Causal interactions and delays in a neuronal ensemble

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We analyze a neural system which mimics a sensorial cortex, with different input characteristics, in presence of transmission delays. We propose a new measure to characterize collective behavior, based on the nonlinear extension of the concept of Granger causality, and an interpretation is given of the variation of the percentage of the causally relevant interactions with transmission delays.

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I. INTRODUCTION

Orientation selectivity and perception are connected with the collective behavior in neural ensembles\textsuperscript{1, 2}. Previous work has shown that networks of excitatory and inhibitory leaky integrate-and-fire neurons tend to oscillate under some general conditions\textsuperscript{3}, provided that the excitatory neurons receive a sufficiently large input, while other studies have shown how oscillatory activity depends on the spatiotemporal properties of the external input\textsuperscript{4}. Due to the finite-velocity propagation of action potentials and to the spike generation dynamics, the presence of delays is physiological in networks of neurons. Sometimes delays are seen as an annoying presence and are thus neglected. In other studies is shown that they can give rise to a wide gamma of behaviors\textsuperscript{5}; also groups of neurons with reproducible time-locked but not synchronous firing patterns have been individuated\textsuperscript{6}. Furthermore, the role of synchronization is controversial. Undoubtedly, when this phenomenon is limited to a small time interval, it is the index of something going on. On the other hand, when facing a fully synchronized network, is difficult to extract any kind of information when all the neurons behave as a single one. We try then to get a better insight on this issue starting from the idea that the essence of collective behavior is the presence of causal interactions. We thus want to individuate the causally relevant relationships between the neurons in the network. The notion of Granger causality\textsuperscript{7} between two time series examines if the prediction of one series could be improved by incorporating information of the other. In particular, if the prediction error of the first time series is reduced by including measurements from the second time series, then the second time series is said to have a causal influence on the first one. The interactions between individual neurons in a network are nonlinear. We thus propose a radial basis function approach to nonlinear Granger causality\textsuperscript{8}, and show how these causal influences are related to the input signal and to the internal delays.

II. THE MODEL

Our network is a basic model of a mammal cortex, similar to the one in\textsuperscript{6}, and consists of $N_E = 400$ excitatory neurons and $N_I = 100$ inhibitory neurons. Each excitatory neuron is connected to 50 random neurons, both excitatory and inhibitory, while each inhibitory neuron is connected to 50 excitatory random neurons.

The membrane potential of a LIF neuron satisfies:

$$\frac{dV(t)}{dt} = -(V(t) - V_r) + I(t),$$

where the membrane resistance is normalized to one. Every time, when the potential of the neuron reaches the threshold value $V_{th}$, a spike is fired. This resets the potential to the rest potential $V_r$ and remains bound to this value for an absolute refractory period $\tau_{ref}$. Each inhibitory neuron $j$ ($j = 1 \ldots N_I$) receives an input $I_j(t)$:

$$I_j(t) = \mu + \eta_j(t) + ST_{E,j}(t),$$

which consists of a constant base current $\mu$, internal Gaussian white noise $\eta$ with intensity $D$, and where $ST_{E,j}(t)$ is the sum of the post-synaptic potentials (PSPs) of the afferent excitatory neurons.
On the other end, each excitatory neuron \( i \) \(( i = 1 \ldots N_E \rangle \) receives an input \( I_i(t) \):

\[
I_i(t) = \mu + \eta_i(t) + ST_{E,i}(t) + ST_{I,i}(t) + \sigma[\sqrt{1-c\xi_i(t)} + \sqrt{c\xi_G(t)}],
\]

with the same internal current \( \mu \) and noise \( \eta \) as in the previous equation, and where \( ST_{E,i}(t) \) and \( ST_{I,i}(t) \) are the sums of the PSPs of the afferent excitatory and inhibitory neurons, respectively. Furthermore we have an additional term \( s_j(t) = \sigma[\sqrt{1-c\xi_j(t)} + \sqrt{c\xi_G(t)}] \), where \( \xi_j(t) \) and \( \xi_G(t) \) are both Gaussian white noise with zero mean and unit power. This term mimics an external stimulus. Varying \( c \) increases or decreases the degree of spatial correlation of the external stimuli, while the total input power to each neuron remains constant. In our model we use dynamical depressing synapses, such that PSPs are delivered through synapses whose effective strength is given by the following equations:\3:

\[
\begin{align*}
\frac{dx}{dt} &= \frac{x}{\tau_{rec}} - U_x s^P(t), \\
\frac{dy}{dt} &= \frac{y}{\tau_{in}} - U_y s^P(t), \\
\frac{dz}{dt} &= \frac{z}{\tau_{rec}},
\end{align*}
\]

where \( x, y \) and \( z \) are the fraction of synaptic resources in the recovered, active and inactive state, respectively, and \( s^P(t) \) is the sum of all the presynaptic activity at time \( t \). Without any spike input all neurotransmitter is recovered and the fraction of available neurotransmitter is one: \( x(t) = 1 \). After each spike arriving at the synapse, a fraction \( U \) of the available (recovered) neurotransmitter is released. The fraction \( y \) of active neurotransmitter is then inactivated into the inactive state \( z \). \( \tau_{in} \) is the time constant of the inactivation process and \( \tau_{rec} \) is the recovery time constant for conversion of the inactive to the active state.

Furthermore we have inserted time delays in the connections. We performed different simulations, where the delays in excitatory (inhibitory) connections were randomly chosen between zero and a maximum value \( \tau_{E,max} \) (\( \tau_{I,max} \)). This maximum value was varied from zero to 40 ms, with a step of 2.5 ms. This values take into account of the measurements performed in mammal cortex \( \ref{10} \).

We used the following parameter values in the model simulations: \( V_r=0, V_{th}=1, \tau_{ref}=3 \) ms, \( \tau_m=10 \) ms, base current \( \mu=0.5 \), intensity of the internal Gaussian white noise \( \sigma=0.4 \) (or 0 in case of absence of external input), \( \tau_m=3 \) ms, \( \tau_{rec}=800 \) ms, \( U(c)=0.5 \). All simulations were integrated using an Euler integration scheme with a time step of 0.1 ms.

### III. GRANGER CAUSALITY

Let \( \{x_i\}_{i=1..N} \) and \( \{y_i\}_{i=1..N} \) be two time series of \( N \) simultaneously measured quantities. In the following we will assume that time series are stationary. We aim at quantifying how much \( y \) is cause of \( x \). For \( k = 1 \) to \( M \) (where \( M = N - m, \ m \) being the order of the model), we denote \( x^k = \bar{x}_{k+m}, X^k = (\bar{x}_{k+m-1}, \bar{x}_{k+m-2}, ..., \bar{x_k}), \ Y^k = (\bar{y}_{k+m-1}, \bar{y}_{k+m-2}, ..., \bar{y_k}) \) and we treat these quantities as \( M \) realizations of the stochastic variables \( x, X, Y \) \( \ref{14} \). Let us now consider the general nonlinear model:

\[
x = w_0 + w_1 \cdot F(X) + w_2 \cdot S(Y) + w_3 \cdot K(X,Y),
\]

where \( w_0 \) is the bias term, \( \{w\} \) are real vectors of free parameters, \( F = (\phi_1, ..., \phi_{n_x}) \) are \( n_x \) given nonlinear real functions of \( m \) variables, \( S = (\psi_1, ..., \psi_{n_y}) \) are \( n_y \) other real functions of \( m \) variables, and \( K = (\xi_1, ..., \xi_{n_{xy}}) \) are \( n_{xy} \) functions of \( 2m \) variables. Parameters \( w_0 \) and \( \{w\} \) must be fixed to minimize the prediction error (we assume \( M \gg 1 + n_x + n_y + n_{xy} \)):

\[
\epsilon_{xy} = 1/M \sum_{k=1}^{M} (x^k - w_0 - w_1 \cdot F(X^k) - w_2 \cdot S(Y^k) + w_3 \cdot K(X^k,Y^k))^2.
\]

We also consider the model:

\[
x = v_0 + v_1 \cdot F(X),
\]

and the corresponding prediction error \( \epsilon_x \). If the prediction of \( \bar{x} \) improves by incorporating the past values of \( \{y_i\} \), i.e. \( \epsilon_{xy} \) is smaller than \( \epsilon_x \), then \( y \) is said to have a causal influence on \( x \). We must require that, if \( Y \) is statistically independent of \( x \) and \( X \), then \( \epsilon_{xy} = \epsilon_x \) at least for \( M \to \infty \). For a detailed discussion on how this condition is achieved in the present case, see \( \ref{8} \) and \( \ref{11} \).
We choose the functions $F$, $S$ and $K$, in model (5), in the frame of Radial Basis Function (RBF) methods. We fix $n_x = n_y = n_{xy} = n < M$: $n$ centers $\{ \tilde{X}_\rho, \tilde{Y}_\rho \}_{\rho=1}^n$, in the space of $(X, Y)$ vectors, are determined by a clustering procedure applied to data $\{(X^k, Y^k)\}_{k=1}^M$. To find prototypes we use fuzzy $c$-means, a well known algorithm which introduces fuzzy memberships to clusters, so that a point may belong to several clusters with some degree in the range $[0,1]$: in calculating the center of a cluster the coordinates of each instance are weighted by the value of the membership function. We then make the following choice for $\rho = 1, \ldots, n$:

\[
\begin{align*}
\phi_\rho(X) &= \exp\left(-\|X - \tilde{X}_\rho\|^2/2\sigma^2\right), \\
\psi_\rho(Y) &= \exp\left(-\|Y - \tilde{Y}_\rho\|^2/2\sigma^2\right), \\
\xi_\rho(X, Y) &= \phi_\rho(X) \psi_\rho(Y),
\end{align*}
\]

$\sigma$ being a fixed parameter, whose order of magnitude is the average spacing between the centers. The RBF model here proposed can approximate any function of $X$ and $Y$. We conclude this section stressing that, according to our experience, the proposed method is insensitive to details of the clustering procedure used to find prototypes, provided that $n$ is at least two orders of magnitude smaller than $M$.

IV. RESULTS AND DISCUSSION

The simulation is run for 30 seconds of model time, such that the network is allowed to stabilize itself, and then for further 60 seconds (60000 points). We extracted then 12 time series of length 5000 points, from the PSP of any presynaptic neuron, and from the membrane potential of the corresponding postsynaptic neuron. Doing this we take also into account the effects of the external input on the subthreshold behavior of the neurons [12]. The series were checked for covariance stationarity with a Dickey-Fuller test ($p < 0.01$). The Granger causality algorithm was then applied. We identified statistically relevant interactions performing an $F$-test (Levene test) of the null hypothesis that the error on the prediction of one series is not decreased when information on the other series is added to the model. This analysis was repeated for every possible delay time in both excitatory and inhibitory connections, up to $\tau_{E,max}$ and $\tau_{I,max}$, and the results were averaged over the 12 trials.

In absence of external input ($\sigma=0$), the percentage of statistically relevant causal interactions decreases slowly but uniformly with $\tau_{E,max}$ and $\tau_{I,max}$ (Figure 1).

\begin{figure}[h]
\centering
\includegraphics[width=0.7\textwidth]{fig1.png}
\caption{Percentage of causally relevant interactions as a function of the delays of excitatory connections (horizontal axis), and inhibitory connections (vertical axis), in absence of external input.}
\end{figure}

In the presence of spatially uncorrelated external input ($c=0$), there is some structure in the percentage of causal interactions. The major differences are observed varying the delays in the inhibitory connections, with a maximum between 20 and 25 milliseconds. This region characterized by an increased amount of relevant interactions becomes narrower as the maximum delay in excitatory connections increases (Figure 2).

\begin{figure}[h]
\centering
\includegraphics[width=0.7\textwidth]{fig2.png}
\caption{Percentage of causally relevant interactions as a function of the delays of excitatory connections (horizontal axis), and inhibitory connections (vertical axis), in absence of external input.}
\end{figure}
When the external input is spatially correlated (c=1), the structure becomes much more pronounced, this time with a maximum around $\tau_{I,max} = 15$ ms for $\tau_{E,max} = 0$, which becomes narrower and drifts down to $\tau_{I,max} = 10$ ms for increasing values of $\tau_{E,max}$ (Figure 3).

In order to explain the structures that appear in presence of external input, some remarks are in order. A delayed inhibitory feedback is necessary in order to discriminate an external input $4$, and this explains the lack of causal interactions in the absence of delays in the inhibitory connections. Furthermore, if too many inhibitory spikes reach an excitatory neuron at the same time, the overall inhibitory effect is depressed. On the other hand, when the delays in the inhibitory connections are scattered along a too wide interval, the feedback effect is inactivated. As it concerns the delays in the excitatory connections, it is worth to recall that a neuron behaves as a coincidence detector when its time constant is small, changing into an integrator when the time constant increases. Since the external input is continuous, the information is constantly carried to the inhibitory neurons, and this makes the number of causally relevant interaction less sensitive to the value of $\tau_{E,max}$. Though, when the input is spatially correlated, the timing is more important if we don’t want to lose the important information that all excitatory neurons receive the same input.
at the same time. We observe that the narrowing of the region with highest percentage of causally relevant interactions becomes more critical as $\tau_{E,\text{max}}$ increases, remaining optimal only in a small region around a value of $\tau_{I,\text{max}}$ for which the excitatory neurons are still able to resolve the individual inhibitory spikes. This preferred value in inhibitory delays can be useful in choosing the optimal window length in the case of spike-time dependent plasticity\textsuperscript{13}.

V. CONCLUSIONS

We have introduced the concept of causality, which can give a better insight on the collective behavior in neural systems. We have shown how to extend the original definition of causality to nonlinear systems. We have built a basic model of a sensory cortex and performed a quantitative analysis of the causally relevant interactions for different characteristics of the external input.

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[1] R Ben-Yishai, R L Bar-Or, and H Sompolinsky. Theory of orientation tuning in visual cortex. \textit{Proc Natl Acad Sci U S A}, 92(9):3844–3848, Apr 1995.
[2] D R Moore, J W Schnupp, and A J King. Coding the temporal structure of sounds in auditory cortex. \textit{Nat Neurosci}, 4(11):1055–1056, Nov 2001.
[3] C B"orgers and N Kopell. Synchronization in networks of excitatory and inhibitory neurons with sparse, random connectivity. \textit{Neural Comput}, 15(3):509–538, Mar 2003.
[4] Brent Doiron, Benjamin Lindner, Andre Longtin, Leonard Maler, and Joseph Bastian. Oscillatory activity in electrosensory neurons increases with the spatial correlation of the stochastic input stimulus. \textit{Physical Review Letters}, 93(4):048101, 2004.
[5] Alex Roxin, Nicolas Brunel, and David Hansel. Role of delays in shaping spatiotemporal dynamics of neuronal activity in large networks. \textit{Physical Review Letters}, 94(23):238103, 2005.
[6] E M Izhikevich. Polychronization: computation with spikes. \textit{Neural Comput}, 18(2):245–282, Feb 2006.
[7] C W J Granger. Investigating causal relations by econometric models and cross-spectral methods. \textit{Econometrica}, 37(3):424–38, July 1969.
[8] Daniele Marinazzo, Mario Pellicoro, and Sebastiano Stramaglia. Nonlinear parametric model for granger causality of time series. \textit{Physical Review E (Statistical, Nonlinear, and Soft Matter Physics)}, 73(6):066216, 2006.
[9] M V Tsodyks and H Markram. The neural code between neocortical pyramidal neurons depends on neurotransmitter release probability. \textit{Proc Natl Acad Sci U S A}, 94(2):719–723, Jan 1997.
[10] H A Swadlow. Monitoring the excitability of neocortical efferent neurons to direct activation by extracellular current pulses. \textit{J Neurophysiol}, 68(2):605–619, Aug 1992.
[11] N Ancona and S Stramaglia. An invariance property of predictors in kernel-induced hypothesis spaces. \textit{Neural Comput}, 18(4):749–759, Apr 2006.
[12] W Gerstner, R Kempter, J L van Hemmen, and H Wagner. A neuronal learning rule for sub-millisecond temporal coding. \textit{Nature}, 383(6695):76–81, Sep 1996.
[13] S. Song, K. Miller, and L. Abbott. Competitive hebbian learning through spiketime-dependent synaptic plasticity. \textit{Nat. Neurosci.}, 3:919–926, 2000.
[14] the series are normalized to zero mean and unit variance