaptic neurons depends on the timing of the spikes. That is, the weight of the synaptic connection from the pre- to postsynaptic neurons increases as $0.1 \times \exp -(t/t_0)$ if the postneuron fires after the presynaptic spike, where $t_0 = 20$ ms and $t$ is the interspike interval. Otherwise, if the order of the spikes is reversed, it decreases as $0.12 \times \exp (t/t_0)$ [65]. Each neuron in the network is described by the simple model of spiking neurons of [63], which has been described above in Eq. (22) to Eq. (24). We considered different stimulus configurations by changing the parameter $a$ that describes the time scale of the recovery variable (we have always taken values of $a > 0$). The parameter $a$ describes the time scale of the recovery variable $u$ (smaller values result in slower recovery). For the computational modeling we take ten different stimuli $s$ as ten different equispaced values of $a$ that span from 0.01 to 0.1 (a typical value is $a = 0.02$ [63]). In order to perform our information theoretical estimation we considered 10 000 trials and 10 different stimuli and performed an average over a time window of 10 ms. Then on the basis of the data generated by our computational model, we build the probabilities of having a particular response **r** equal to 0 or 1 (where 0 denotes no spike events and 1 that a spike is being fired in the considered time window) conditional to the stimulus $s$ described above.

Let us consider a network consisting of three neurons taking into account two cases: one in which the neurons have just pairwise common inputs in their excitatory synapsis ($M = 2$) and the other with triplewise ($M = 3$) common inputs in their excitatory synapsis. That is, Fig. 6 shows the different stimulus-dependent correlation components considering these two Hebbian networks in which the excitatory synapsis per
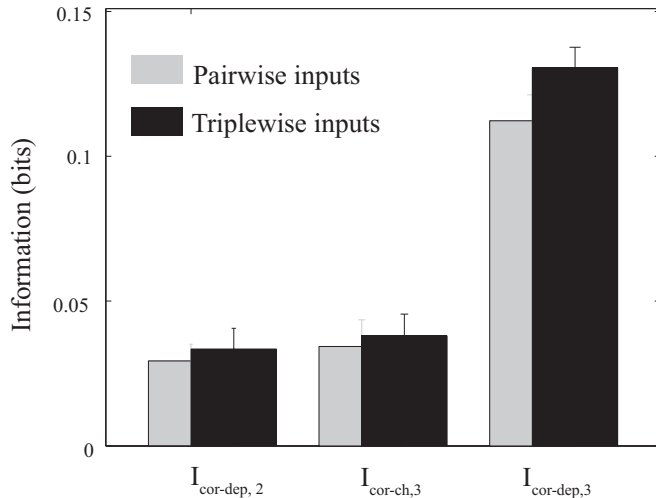
FIG. 6. Izhikevich spiking network. Gray and black bars represent networks with pairwise and triplewise input connectivity, respectively. Note that triplewise connectivity is reflected in a higher amount of stimulus-dependent correlations, and $I_{\text{cor-ch},3}$ contributes in either case with an important amount of information.

neuron is equal to $M = 2$ and $M = 3$, respectively. The number of excitatory synapses per neuron is implemented here in the same way as in Ref. [65], which is the standard way of implementing this kind of modeling. We illustrate how increasing the network input connectivity may affect the stimulus-dependent correlation. Notice that $I_{\text{cor-ch},3}$ contributes in both cases with an important amount of information. In this case, the possible "chance" triplets of spikes that may have arisen from second-order correlations would contribute to an underestimation of information if they were not taken into account. In the current model, the stimulus-dependent correlations of second and third order increase the total amount of information as the input connectivity becomes larger. Note that triplewise connectivity is reflected in a higher amount of stimulus-dependent correlations.

## VII. DISCUSSION AND CONCLUSIONS

The emergent properties of any complex system cannot be reduced, in general, to pairwise interactions [14–19,44]. Importantly, if triplet or higher-order correlations are present in the data, they could not be visible, and they may just be perceived as pairwise correlations [66]. Unlike other simpler correlation measures, information has the unique advantage of capturing all nonlinear dependencies of any statistical order that may be present in the data. The simple comparison between the information of an ensemble of neurons and the sum of information provided by individual neurons combines several forms of correlations [11,41]. It is therefore natural to ask under what conditions groups of neurons represent stimuli and direct behavior in either a synergistic, redundant, or independent manner. In this sense, a crucial point in understanding the representation of external stimuli by the activity of a population of neurons is how the information conveyed by individual cells combines together [42].

The main advantage of our current approach is that it allows us to account for hidden variables dynamically linked together that are not accessible to measure. They are expressed in our numerical estimations through a mixed term of pairwise and triplewise stimulus-dependent correlations by chance, $I_{\text{cor-ch},3}$. We provide, for any order, the analytical estimation of the correction that might be produced by hidden variables through the novel term $I_{\text{cor-ch},3}$. Note that the series expansion approach should not be applied to long poststimulus windows or large populations. These limitations were previously explored in [50], where the generality of this framework is challenged even further. However, a powerful feature of our current approach is that we are in absolute control of which correlation order dominates the data and the proper quantification of the possible stimulus-dependent correlations by chance through $I_{\text{cor-ch},3}$.

We investigated the limitations of performing a pairwise analysis, using an extension of the MI series expansion for short time scales. Moreover, as it has been previously pointed out by Martignon *et al.* [45], independent inputs can be such that firing rates of individual neurons and pairwise correlations may lead to triplewise correlations by chance. Thus, if we were considering two populations of neurons, one with just pure pairwise correlations and the other with pure pairwise correlations as well but also with chance coincidence at triplewise level, the differences between these two populations would not be detected by a cross correlogram or even using standard information breakdown methodologies [11,41,44,67–69]. It is HOCs that determine whether coincident spikes of two neurons are also coincident with the spikes of the third neuron through the stimulus-dependent correlational component by chance term, $I_{\text{cor-ch},3}$.

This paper was intended as a study of HOCs and not an improved pairwise framework. In this sense, our work aims to quantify the effect of chance correlations on information processing in a population of neurons. We show that to properly quantify pairwise correlations it is also necessary to account for triplewise correlations, as the term $I_{\text{cor-ch},3}$ defines a new scenario even if there is no impact from pure triplewise interactions. More specifically, depending on the value of $f(\bar{\mathbf{r}})$ (a function of the mean values of the firing rates of the neurons considered, e.g., a triplet of cells), which is directly related to the mixed stimulus-dependent correlation term (see Sec. IV), when the $I_{\text{cor-ch},3}$ term is nonzero, there is a substantial modification in the correlational dynamics. When this function $f(\bar{\mathbf{r}})$ is positive, it results in a coding regime more similar to the traditional intuition in which correlations tend to result in redundancy and thus limit the number of neurons whose output could usefully be combined to represent the stimulus variable. On the contrary, if $f(\bar{\mathbf{r}})$ is negative, it leads to larger regions of synergy in the plane noise versus signal correlations. Importantly, when $f(\bar{\mathbf{r}}) = 0$, which means $I_{\text{cor-ch},3} = 0$, the regions of synergy and redundancy in the plane noise versus signal correlations are qualitatively equivalent as the one defined by pure pairwise correlations as in [42]. The present study is the first attempt to provide an analytical expression to quantify the mixed stimulus-dependent correlation by chance involving an order higher than two neuronal interactions. Our current study does not only rigorously demonstrate that correlations do not imply redundancy, but also that HOCs

could increase the amount of synergy. Moreover, using a Poisson simulation with von Mises stimuli dependency, we have shown that stimulus-dependent correlations should not be neglected: The effect of stimulus-dependent correlations of third order increases the synergy fraction. In addition, using a spiking network simulation, we convey that the possible "chance" triplets of spikes that may have arisen from second-order correlations would contribute to an underestimation of information if they were not taken into account and also that an increase in the connectivity might be reflected in a higher amount of stimulus-dependent correlations.

The possibility of synergy with correlations of order higher than two is an important issue as they prove to be an inherent property of cortical dynamics. The extension of the information expansion we have introduced shows excess synchrony that cannot be explained by simply considering up to pairwise correlations, and HOCs redefine the boundaries of the regions of synergy and redundancy. We have conveyed this issue on a solid mathematical background, and, for short time windows at third-order level, we have presented the exact boundaries of the regions of synergy and redundancy. Thus, the structure of higher-order interactions and their contributions to cortical dynamics are still open to debate. Furthermore, if one is interested in studying the interaction structure, the present approach can be useful to reveal the underlying structure of the neural cortex. As our results demonstrate that true pairwise interactions can only be completely captured if potential higher-order interactions are taken into account, our current approach could also be a very useful complementary tool to other large population methods [21,26,27] to quantify the degree of synchronous activity in neuronal avalanches [70].

## APPENDIX A

A natural mathematical definition [30] for the normalized cross-correlation strength of population response $\mathbf{r}$ (noise correlation) is the following:

$$\gamma(\mathbf{r}|s) = \begin{cases} \frac{P(\mathbf{r}|s)}{P_{\text{ind}}(\mathbf{r}|s)} - 1 & \text{if } P_{\text{ind}}(\mathbf{r}|s) \neq 0, \\ 0 & \text{if } P_{\text{ind}}(\mathbf{r}|s) = 0. \end{cases} \quad \text{(A1)}$$

The probability of independent population responses $P_{\text{ind}}(\cdot)$ can be obtained by taking the product of the probability distributions of individual cells:

$$P_{\text{ind}}(\mathbf{r}|s) = \prod_{i=1}^{N} P(r_i|s). \quad \text{(A2)}$$

Since $\gamma(\mathbf{r}|s)$ are response-dependent quantities, they have to satisfy (for each stimulus $s$) a zero-sum constraint:

$$\sum_{\mathbf{r}} P_{\text{ind}}(\mathbf{r}|s)\gamma(\mathbf{r}|s) = 0. \quad \text{(A3)}$$

This constraint stems directly from the normalization to one of the response probabilities. We name $P_{\text{ind}}(\mathbf{r}) = \langle P_{\text{ind}}(\mathbf{r}|s)\rangle_s$. The "signal similarity" coefficient (signal correlation) is defined as

$$\nu(\mathbf{r}) = \begin{cases} \frac{P_{\text{ind}}(\mathbf{r})}{\prod_{i=1}^{N} P(r_i)} - 1 & \text{if } \prod_{i=1}^{N} P(r_i) \neq 0, \\ 0 & \text{if } \prod_{i=1}^{N} P(r_i) = 0. \end{cases} \quad \text{(A4)}$$

It depends only on response probabilities of individual neurons and, thus, satisfies a normalization condition similar to (A3), as follows:

$$\sum_{\mathbf{r}} \left[ \prod_{i=1}^{N} P(r_i) \right] \nu(\mathbf{r}) = 0. \quad \text{(A5)}$$

As a ratio of the full and independent probabilities, they convey how likely it would be to find correlated (in comparison to independent) events in the ensemble. Despite being similarly defined, the main difference between these two measures is stimulus modulation.

## APPENDIX B

The components of the exact information breakdown are given below, as in [11,30]. The activity of $C$ cells is observed and each possible population response $\mathbf{r}$ is composed by the individual cell responses $r_1, \ldots, r_C$. The total amount of information that would be conveyed if all of the cells were independent, $I_{\text{lin}}$, reads as

$$I_{\text{lin}} = \frac{1}{\ln 2} \sum_c \sum_{r_c} \left\langle P(r_c|s) \ln \frac{P(r_c|s)}{P(r_c)} \right\rangle_s. \quad \text{(B1)}$$

Here sums are carried on for each cell $c$ and each possible response of such cell, since no further assumption was made about the response probability. The signal similarity term, $I_{\text{sig-sim}}$, is given by

$$I_{\text{sig-sim}} = \frac{1}{\ln 2} \sum_{\mathbf{r}} \left[ \prod_c P(r_c) \right] \left\{ \nu(\mathbf{r}) + [1 + \nu(\mathbf{r})] \right.$$
$$\left. \times \ln\left[ \frac{1}{1 + \nu(\mathbf{r})} \right] \right\}. \quad \text{(B2)}$$

The total amount of information attributable to the correlated activity on the overall neural coding ($I_{\text{cor}}$) is defined as $I_{\text{cor}} = I_{\text{cor-ind}} + I_{\text{cor-dep}}$, where the stimulus-independent component, $I_{\text{cor-ind}}$, reads as

$$I_{\text{cor-ind}} = \sum_{\mathbf{r}} \langle P_{\text{ind}}(\mathbf{r}|s)\gamma(\mathbf{r}|s)\rangle_s \log_2\left[ \frac{1}{1 + \nu(\mathbf{r})} \right] \quad \text{(B3)}$$

and a stimulus-dependent component, $I_{\text{cor-dep}}$, reads as

$$I_{\text{cor-dep}} = \sum_{\mathbf{r}} \left\langle P_{\text{ind}}(\mathbf{r}|s)[1 + \gamma(\mathbf{r}|s)] \right.$$
$$\left. \times \log_2\left\{ \frac{\langle P_{\text{ind}}(\mathbf{r}|s')\rangle_{s'}[1 + \gamma(\mathbf{r}|s)]}{\langle P_{\text{ind}}(\mathbf{r}|s')[1 + \gamma(\mathbf{r}|s')]\rangle_{s'}} \right\} \right\rangle_s. \quad \text{(B4)}$$

## APPENDIX C

The mutual information about the whole set of stimuli transmitted by the population response [46,71,72] can alternatively

be written to Eq. (1) as

$$I = H(\mathbf{r}) - H(\mathbf{r}|s), \tag{C1}$$

where $H(\mathbf{r})$ is the total response entropy

$$H(\mathbf{r}) = -\sum_{\mathbf{r}} P(\mathbf{r}) \log_2 P(\mathbf{r}) \tag{C2}$$

and $H(\mathbf{r}|s)$ is the noise entropy that quantifies the variability to repeated presentations of the same stimulus,

$$H(\mathbf{r}|s) = -\sum_{s \in \{s\}} P(s) \sum_{\mathbf{r}} P(\mathbf{r}|s) \log_2 P(\mathbf{r}|s). \tag{C3}$$

Equations (3)–(5) are the main basis of the series expansion approach [3,4,42]. For example, in the pairwise framework, the probability of having no spike fired [3,4,42] reads as

$$P(0;s) = 1 - \sum_{i=1}^{N} \bar{r}_i(s)t + \frac{1}{2} \sum_{i,j=1}^{N} \bar{r}_i(s)\bar{r}_j(s)[1 + \gamma_{ij}(s)]t^2$$
$$+ O(t^3), \tag{C4}$$

and the probability $P(r_i;s)$ of observing just one spike fired by the cell $i$ is [3,4,42]

$$P(r_i;s) = \bar{r}_i(s)t + \bar{r}_i(s)t^2 \sum_{j=1}^{N} \bar{r}_j(s)[1 + \gamma_{ij}(s)] + O(t^3), \tag{C5}$$

where $N$ denotes the number of neurons. In this framework we can write the probability of having two neurons $(r_i, r_j)$ firing a pair of spikes as [3,4,42]

$$P(r_i, r_j;s) = \bar{r}_i(s)\bar{r}_j(s)t^2[1 + \gamma_{ij}(s)] + O(t^3), \tag{C6}$$

where

$$\gamma_{ij}(s) = \frac{\overline{r_i(s)r_j(s)}}{\bar{r}_i(s)\bar{r}_j(s)} - 1 \tag{C7}$$

denotes the pairwise noise correlation. We use the overline notation to denote the averaged quantities over trials and to distinguish them from averages over stimuli. Pairwise signal correlation is defined as (see [42])

$$\nu_{ij} = \frac{\langle \bar{r}_i(s)\bar{r}_j(s) \rangle_s}{\langle \bar{r}_i(s) \rangle_s \langle \bar{r}_j(s) \rangle_s} - 1. \tag{C8}$$

Note that we can extend the previous definitions for the $n$th order of noise correlation as

$$\gamma_{i_1,\dots,i_n}(s) = \frac{\overline{r_{i_1}(s) \cdots r_n(s)}}{\bar{r}_{i_1}(s) \cdots \bar{r}_n(s)} - 1. \tag{C9}$$

Similarly, the $n$th order of signal correlation is given by

$$\nu_{i_1,\dots,i_n} = \frac{\langle \bar{r}_{i_1}(s) \cdots \bar{r}_n(s) \rangle_s}{\langle \bar{r}_{i_1}(s) \rangle_s \cdots \langle \bar{r}_n(s) \rangle_s} - 1. \tag{C10}$$

Considering this, the probability of having three neurons firing (in the third order framework) is given by Eq. (6). Moreover, the probability of having four neurons firing (up to fourth order) is written as

$$P(r_i, r_j, r_k, r_l;s) = \bar{r}_i(s)\bar{r}_j(s)\bar{r}_k(s)\bar{r}_l(s)t^4[1 + \gamma_{ijkl}(s)]$$
$$+ O(t^5), \tag{C11}$$

which is generalized for $n$ neurons that fire $n$ spikes simultaneously (in an $n$th-order framework) as

$$P(r_{i_1}, r_{i_2}, \dots, r_{i_n};s) = \bar{r}_{i_1}(s) \cdots \bar{r}_{i_n}(s)t^n[1 + \gamma_{i_1,\dots,i_n}(s)]$$
$$+ O(t^{n+1}). \tag{C12}$$

The following additional assumptions are to be made to be able to compute the series expansion: first, that the mutual information is analytic in time and, second, that different trials are random realizations of the same process. The validity of these and previous assumptions has been examined elsewhere [3,4,42,50]. Then the mutual information can be expanded as a series of the poststimulus time window as in Eq. (9). That is, we take advantage of the fact that the mutual information can be estimated in terms of signal and noise correlation contributions.

Summarizing, the information derivatives are calculated in terms of the probabilities given by Eqs. (C4), (C5), (C6), (6), (C11), and (C12) as follows. First, one inserts the probabilities of Eqs. (C4), (C5), (C6), (6), (C11), and (C12) into the sum over responses in Eq. (1). Then, for each term of the sum over responses, one uses the power expansion of the logarithm as a function of $t$,

$$\log_2(1 - tx) = -\frac{1}{\ln 2} \sum_{i=1}^{\infty} \frac{(tx)^i}{i}, \tag{C13}$$

as in [3,42]. Finally, grouping together all the terms in the sum which have the same power in $t$, and using Eq. (9), one obtains the expressions for the information derivatives reported in this paper and its encoding components of all orders.

As we mentioned in Sec. III the first and second orders of the expansion were originally reported in [42]. Moreover, the first order of the expansion (and also the first term of the information breakdown) corresponds to $I_{\text{lin}}$; i.e., no redundancy or synergy is considered. The second order, the terms which have $t^2$, is decomposed in the following components (noted by 2 to distinguish them from higher-order ones), as in [30]: $I_{\text{sig-sim,2}}$, which takes into account redundancy that can arise even in the absence of cross correlation; and the two correlational terms, $I_{\text{cor-ind,2}}$ and $I_{\text{cor-dep,2}}$, which measure the amount of information truly available from the pairwise correlated activity of the whole population. Each component expression in the series expansion up to second order is given in the following equations:

$$I_1 = I_{\text{lin}} = \sum_{i=1}^{N} \left\langle \bar{r}_i(s) \log_2 \left[ \frac{\bar{r}_i(s)}{\langle \bar{r}_i(s') \rangle_{s'}} \right] \right\rangle_s. \tag{C14}$$

At second order, the nonlinear contribution is

$$I_2 = I_{\text{sig-sim,2}} + I_{\text{cor-ind,2}} + I_{\text{cor-dep,2}} \tag{C15}$$

in which

$$I_{\text{sig-sim},2} = \frac{1}{2\ln 2} \sum_{i,j=1}^{N} \langle \overline{r}_i(s) \rangle_s \langle \overline{r}_j(s) \rangle_s$$

$$\times \left[ v_{ij} + (1 + v_{ij}) \ln\left(\frac{1}{1 + v_{ij}}\right) \right], \quad \text{(C16)}$$

$$I_{\text{cor-ind},2} = \frac{1}{2\ln 2} \sum_{i,j=1}^{N} \langle \overline{r}_i(s) \overline{r}_j(s) \gamma_{ij}(s) \rangle_s \ln\left(\frac{1}{1 + v_{ij}}\right),$$

$$\text{(C17)}$$

and

$$I_{\text{cor-dep},2} = \frac{1}{2\ln 2} \sum_{i,j=1}^{N} \left\langle \overline{r}_i(s) \overline{r}_j(s) [1 + \gamma_{ij}(s)] \right.$$

$$\times \left. \ln\left\{ \frac{\langle \overline{r}_i(s') \overline{r}_j(s') \rangle_{s'} \, [1 + \gamma_{ij}(s)]}{\langle \overline{r}_i(s') \overline{r}_j(s') [1 + \gamma_{ij}(s')] \rangle_{s'}} \right\} \right\rangle_s, \quad \text{(C18)}$$

The third-order terms are shown in Eqs. (10)–(13). In the following we provide a detailed explanation of how to perform the derivation of the third-order terms ($I_3$) and the terms displayed in Eqs. (10)–(13). Equation (6) represent the probability of having three neurons firing (up to third order in $t$), where the triplewise noise correlation and the triplewise signal correlation are given by Eqs. (7) and (8), respectively. Lower-order event (that is, one, two or zero spikes) probabilities are defined by taking into account the definitions of the pairwise correlation coefficients. In the triplewise framework, the probability of having no spikes fired reads as

$$P(0; s) = 1 - \sum_{i=1}^{N} \overline{r}_i(s) t + \frac{1}{2} \sum_{i,j=1}^{N} \overline{r}_i(s) \overline{r}_j(s) [1 + \gamma_{ij}(s)] t^2$$

$$+ \frac{5}{6} \sum_{i,j,k=1}^{N} \overline{r}_i(s) \overline{r}_j(s) \overline{r}_k(s) [1 + \gamma_{ijk}(s)] t^3 + O(t^4),$$

$$\text{(C19)}$$

the probability of observing just one spike fired by the cell $i$ is

$$P(r_i; s) = \overline{r}_i(s) t - \overline{r}_i(s) \sum_{j=1}^{N} \overline{r}_j(s) [1 + \gamma_{ij}(s)] t^2$$

$$- \frac{1}{2} \overline{r}_i(s) \sum_{j,k=1}^{N} \overline{r}_j(s) \overline{r}_k(s) [1 + \gamma_{ijk}(s)] t^3 + O(t^4),$$

$$\text{(C20)}$$

and the probability of having two neurons firing (labeled as $i$ and $j$) is expressed as

$$P(r_i, r_j; s) = \overline{r}_i(s) \overline{r}_j(s) [1 + \gamma_{ij}(s)] t^2 - \overline{r}_i(s) \overline{r}_j(s)$$

$$\times \sum_{k=1}^{N} \overline{r}_k(s) \{ [1 + \gamma_{ijk}(s)] \} t^3 + O(t^4). \quad \text{(C21)}$$

Note that $N$ denotes the number of neurons. We put then the probabilities defined in the triplewise framework by Eqs. (C19), (C20), and (C21) and Eq. (6) into the sum over $\mathbf{r}$ in

Eq. (1). Additionally, for each term of such sum we consider the power expansion of Eq. (C13) as a function of $t$. Gathering together all the terms in the sum which have the same power in $t$ and using Eq. (9) for the third order, that is, the terms with $t^3$, one obtains

$$I_3 = \frac{1}{6\ln 2} \sum_{i,j,k=1}^{N} \langle \overline{r}_i(s) \rangle_s \langle \overline{r}_j(s) \rangle_s \langle \overline{r}_k(s) \rangle_s$$

$$\times \left[ v_{ijk} + (1 + v_{ijk}) \ln\left(\frac{1}{1 + v_{ijk}}\right) \right]$$

$$+ \langle \overline{r}_i(s) \overline{r}_j(s) \overline{r}_k(s) \gamma_{ijk}(s) \rangle_s \ln\left(\frac{1}{1 + v_{ijk}}\right)$$

$$+ \langle \overline{r}_i(s) \overline{r}_j(s) \overline{r}_k(s) [1 + \gamma_{ijk}(s)]$$

$$\times \ln\left\{ \frac{\langle \overline{r}_i(s') \overline{r}_j(s') \overline{r}_k(s') \rangle_{s'} [1 + \gamma_{ijk}(s)]}{\langle \overline{r}_i(s') \overline{r}_j(s') \overline{r}_k(s') [1 + \gamma_{ijk}(s')] \rangle_{s'}} \right\} \right\rangle_s$$

$$- 3 \langle \overline{r}_i(s) \overline{r}_j(s) \overline{r}_k(s) [1 + \gamma_{ijk}(s)]$$

$$\times \ln\left\{ \frac{\overline{r}_i(s) \overline{r}_j(s) \, [1 + \gamma_{ij}(s)]}{\langle \overline{r}_i(s') \overline{r}_j(s') [1 + \gamma_{ij}(s')] \rangle_{s'}} \right\} \right\rangle_s. \quad \text{(C22)}$$

Thus, at third order, the nonlinear contribution is $I_3 = I_{\text{sig-sim},3} + I_{\text{cor-ind},3} + I_{\text{cor-dep},3} + I_{\text{cor-ch},3}$ (in analogy to [3,4,30,42,50]). The signal similarity contribution, $I_{\text{sig-sim},3}$, is specified by Eq. (10). The total amount of information attributable to third-order correlated activity on the overall neural coding is given by the stimulus-independent contribution, $I_{\text{cor-ind},3}$, and the stimulus-dependent correlation component, $I_{\text{cor-dep},3}$. The extra term that takes into account "chance" correlations is denoted as $I_{\text{cor-ch},3}$. Equations (11), (12), and (13) are the expressions of $I_{\text{cor-ind},3}$, $I_{\text{cor-dep},3}$, and $I_{\text{cor-ch},3}$, respectively.

For the sake of completeness, the fourth order of the series expansion is given below. At fourth order, the nonlinear contribution is

$$I_4 = I_{\text{sig-sim},4} + I_{\text{cor-ind},4} + I_{\text{cor-dep},4} + I_{\text{cor-ch},4}. \quad \text{(C23)}$$

The signal similarity contribution, the stimulus-independent correlation contribution, and the stimulus-dependent correlation component are, respectively,

$$I_{\text{sig-sim},4} = \frac{1}{24\ln 2} \sum_{i,j,k,l=1}^{N} \langle \overline{r}_i(s) \rangle_s \cdots \langle \overline{r}_l(s) \rangle_s$$

$$\times \left[ v_{ijkl} + (1 + v_{ijkl}) \ln\left(\frac{1}{1 + v_{ijkl}}\right) \right], \quad \text{(C24)}$$

$$I_{\text{cor-ind},4} = \frac{1}{24\ln 2} \sum_{i,j,k,l=1}^{N} \langle \overline{r}_i(s) \cdots \overline{r}_l(s) \gamma_{ijkl}(s) \rangle_s$$

$$\times \ln\left(\frac{1}{1 + v_{ijkl}}\right), \quad \text{(C25)}$$

$$I_{\text{cor-dep},4} = \frac{1}{24 \ln 2} \sum_{i,j,k,l=1}^{N} \left\langle \overline{r}_i(s) \cdots \overline{r}_l(s)[1 + \gamma_{ijkl}(s)] \right.$$
$$\times \ln \left\{ \frac{\langle \overline{r}_i(s') \cdots \overline{r}_l(s') \rangle_{s'}[1 + \gamma_{ijkl}(s)]}{\langle \overline{r}_i(s') \cdots \overline{r}_l(s')[1 + \gamma_{ijkl}(s')] \rangle_{s'}} \right\} \right\rangle_s.$$
(C26)

Finally, $I_{\text{cor-ch},4}$ reads as

$$I_{\text{cor-ch},4} = -\frac{1}{24 \ln 2} \sum_{i,j,k,l=1}^{N} \left\langle \overline{r}_i(s) \cdots \overline{r}_l(s)[1 + \gamma_{ijkl}(s)] \right.$$
$$\times \left\{ 6 \ln \left( \frac{\overline{r}_i(s)\overline{r}_j(s)\,[1 + \gamma_{ij}(s)]}{\langle \overline{r}_i(s')\overline{r}_j(s')[1 + \gamma_{ij}(s')] \rangle_{s'}} \right) \right.$$
$$\left. + 4 \ln \left( \frac{\overline{r}_i(s)\overline{r}_j(s)\overline{r}_k(s)\,[1 + \gamma_{ijk}(s)]}{\langle \overline{r}_i(s')\overline{r}_j(s')\overline{r}_k(s')[1 + \gamma_{ijk}(s')] \rangle_{s'}} \right) \right\} \right\rangle_s.$$
(C27)

Extending these calculations to higher orders, we derive the $n$th-order $I_{\text{cor-ch},n}$ component of the series expansion of Eq. (14). To illustrate the derivation of a general equation for the correlation-dependent chance information term, the $n$th-order contribution of the information series expansion is specified in the following expressions. The signal similarity contribution of such order reads as

$$I_{\text{sig-sim},n} = \frac{1}{n! \ln 2} \sum_{i_1,\dots,i_n=1}^{N} \langle \overline{r}_{i_1}(s) \rangle_s \cdots \langle \overline{r}_{i_n}(s) \rangle_s$$
$$\times \left[ \nu_{i_1 \cdots i_n} + \left(1 + \nu_{i_1,\dots,i_n}\right) \ln \left( \frac{1}{1 + \nu_{i_1,\dots,i_n}} \right) \right].$$
(C28)

The stimulus-independent correlation contribution reads as

$$I_{\text{cor-ind},n} = \frac{1}{n! \ln 2} \sum_{i_1,\dots,i_n=1}^{N} \left\langle \overline{r}_{i_1}(s) \cdots \overline{r}_{i_n}(s) \gamma_{i_1,\dots,i_n}(s) \right\rangle_s$$
$$\times \ln \left( \frac{1}{1 + \nu_{i_1,\dots,i_n}} \right),$$
(C29)

and the stimulus-dependent correlation component reads as

$$I_{\text{cor-dep},n} = \frac{1}{n! \ln 2} \sum_{i_1,\cdots,i_n=1}^{N} \left\langle \overline{r}_{i_1}(s) \cdots \overline{r}_{i_n}(s)\big[1 + \gamma_{i_1,\dots,i_n}(s)\big] \right.$$
$$\times \ln \left\{ \frac{\langle \overline{r}_{i_1}(s') \cdots \overline{r}_{i_n}(s') \rangle_{s'}\big[1 + \gamma_{i_1,\dots,i_n}(s)\big]}{\langle \overline{r}_{i_1}(s') \cdots \overline{r}_{i_n}(s')\big[1 + \gamma_{i_1,\dots,i_n}(s')\big] \rangle_{s'}} \right\} \right\rangle_s.$$
(C30)

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