Interspike interval attractors from chaotically driven neuron models

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Abstract

Sequences of intervals between firing times (interspike intervals (ISIs)) from single neuron models with chaotic forcing are investigated. We analyze how the dynamical properties of the chaotic input determine those of the output ISI sequence, and assess how various biophysical parameters affect this input–output relationship. The attractors constructed from delay embeddings of ISIs and of the chaotic input are compared from the points of view of geometry and nonlinear forecastability. For the three integrate-and-fire (IF) models investigated, the similarity between these attractors is high only when the mean firing rate is high, and when firings occur over a large range of the input signal. When these conditions are satisfied, ISIs are related to input values at which firings occur by a simple map, and their distribution can be derived from that of input signal values. Attractor reconstruction is found to be more sensitive to mean firing rate than to ISI distribution. At low firing rates, for which the input is under sampled and ISIs become larger than the short-term prediction horizon, or when the dynamics do not allow a smooth invertible mapping between signal and ISIs, information is lost. Our results, relevant to all dynamical systems generating events, show that information about continuous-time dynamics is difficult to retrieve at low event rates, and that information about inputs can be isolated only under restricted conditions.

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1. Introduction

Many dynamical systems generate “events” in the course of their continuous-time evolution. An event can be defined as a sudden change in a measured continuous physical variable. These changes occur on a fast time scale compared to other potentially interesting variations. Systems characterized by the occurrence of events abound in the physical, chemical, and biological sciences [1–4]. Epileptic seizures, cell division or neuron firing are examples of events in the time evolution of the corresponding biological systems. During “events”, the state variables in such systems execute large stereotyped excursions in phase space.

Of interest in the present study is the case of neurobiology, where events correspond to nerve cell “action potentials” or voltage “spikes”. It is usual to describe excitable systems by the times at which events occur [4,5]. Technical limitations can also make a description of the underlying systems in terms of these times unavoidable. Such is the case when only the firing times of a neuron can be obtained through extracellular recordings, i.e. when the transmembrane
potential cannot be recorded. The analysis of firing times can then be used to quantify the information about their internal dynamics and about their inputs.

There is an extensive literature on the information transfer between time-varying input signals to sensory neurons and resulting output spike trains (see e.g. [6–9], and [10] for a review of earlier work). In particular, the approach in [7,9] revolves around the possibility of reconstructing the stimuli to sensory cells from the spike trains generated by these cells. The way in which specific neural properties affect this information transfer is, however, less well understood. These properties include temporal integration, recovery from firing (refractoriness), distance from resting potential to threshold, the type of threshold, the membrane time constant, and pacemaker activity. Such knowledge could lead to principles of neural information processing that apply across different classes of neurons, sensory and other.

From a dynamical systems perspective, the time evolution of the neuron state variables (membrane voltage, ionic conductances, etc.) is mapped by the “thresholding” process into a point process (the set of firing times) and derived quantities such as interspike intervals (ISIs). Under conditions discussed in the present study, an ISI may then be seen as a new state variable by which the temporal dynamics of the neuron can be characterized. In analogy with the Takens theorem [11] for discrete- or continuous-time dynamical systems, later generalized in [12], it should then be possible to reconstruct the essential features of the attractor dynamics of a neuron from measurements of only one variable, using e.g. delay embeddings on ISI sequences.

This is the starting point of an interesting numerical study [13] which showed that the attractor of a chaotic input to a simple integrate-and-fire (IF) neuron (see [10], and Section 2) can be “reconstructed” by performing a delay embedding of the ISIs generated by the neuron. Thus, for the simplest neuron dynamics, there is a similarity (in the sense of a diffeomorphism) between these two attractors. The present study investigates these findings in the context of neural models of increasing complexity, in order to circumscribe the domain of applicability of this result. In particular, we determine whether the generic properties of neurons change the conclusions in [13]. These properties are the distance between resting potential and threshold, pacemaker activity, signal strength in the presence of leakiness, and refractoriness. Accordingly, our study focuses on four standard models in the neural dynamics literature, each of which embodies one or more of these properties. We assess, using measures inspired from nonlinear dynamics, the effect of these properties on the reconstruction of the input signal attractor from ISIs.

Our paper is organized as follows. Section 2 provides background on nonlinear dynamical analyses of point processes, and summarizes the results in [13]. Section 3 introduces the nonlinear forecasting method used throughout our study. The analysis of the reconstruction of inputs in neuron models of increasing complexity is the subject of Section 4. The influence of the distance-to-threshold is investigated in the generic IF model used in [13]. The model in [14] is given a chaotically modulated threshold to assess the influence of pacemaker activity. The model studied in [15] is given a chaotic input to assess the effect of leakiness and signal strength. Finally, the Fitzhugh–Nagumo equations [16,17] are chaotically forced to study more realistic dynamics with refractoriness and recovery. Section 5 validates the nonlinear prediction errors obtained in Section 4 using surrogate data. Section 6 compares the ability of the ISIs from the three IF models to reproduce properties of the input signal. Section 7 correlates the quality of reconstruction with the ISI histograms. A discussion and outlook onto future investigations follow in Section 8.

2. Background

In recent years, much effort has gone into the characterization of the dynamics underlying experimental ISI sequences from neurobiology (see e.g. [18–23]). These studies contrast with traditional stochastic process analyses (see e.g. [4,5] for reviews). Their underlying assumption is that the
nonlinear dynamical properties of neurons, in isolation or in networks, can be studied despite the presence of noise and possible non-stationarity. The underlying hope is that the continuous-time dynamics of the neurons are of low dimension, and that some information about them filters in some way to the ISI sequence, from which it may be extracted.

A number of nonlinear dynamical systems can be analyzed from event times. The classic study of the chaotic dripping faucet [3] used return maps and dynamical information measures to analyze inter-drop times. The dynamics of certain delay-differential equations with piecewise constant feedback can be completely analyzed from the times at which the state variable switches between domains of the feedback function [24]. Particularly relevant to the area of mathematical biology is the analysis in [1] of simple autonomous systems in terms of the asymptotic time behavior of densities of inter-event intervals. The phase locking of biological oscillators to periodic driving signals has been studied using firing intervals in [14]. That study deals with IF dynamics with a periodically modulated threshold, and motivates one of the models studied in Section 4. A related study, in a similar but more elaborate model with leakiness and higher-order dynamics, can be found in [25]. Keener et al. [15] have investigated the dynamics of a periodically forced leaky IF model using a map of firing times derived analytically from the equation of motion. Also, a study of the detectability of chaos in sequences of intervals between "spikes" generated by threshold crossings in a bistable delay-differential equation can be found in [26].

The chaotic input to the IF neuron in [13] is the same as that used in the present study, namely the $x$-component of the three-dimensional Rössler system,

\begin{align*}
\frac{dx}{dr} &= -y - z, \\
\frac{dy}{dr} &= x + ay, \\
\frac{dz}{dr} &= b + z(x - c)
\end{align*}

with parameters $a = 0.36$, $b = 0.4$ and $c = 4.5$. The ISI attractors can then be compared to the attractor constructed from a delay-embedding on the $x$-component (Fig. 1(a)). The main characteristics of this attractor are its funnel shape (visible only in three dimensions) and its banded structure. The neuron voltage in the IF model results from the perfect integration of the input signal $S(t)$, itself a function of $x$:

$$V(t) = \int_{t_n}^{t} S(t') dt'.$$

This equation is valid for $t > t_n$, where $T_n$ is the last firing time. A spike is generated when $V(t)$ reaches a fixed threshold, $V(T_{n+1}) = \Theta$, after which the voltage is immediately reset to zero, $V(T_{n+1}) = 0$, and the integration begins anew. The ISIs are simply $t_{n+1} - T_n$. Also, parameters are such that $S(t)$ is always positive, with the result that $V(t)$ is monotonically increasing. This is achieved by scaling the input $x$ after adding a positive constant:

$$S(t) = \delta \cdot (x(t) + C).$$

This scaling and shifting of the input is necessary, as we will see below, to obtain proper reconstructions.

The results in [13] imply that the ISI sequence has similar dynamical invariants as the input signal, and that the IF neuron does nothing more than some kind of non-uniform sampling of the input signal. The Takens embedding theorem [11,12] can then be applied to a map (such as the one in [15]) that underlies ISI sequences in the combined “neuron + input” system. For example, the Hodgkin–Huxley neuron model (4D) forced by the Rössler system (3D) would be a seven-dimensional system. Thus, the map generating the successive ISIs would have to be of dimension $D = 7$ or less. The correlation dimension of an attracting set of ISI values, if it exists and can be determined, would then be smaller than $D$ (just as the dimension of the attractor of the two-dimensional Hénon map is less than two). In fact, Sauer’s result implies that, for a simple IF neuron, the attractor dimension of this ISI map should be similar to that of the Rössler attractor. Thus, whatever extra dimension the IF dynamics add to the input, the thresholding process removes, just
like a Poincaré section removes one dimension from the dynamics. We will see in Section 4 that, in the limit of high firing rate, the ISI dynamics can be understood as arising from a “Poincaré-like section” on the combined system, followed by a static nonlinear transformation.

One can also find an abundance of counterexamples to the reconstruction result of [13] in the literature on excitable cells (see e.g. [19,27,28]). Some neurons have a phasic behavior, firing only during positive or negative going portions of an input stimulus. Neurons often fire in an $n:1$ phase locking regime, firing only once in response to $n$ stimulating pulses. Hence, the periodic input has a one-dimensional attractor, while the ISI attractor would be zero-dimensional, with only a single point at the firing interval. These observations further motivate our study into the properties of neurons that determine the flow of information from an input signal to an output spike train.

3. Nonlinear forecasting of interspike intervals

A priori, two factors could determine the influence of an input on ISI reconstructions. The first is the mean firing rate. If this rate is low, ISIs tend to be long. This hampers the extraction of information about the fine structure of the voltage fluctuations between spikes which is lost or averaged out in the process. A second and related factor is the intrinsic short-term forecastability of ISIs due to chaos. ISIs become uncorrelated when they are larger than the prediction horizon of the dynamics, i.e. larger than one or more Lyapunov times, the reciprocal of the maximal Lyapunov exponent [29]. Points with low nonlinear correlations produce poor delay embeddings, which weaken our ability to compute dynamical properties.

In this study, we use the nonlinear forecastability, which is a dynamical invariant of a nonlinear dynamical system [29], to quantify the information in the ISIs.
about the input. As this measure is sensitive to ISI correlations and patterning, it is particularly relevant to neurobiology [21–23, 30]. In the first step, a delay embedding is constructed from a sequence of $N$ ISIs $(I_1, I_2, I_3, \ldots, I_N)$ in the same way as for a time series [29]. An $m$-dimensional embedding yields vectors of the form $x_n = (I_{n-m+1}, I_{n-m+2}, \ldots, I_{n-1}, I_n)$. The endpoints of these vectors can be plotted in $m$-space, and either joined or not by straight lines. As the mean time between firings increases, a representation without the straight lines is more adequate, as the attracting sets resemble that of a map. When the attracting sets resemble continuous-time flows, joining the endpoints highlights the flow lines.

Nearest neighbors in the embedding space correspond to similar sequences of $m$ successive ISIs in the data. These neighbors can be used for prediction purposes. We use the simple nearest-neighbor method described in [13]. For each $x_n$, one identifies $\beta N$ ($\beta < 1$) nearest neighbors $x_n^j = (I_{n-m+1}^j, I_{n-m+2}^j, \ldots, I_{n-1}^j, I_n^j)$, $j = 1, \ldots, \beta N$. For all calculations in this paper, $\beta = 0.01$. The whole data set serves as the training and the test sets. Nearest neighbors close in time to $x_n$ are omitted to avoid biasing predictions by insample interpolation. One-step ahead predictions are based on the range of the $x_n^j$ under one iteration, i.e. the $x_{n+1}^j$. The predicted interval $f_n$ is the average of the last components $I_{n+1}^j$ of the $x_{n+1}^j$, i.e.

$$ f_n = \frac{1}{\beta N} \sum_{j=1}^{\beta N} I_{n+1}^j. $$

(6)

This prediction is compared to the actual value $I_{n+1}$ of the next ISI. A normalized prediction error (NPE) is computed by averaging the squares of all the prediction errors over the whole data set, and then dividing this result by the average error incurred by always predicting $\bar{I}$, the mean of the ISI sequence:

$$ \text{NPE} = \left[ \frac{(f_n - I_{n+1})^2}{(\bar{I} - I_{n+1})^2} \right]^{1/2}. $$

(7)

This NPE is calculated as a function of $m$, i.e. of the number of intervals used to identify neighbors and carry out the predictions. This NPE is sensitive to non-linear dynamical structure in the data [13, 21, 29]. An NPE value close to zero signifies high predictability in the ISI sequence; a value near one signifies low predictability, with $\bar{I}$ being the best forecast. Linear correlations can, however, fool such algorithms by giving NPE values less than one [21–23, 31]. It is important therefore to test the predictions against appropriate surrogate data sets (see [32] and references therein), as done in Section 5.

4. Reconstructing the input to simple neuron models

This section studies ISI embeddings for three IF models and the FitzHugh–Nagumo model. We define the “sampling rate” of the input as the mean number of spikes per unit of time. For simplicity, this rate is expressed in Hz, even though for a real neuron the firing rate can approach 1000 Hz. Comparison between models and actual experiments requires matching the time scale of the input variations to the relevant firing frequencies, which depend mainly on membrane time constant and refractory period. The concept of “sampling rate” is suggested by its use in the context of uniformly sampled time series. Here, we can think rather that the ISIs produce a sampling of the input which is non-uniform in time, since firings occur at varying time steps and values of the input.

4.1. Generic integrate-and-fire device

This generic IF model, described in Section 2, is driven by the same input signal $S$ as in [13]: $S(t) = x(t) + 40$. Firing times are determined by integrating the Rössler equations using a fourth-order Runge–Kutta method with time step 0.001. The contribution to the integral $V(t)$ is computed every time step. When $V(t)$ crosses the threshold, the time step is reduced and the step is repeated until $|V(t) - \Theta| < \Delta = 10^{-3}$. The threshold, fixed for each simulation, can be varied to alter the sampling rate: as $\Theta$ increases, the sampling rate decreases.
where \( \overline{S}_n \) is the mean value of the input signal \( S(t) \) over the interval \( I_n \). For successive intervals, we then have
\[
I_1 \overline{S}_1 = I_2 \overline{S}_2 = I_3 \overline{S}_3 = \ldots = I_N \overline{S}_N = \Theta.
\] (9)

This IF model can fire at a high rate if \( \Theta \) is low. As this firing rate increases, the ISI attractor becomes as smooth as that of the input attractor. For a high firing rate, one can approximate \( \overline{S}_n \) by \( S_n \), i.e., the value of the input signal at time \( T_n \). Consequently, one can write
\[
(I_1, I_2, I_3, \ldots, I_N)
\]
\[
\approx \Theta \left( 1/S_1, 1/S_2, 1/S_3, \ldots, 1/S_N \right). \] (11)

Hence, at high firing rate, the ISI sequence and the signal values at which firings occur are related by a simple static nonlinear transformation. Hence, both sequences will have the same dynamical invariants.

Fig. 1(c) shows the attractor that results from the action of this map on the \( x \)-component of the Rössler, namely \( I_n = 100/(x + 40) \), with an embedding delay of 10 time units as in Fig. 1(a). The factor 100 is for scaling purposes. The ISI attractor for the generic IF model with \( \Theta = 15 \) is shown in Fig. 1(d), with an embedding delay of one ISI. A comparison of Figs. 1(c) and (d) shows that the attractors have the same topology and orientation, as predicted by our analysis. Reconstructions for \( \Theta < 15 \), while being even more similar to that in Fig. 1(c), are too concentrated along the diagonal, and embedding delays of two or more ISIs must be used to properly visualize the attractor.

The fact that ISIs are related to sampled values of the input when the voltage reaches threshold suggests that this sampling arises from the action of a “Poincaré-like section” on the dynamics of the combined “neuron + input” system. In fact, the situation is similar to taking a Poincaré section in a periodically forced system by sampling all the system variables at a given phase of the forcing. However, in our case, samples are taken on the input signal. They occur non-uniformly in time, i.e., whenever the voltage variable reaches threshold. Further, the sample is of the Rössler \( x \)-component, not of \( x, y \) and \( z \). Thus the reduction in
dimensionality is higher than for a Poincaré section. Information about the dynamics giving rise to $x$ can of course be extracted from $x$ using delay-embeddings, due to the low-dimensional chaotic nature of the input, but not about $y$ and $z$ per se.

Eq. (11) shows that the ISIs are proportional to $\Theta$. Also, since Eq. (11) reveals that ISIs are inversely proportional to the signal value, small values of $x$ lead to large ISIs, and thus, less firings occur on the lower portions of the input signal. This is not necessarily obvious from Fig. 2, since for the offset value (40) used (the left-hand side plot does not show this offset), there is only a small difference in firing rate over the range of signal values. Thus, some portions of the signal are sampled more often than others, affecting ISI forecastability and distribution. In Section 7, it will be shown that Eq. (11) can be used to derive the distribution of ISIs from a knowledge of the distribution of the input signal values.

Fig. 3 plots the NPE versus the embedding dimension $m$. We find that the better reconstruction has a lower NPE than the poor one, as expected. The NPE for $\Theta = 35$ is low for $m > 1$ and relatively constant for $m > 2$, suggesting that the ISIs are governed by at least two-dimensional dynamics. However, the poor reconstruction also has a low NPE value, which implies that there is still much information about the combined neuron + input system in these ISIs (see also Section 5). The loss of predictability as the sampling rate decreases can be understood from the previous analysis in terms of the increasing discrepancy between $S_n$ and $\overline{S}_n$. The forecasts will worsen as the firing times are further apart, because the finer structure of the input signal is no longer mapped to the ISI sequence. Further, as $\Theta$ increases, there is a progressive loss of the short-term nonlinear forecastability. This is due to the ISIs being larger on an average than the Lyapunov time of the input, equal here to the reciprocal of the maximal Lyapunov exponent of the Rössler system, i.e., approximately $1/0.15 = 6.7$ s. Finally, for very high $\Theta$ values, the firings are very far apart. The mean values of the $S_n$'s then approach the mean value $\overline{S}$ of $S(t)$ itself, and the NPE goes to one (not shown).

4.2. Glass–Mackey integrate-and-fire model

In the previous example, the dynamics were biased into the periodic firing regime using a constant input $C$ (set equal to 40), to which a chaotic modulation was added. We now present reconstruction results for the Glass–Mackey (GM) IF model [14,25]. It is similar to the generic IF model, except that it fires periodically in the absence of any input. Further, the input modulates the threshold rather than the state variable. In the context of our study, the input is made to be the same chaotic signal as for the generic IF model. As we will see below, the GM model fires more often when the input is low, a behavior opposite to that of the generic IF model, and is thus an appropriate simple model for neurons that fire in this manner.

The neural activity now increases in a linear fashion towards the chaotic threshold $S(t)$:

$$V(t) = \alpha t + \beta. \quad (12)$$

$$V(T_n^+) = 0 \quad \text{if} \quad V(T_n) = S(T_n). \quad (13)$$

We use $S(t) = x(t) + 10$. The constant is added to make $S(t)$ positive everywhere, since the threshold must always be above the resetting point of the voltage. The Rössler equations are integrated as for the generic IF model. When $V(t)$ crosses the threshold, a linear
Reconstructions are shown for $\alpha = 10$ and $\alpha = 1$ in Fig. 4 ($\beta = 0$ in both cases). Both left panels show the dynamics $V(t)$ and the threshold. Spikes occur whenever a straight line intersects the chaotic threshold. The sampling rate for these two reconstructions are 1.15 and 0.15 Hz, respectively. The reconstruction for the high sampling rate still has funnel shape and a somewhat banded structure. This is not the case for $\alpha = 1$. The low sampling rate leads to significant jumps from one point to another on the attractor, a property usually associated with discrete-time maps rather than with flows. In Fig. 5, the NPE results for both reconstructions are shown. Once again the better reconstruction has a low NPE across all embedding dimensions ($m > 1$), yet the poor reconstruction still has an NPE less than one.

As for the generic IF model, it is possible to derive the form of the mapping between the input signal and the output ISI sequence. Since $V(t) = \alpha t$, and firing occurs when $V(T_n) = S(T_n) \equiv S_n$, there exists a relationship between intervals $I_n = T_n - T_{n-1}$ and signal values $S_n$ at which firings occur. Let

\begin{align*}
\alpha(T_n - T_{n-1}) &= S_n, \\
\alpha(T_{n+1} - T_n) &= S_{n+1}.
\end{align*}

Consequently,

\begin{equation}
\alpha = \frac{S_2}{I_1} = \cdots = \frac{S_n}{I_{n-1}} = \cdots = \frac{S_{N+1}}{I_N},
\end{equation}

and the relationship between intervals and signal values at the end of these intervals is

\begin{equation}
(I_1, I_2, \ldots, I_N) = \alpha^{-1}(S_2, S_3, \ldots, S_{N+1}).
\end{equation}

This analysis holds for all firing rates. It predicts that when $S$ is large, $I$ is also large, and vice versa. This is the opposite of what was found for the generic IF model, and is a consequence of this type of pacemaker dynamics. Hence, more firings occur on the lower portions of the signal. As the pacemaker rate $\alpha$ decreases, the firing rate decreases by first dropping out firings on higher values of the input signal. The loss of representation of the corresponding higher $S_N$ values thus leads to loss of forecastability. As in the generic IF model for high $\Theta$, a low $\alpha$ also separates firings by more than one Lyapunov time, resulting in a further loss of nonlinear forecastability.

Another interesting aspect of this model is that values on the rising portions of the input signal can be
sampled only if $\alpha$ is sufficiently large. The derivative at a sample can be estimated as

$$\dot{S}_n \approx \frac{S_{n+1} - S_n}{I_n} \approx \alpha \left( 1 - \frac{I_{n-1}}{I_n} \right).$$  \hspace{1cm} (18)$$

For example, $I_{n-1} \approx I_n$ occurs when $\dot{S}_n \approx 0$, i.e. when the signal is almost constant, or near its maxima or minima. Defining $\epsilon \equiv I_{n-1}/I_n$, we have that

$$0 < \epsilon < \frac{I_{\text{max}}}{I_{\text{min}}} \equiv \epsilon_{\text{max}}.$$  \hspace{1cm} (19)$$

Consequently, we have the following bounds on the derivative of the signal when it is being sampled:

$$\alpha(1 - \epsilon_{\text{max}}) < \dot{S}_n < \alpha.$$  \hspace{1cm} (20)$$

We thus see that the derivative at a sampling point is bounded above by the rate of increase of the voltage. For the high rate case of Fig. 4, $\alpha$ is greater than the maximal derivative of the input; the opposite holds for the low rate case, where portions of the input with significant positive slope cannot be sampled.

4.3. Leaky integrate-and-fire model

The study of Keener et al. [15] of a leaky integrator neuron forced by a cosine wave showed that all the "interesting dynamics" commonly seen in experiments, such as phase locking and chaos, [19,27], can be understood from the spike times. They analytically derived a map governing the sequence of firing times. The dynamics of the leaky IF are based on the generic IF dynamics, but include a dissipative term $-\sigma V$ which accounts for the tendency of the membrane potential to always decay to the resting potential, as long as the threshold is not crossed. The value of $\sigma$ is typically the reciprocal of the charging (RC) time constant of the neuron's membrane. The voltage is governed by

$$V = -\sigma V + S_0 + S(t),$$  \hspace{1cm} (21)$$

where we have added a chaotic input $S(t) = \gamma(x(t) + 10)$ with $\sigma = 0.5$ and $S_0 = 0.4$. A spike is generated whenever $V(t) = \Theta$, and we set $\Theta = 1$ without loss of generality. The dynamics for this model can also be written in integral form:

$$V(t) = \int_{T_n-1}^t \left[ S_0 + S(t') \right] e^{-\sigma(t-t')} \, dt', \hspace{1cm} T_{n-1} < t < T_n.$$  \hspace{1cm} (22)$$

in which it is immediately apparent that the generic IF model is the limiting case of this model as $\sigma \to 0$, i.e. as the leakiness disappears. The effect of $\sigma$ is to slow down the upward trend of the voltage in the generic IF case, since the voltage now is always attracted by the resting potential $V = 0$. Also, for a given $\sigma$, there is a range of small inputs (larger inputs when $\gamma$ is small) for which the voltage never reaches threshold.

To determine the spike times, the coupled differential equations for $S(t)$ and $V(t)$ are numerically integrated with a fixed time step of 0.001. Linear interpolation between two points straddling the threshold is used to determine a precise value of the crossing time $T_n$. The forcing parameter $\gamma$ can then be varied to change the influence of the Rössler system on the ISIs in the presence of leakiness. As $\gamma$ increases, so does the sampling rate since the enhanced signal brings the voltage to threshold more often. A preliminary account of the results in this section can be found in [33].

Fig. 6 shows the ISI embeddings for $\gamma = 0.154$ and $\gamma = 0.01$, corresponding respectively to sampling rates of 1.15 and 0.30 Hz. For $\gamma = 0.154$, the reconstruction resembles the Rössler attractor, although the quality of this "good" reconstruction is perhaps slightly lower than in the previous examples. The attractor seems to be evolving mostly in a planar region, and the banded structure is not readily apparent. The lower left panel ($\gamma = 0.01$) shows 2000 points while the lower right panel shows 500 points joined by lines. This Rössler attractor is not recognizable in this ISI attractor, a consequence of the low sampling rate. In Fig. 7, ISI forecasting results for the two cases $\gamma = 0.15$ and $\gamma = 0.01$ are presented. Once again the better reconstruction has a lower NPE across all $m > 1$ values, yet surprisingly the NPE for the sequence with the lower sampling rate is still significantly less
At large $\sigma$, the input has to be very high for threshold crossings to occur. The behavior of the NPE as a function of $\sigma$ for constant $\gamma$ is more complicated (not shown). As $\sigma$ initially increases, the NPE also increases since the sampling rate decreases. However, at certain values of $\sigma$, the NPE falls back to lower values. These cases were usually associated with a simplification in the structure of the ISI histogram (ISIH). For example, the ISIH would go from a broad gamma type distribution to a sharp bimodal distribution, with ISIs alternating between the two modes. Thus, these drops in NPE seem to correspond to some kind of statistical phase locking between firings and the input (we note that the Rössler signal used in our study has a strongly dominant frequency). An in-depth study of the leaky IF dynamics with chaotic inputs may reveal other regions in the $(\sigma, \gamma)$ parameter space where such phase lockings occur.

The integral form of the dynamics can be used here to obtain an approximate expression for the mapping between signal values at which spikes occur and ISIs. Denoting the threshold by $\Theta$ instead of one, and letting $s(t) \equiv S_0 + S(t)$, we have

$$V(T_n) = \int_{T_{n-1}}^{T_n} s(t') e^{-\sigma(T_n-t')} \, dt' = \Theta. \quad (23)$$

When $\sigma$ is small, and the sampling rate is high, the firings are close in time. One can then approximate the integral using the midpoint rule,

$$V(T_n) \approx T_{n-1} s \left( \frac{T_n + T_{n-1}}{2} \right) e^{-\sigma T_{n-1}/2} = \Theta. \quad (24)$$

Denoting

$$s_{n-1} = S_0 + s_{n-1} \equiv s \left( \frac{T_n + T_{n-1}}{2} \right), \quad (25)$$

we then have the following map between intervals and sample values:

$$s_0 + s_n \equiv \frac{\Theta}{T_n} e^{\sigma T_{n}/2}. \quad (26)$$

Thus, the hyperbolic behavior found in Eq. (11) is modified by an exponential factor which causes the relationship between $s_0$ and $T_n$ to become transcendental, i.e. we cannot solve for $T_n$. Our simple analysis
captures all the behaviors of the ISIs as a function of $S_x$, $\Theta$ and $\sigma$, provided that the physically significant negatively sloped branch of the function of $I_n$ on the right-hand side of Eq. (26) is used. In fact, there now exists a maximum interval $I_{max} = 2/\sigma$, corresponding to the smallest possible sample $s_{min} = \frac{1}{2}\sigma$. As $\sigma \to 0$, $I_{max} \to \infty$ and $s_{min} \to 0$. In this same limit and when the sampling rate is high, the map reduces to that for the generic IF model. This rate increases for low $\Theta$ or high $\gamma$. Thus, our analysis shows that there should be some similarity between ISI attractors for the generic IF and leaky IF models. A comparison of the good reconstructions for both these cases (Figs. 2 and 6) supports this conclusion.

4.4. FitzHugh–Nagumo equations

We now shift our focus to the more complicated FitzHugh–Nagumo (FHN) model [16,17]. Its main additional features are: (1) its more realistic action potential with refractory period and (2) its fully continuous dynamics, i.e. no abrupt reset of the voltage after an action potential. It also has one more fixed points. This model is modified here by adding a chaotic input current $S(t)$:

$$\epsilon \frac{dV}{dt} = V(V - a)(1 - V) - W + S(t),$$

$$\frac{dW}{dt} = V - d W - b,$$

where $S(t) = \mu x(t)$, $x(t)$ being as usual the $x$-component of the Rössler system. This modified model is thus a set of five coupled ordinary differential equations. Spiking times are determined by numerically integrating Eq. (27) and by finding, via linear interpolation, the times at which the variable $V$ makes positive-going crossings of a fixed threshold (set to 0.7). The scaling factor $\mu$ is varied to increase the effect of the chaotic input on the neuron model.

For the parameters chosen, the FHN equations cannot generate spikes without an input current, i.e. there is a globally stable fixed point. A minimum value of $\mu \approx 0.007$ exists below which firings do not occur. There is also an upper limit on $\mu$ beyond which the range of $S(t)$ becomes much larger than the $(-0.4, 1.1)$ range of $V(t)$. A value of $\mu = 0.075$ gives $S(t) \in (-0.6, 0.9)$. At this and higher values of $\mu$, some of the spikes (e.g. the first one in Fig. 8(b)) are distorted, as the voltage remains high for a long time in comparison with a proper action potential for this model. To investigate the effect of the chaotic input current on the FHN model in a physiologically relevant regime, only values of $\mu \leq 0.075$ were used.

In Fig. 9, typical ISI return maps (2D embeddings) are shown, corresponding to $\mu = 0.04$ and $\mu = 0.075$. 

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Fig. 8. Voltage time series from the FHN model equation (27) forced by a chaotic input. (a) $\mu = 0.04$, (b) $\mu = 0.075$. Other parameters are fixed at $a = 0.5$, $d = 1.0$, $b = 0$, and $\epsilon = 0.005$.

Fig. 9. ISI attractors (first return maps) for the FHN model equation (27) with chaotic input current, with points joined (left panels) or not (right panels) by straight lines. Top: $\mu = 0.04$. Bottom: $\mu = 0.075$. Note the scale difference from (c) to (d). 500 points were used in (a), and 5000 points were used in (b)–(d).
Neither of these bear any resemblance to the Rössler attractor. The result of NPE calculations are shown in Fig. 10. Both cases have an NPE less than one, which indicates determinism in the ISI sequence. In comparison with those for the IF models, the NPE values are high, most likely a consequence of the low sampling rate in both cases. The NPE values vary significantly as a function of \( m \), in contrast to those for the good reconstructions from the IF models. Further, the NPE is smaller for the ISI sequence with the smaller value of \( \mu \). This indicates that the FHN dynamics modify the signal flow more than the IF dynamics, as expected from the nonlinear dynamical properties of excitatory cells revealed by experimental studies [19,27,28].

If \( \mu \) is allowed to increase further past 0.075, there exists a value (\( \mu \approx 0.3 \)) beyond which the return map does not change. The return map for \( \mu = 0.4 \) is shown in Fig. 11. The attractor does not look like that of the Rössler system, but rather like that of a two-dimensional map such as a Poincaré map of a higher-dimensional system. In fact, the attractor in Fig. 11 is similar to those that are generated from intervals between threshold crossings of the \( x \)-component of the Rössler system itself (not shown). This is not surprising since the dynamics of the FHN equations are dominated by the forcing current which is this \( x \)-component.

5. Validation of prediction results using surrogate data

In this section we investigate the nature of the correlations in the ISI sequences which give rise to the forecastability revealed by the NPE analyses. This is achieved using the surrogate data method [32] applied to ISI data [21] with the NPE as our discriminating statistic. Three kinds of surrogates are used: shuffled, phase-randomized, and amplitude-adjusted phase-randomized surrogates. Shuffled surrogates have no correlation between successive ISI values, but the distribution of ISI values is exactly preserved. The phase-randomized surrogates mimic the linear correlations of the original ISI sequence, but have a Gaussian distribution. The amplitude-adjusted surrogates mimic the linear properties of the data as well as the ISI distribution. The latter two surrogates preserve the main spectral features of the ISI sequences, but the methods used to generate them cannot reproduce the intricate spectral details.

These surrogates are borrowed from time series analysis, where they were proposed with specific null hypotheses in mind. For the case of shuffled surrogates, the null hypothesis of independent and identically distributed (IID) values carries over to the context of neural ISIs without any interpretation
problem. However, both kinds of phase-randomized surrogates produce a Gaussian-distributed data set; in the case of the amplitude-adjusted surrogates, this set is remapped to another set having the same distribution as the original data. The null hypotheses are, respectively, a linear stochastic process (for example, colored noise), and a linear stochastic process seen through a static nonlinearity.

There is a severe problem of interpretation when the latter null hypotheses are applied to ISI data, because the phase-randomization procedure significantly alters the distribution of intervals between times at which events occur. For example, negative ISIs can be generated. A discussion of this problem can be found in [30]. That study shows that while the rejection of the null hypothesis does not allow the rejection of a physical mechanism for the generation of ISIs, it does argue against linear correlations as the source of the forecastability. That is the spirit in which the surrogate data analysis is carried out in the present study. In particular, it is important to check against both kinds of surrogates, since it has recently been shown, using radioactive decay events to generate intervals, that failure to correct for the distribution of surrogates can lead to spurious identification of non-random structure [2].

Ten sets of each kind of surrogate are generated from each ISI sequence of interest, and the NPE is computed for each surrogate. The NPEs for one kind of surrogate are averaged together, and an error bar equal to $\pm 2\sigma_p$ is calculated, where $\sigma_p$ is the standard deviation across the 10 surrogate values. This procedure is repeated for several values of $m$. There is an error bar on all NPE values for surrogates, equal to or less than the symbol size used to plot the NPE values. Note also that the scales are not the same on all plots.

The data for the good and poor reconstructions for each of the three IF models in Section 4 each contain 3000 ISIs. The NPE values for the raw and surrogate data sets are shown in Fig. 12 for the generic IF, in Fig. 13 for the GM model, and in Fig. 14 for the leaky IF model. In every case for $m > 1$, the null hypothesis of IID data can be rejected, and the results with both types of phase-randomized surrogates clearly indicate that linear correlations make only a small contribution to the forecastability. It is not possible to distinguish the surrogates from certain raw data sets when $m = 1$. This is because the NPE algorithm simply averages one-step ahead predictions over the 30 most similar intervals (1% of the total), while the NPE results suggest that the dynamics are at least two-dimensional.
6. Comparing the three IF models

6.1. NPE and sampling rate

The results in Section 4 established that input attractors can be reconstructed using ISIs in all three IF models considered. This is true even though the firings may not occur over the whole range of the input signal. For example, Fig. 4 shows that even for the good reconstruction, firings occur less frequently when the signal is high, or when the slope of the signal is near its most positive value (Eq. (20)). Likewise, Fig. 6 illustrates that a good reconstruction with low NPE is possible even though no firings occur on the bottom part of the signal.

The parameters from the different IF models were adjusted to yield "good" reconstructions with the same "sampling rate" of 1.15 Hz, in the hope of facilitating the comparison of the ability of these models to reconstruct inputs. A quick inspection of the reconstructed attractors in Figs. 2, 4, and 6 suggests that the best reconstruction is achieved for the generic IF model, and that the quality of the reconstruction diminishes for the GM model, and further still for the leaky IF model. However, such a comparison does not take into account the fact that the input signal is sampled more uniformly in the generic IF case, as we have just discussed. In fact, it is difficult to devise a proper comparison, because as soon as a new biophysical parameter is introduced, the mean firing rate is modified. For example, as soon as leakiness is introduced into the generic IF model, the mean firing rate decreases even though the input signal is the same. Consequently, the reconstruction quality and the NPE decrease. One can then increase the firing rate back to the same value as for the generic IF case, but this requires further alterations, such as modifying the threshold. Since firing rate is a major determinant of reconstruction quality, it is the parameter that is kept constant for the three IF models. The main point then is not that the generic IF gives the best reconstructions, but that all models can give good reconstructions when the firing rate is high.

The dependence of the NPE on sampling rate is illustrated in greater detail for the GM model in Fig. 15, where the NPE is plotted against $\alpha$, itself proportional to the sampling rate. It is clear that, as $\alpha$ increases, the NPE decreases. This decrease is well fitted by the sum of an exponential and a constant term, which suggests that the NPE value has a lower saturation value for very high firing rate. As one would expect, this NPE value ($0.14$) is close to that of the $x$-component of the Rössler itself, i.e. $\approx 0.07$ for $3 < m < 9$. This mean value was determined using a uniform sampling of the $x$-component at every 0.2 s. The NPE increases at a slow rate as the sampling rate decreases. For example, a sampling rate of 0.4 s (i.e. $\approx 15$ samples per basic cycle) produced a mean NPE of $\approx 0.08$ over the same range of $m$ values. The origin of this dependence of NPE on sampling rate is the same as that for the ISIs, and lies in the progressive decorrelation of successive samples, and thus, of successive ISIs.

NPE results for the three IF models with a sampling rate of 1.15 Hz are plotted side by side in Fig. 16. The generic IF device has significantly lower NPE than the other two models. This is probably not due to an intrinsic superiority of the generic IF model, since all models relate signal values to ISIs through some map that does not change dynamical invariants. The difference is more likely due to the fact that, in our study, the generic IF model samples the input more evenly than...
the other two models. Also, for all models, the NPE is almost constant across all \( m > 1 \) values. This suggests that most of the information about the Rössler system is present in the ISIs, and consequently, that good neighbors can be found in any dimension greater than one. In contrast, for the poor reconstructions, the NPE is low only over a narrow range of \( m \) values, namely for \( 2 < m < 4 \) (the minimum is different for each model). In these cases, determinism is lost as the low sampling rates make the ISIs less causally and more statistically related. Consequently, a limited range of embedding dimensions will yield appropriate neighbors, causing a sensitivity of the NPE to the value of \( m \).

6.2. Decay of forecastability with prediction time

Refs. [31,34] describe a method for finding evidence (but not proof) of chaos in time series, based on the dependence of forecasts on prediction time. Here we investigate the extension of this method to the ISI sequences from the three IF models. Since we are dealing with noiseless models, the results presented here reflect the power of this method for ISI data in the best of cases. The basis of this method is the notion that, for a chaotic time series, Pearson’s correlation coefficient \( r \) between the distributions of predicted and actual ISI values varies with prediction time \( T \) according to

\[
r(T) \propto (1 - e^{KT}).
\]

where \( K \) is a positive constant. Thus a plot of \( \ln(1 - r) \) versus \( T \) would produce a straight line if the information about the chaotic input is present in the ISIs. We apply this method to the “good” and “poor” ISI sequences by interpreting \( T \) (absolute continuous or discrete time) as a prediction horizon \( T_h \), i.e. as the number of ISIs ahead one wishes to predict. For example, \( r(T_h = 4) \) is the correlation coefficient for predicting four ISIs ahead. The results are shown in Fig. 17.

For the “good” ISI sequences (\( \theta = 35, \alpha = 10, \gamma = 0.154 \)), the linear scaling associated with chaotic dynamics is present over a long prediction horizon for the generic and leaky IF models, and for \( 1 \leq T_h \leq 4 \) for the GM model. For the “poor” ISI sequences (\( \theta = 90, \alpha = 1, \gamma = 0.01 \)), \( \ln(1 - r) \) tends to climb nonlinearly towards zero (i.e. \( r \to 0 \)), where it levels off. Thus, for these low sampling rate cases, the correlations between ISIs do not capture the chaotic nature of the neuron dynamics, even though they do capture some nonlinear correlations, as revealed by our NPE-surrogate data analysis in Sections 4 and 5. Also, for short-term forecasts, our ability to predict future ISIs falls off more rapidly with \( T_h \) (from an already low level) for the poor ISI sequences. In summary, application of this method to point processes from simple neuron models shows some promise if the sampling rate of the input is sufficiently high.

7. The role of the ISI distribution

This section considers the reconstruction quality as a function of the distribution of ISIs, i.e. of the ISIH. Fig. 18 shows the ISIHs for the two cases of each of the three IF models and the FHN model studied in Section 4. These can be compared to the histogram of values of the \( x \)-component of the Rössler system itself, shown in Fig. 1(b). At first glance, it appears that all ISIHs are very different from one another. All distributions, designated here by \( P_1 \), have counts only in a narrow domain of ISI values (this domain of values where \( P_1 \neq 0 \) is known as the “support” of \( P_1 \)). For the IF models, the counts for the poor reconstructions correspond to ISIs centered around a high mean value in comparison to their “good” counterparts. This is
simply another statement of the fact that poor reconstructions correspond to lower mean sampling rates. Since all the IF models can yield good reconstructions, we can conclude that the quality of the reconstruction is dependent more on the sampling rate (i.e. the ISIH mean) than on the actual distribution of ISIs.

Closer inspection reveals that the ISIH for the “good” sequence from the generic IF has a shape and peaks similar to those of the input signal in Fig. 1(b). This reinforces previous conclusions that the generic IF model with the parameter used in Section 4 produces the best reconstruction of the input signal. We also observe that the good ISIH for the GM model has a significant number of counts across a larger range of ISIs (0.25–2.2), as compared to the other two IF models, even though its mean ISI is the same and equal to the reciprocal of the sampling rate 1/1.15 = 0.87. The presence of many counts at larger ISIs may explain the relatively lower correlation coefficient $r$ for the GM model (see Fig. 17), even though there is little difference between the one-step ahead NPEs for the leaky and GM models. It is also clear that the ISIHs from the FHN model are radically different from the distribution of input signal values. This supports our previous conclusion that the FHN model does not simply generate ISIs that have a simple relation to the input. The regime chosen for FHN in our study is physiologically plausible, and is relevant to many experimental studies (see e.g. [19,28]). Better reconstructions may be obtained by e.g. slowing down the Rössler input and/or by modifying the FHN parameters, although our attempts at this have been unsuccessful.

It is possible to obtain a deeper understanding of the ISIH structure for the IF models when the firing rate is high. As discussed in Section 4, these models sample the input signal when the threshold condition is satisfied. Our analysis showed that these samples
are simply mapped to ISI values. It should then be possible to compute an ISI for one of these models using the (numerically) computed distribution $P_x(x)$ of the Rössler $x$-component in Fig. 1(b). However, this requires more than a standard calculation of the distribution $P_I$ from $P_x$ knowing the transformation $I = F(x)$ from sample to ISI, using $P_I(I) dI = P_x(x) dx$. For example, that approach would lead to the erroneous conclusion for the GM model that the mean ISI, $\mu_I$, is related to the mean of $x$, $\mu_x$ by the equation $\mu_I = \alpha^{-1}(\mu_x + 10)$, since the actual signal is $S(t) = x(t) + 10$, and the analysis in Section 4 yielded $I(S) = S\alpha^{-1}$. In fact, for $\alpha = 10$, we observe that $\mu_I = 0.87$, as for the other two IF models, rather than 1.06 as this simple analysis would predict.

The discrepancy arises because we have not taken into account the relative frequency at which the different values of $x(t)$ (or $S(t)$) are sampled. Inspection of Fig. 4 reveals that lower values of $S(t)$ are sampled more often than higher ones. Since ISIs are directly proportional to sample values, $I = S\alpha^{-1}$, the result is that the mean ISI is lowered by the sampling process, from 10.6 to 0.87. Thus, computing the new distribution after the change in variable from $S$ to $I$ must first be preceded by a weighting of the distribution of sample values $P_S(S)$. We can assume that the weight associated with a given value of $S$ is proportional to the frequency $f(S)$ at which this value is sampled, and that $f(S)$ is proportional to the instantaneous firing frequency $F^{-1}(S)$ at this value of $S$, i.e. to the reciprocal of the firing interval. The probability $Q(S)$ that a value of $S$ is actually sampled and converted to an interval is then proportional to the product of the probability that $S$ occurs in the first place, $P_S(S)$, times the probability that it is sampled by the IF neuron. For the GM model, this latter probability is proportional to $S^{-1}$, and consequently,

$$Q(S) = \frac{1}{N} \frac{P_S(S)}{S},$$

where $N$ is a normalization factor

$$N = \int_{S_{\text{min}}}^{S_{\text{max}}} \frac{P_S(S)}{S} dS.$$  \hspace{1cm} (30)

The distribution of intervals can then be calculated from

$$P_I(I) = Q(S) \frac{dS(I)}{dI} = \alpha Q(S).$$ \hspace{1cm} (31)

We can then, for example, calculate the mean interval $\mu_I$ in the following way:

$$\mu_I = \int S P_I(I) dI$$

$$= \int \frac{S_{\text{max}}}{S_{\text{min}}} I(S) Q(S) dS$$ \hspace{1cm} (33)
\[ R_I = \frac{\int_{S_{\text{min}}}^{S_{\text{max}}} P_S(S) \, dS}{\int_{S_{\text{min}}}^{S_{\text{max}}} P_S(S)^{-1} \, dS}. \]

where \( R_I \) is the support of \( P_I(I) \). Using the data for \( P_S(x) \) in Fig. 1(b), along with \( S(t) = x(t) + 10 \), the ratio of integrals can be computed by numerical integration. This ratio was evaluated using fourth-order interpolating polynomials, and the value was the same as that obtained with the simplest "rectangle method" when the histogram \( P_S(x) \) contains at least 200 bins across its support. The ratio value is 8.47, and thus, for \( \alpha = 10 \), we obtain the value \( \mu_I = 0.847 \), very close to the actual value of 0.87. This analysis holds also if the sampling rate is high enough so that values on the positively sloped portions of the signal are sampled (cf. Eq. (20)). At lower sampling rates (i.e., lower \( \alpha \)), there will be an additional weighting that takes these missing samples into account in computing the ISIH. The result is a fractionated support, as seen in Fig. 18.

A similar analysis can be performed for the IF or leaky models. For the simpler IF case, we recall from Eq. (11) that \( I(S) = \Theta/S \), and also that \( S(t) = x(t) + 40 \). The instantaneous frequency is thus proportional to \( S \), and

\[ Q(S) = \frac{1}{N} P_S(S) S. \]

The mean interval is then given by

\[ \mu_I = \Theta \frac{\int_{S_{\text{min}}}^{S_{\text{max}}} P_S(S) \, dS}{\int_{S_{\text{min}}}^{S_{\text{max}}} P_S(S)^{-1} \, dS}. \]

For \( \Theta = 35 \), the ratio of integrals is found to be 0.0246, resulting in \( \mu_I = 0.861 \), as observed from the simulations of the generic IF model with this value of \( \Theta \). In this case, the weighting function does not alter the distribution of the signal values very much. This could have been guessed by comparing the ISIH to the distribution in Fig. 1(b). Also, the left panel of Fig. 2 shows that firings occur at almost the same mean rate when the signal is low or high. This is due to the high offset (equal to 40), which is the main driving force of the voltage towards threshold, making the proportionality between firing rate and signal (rate-coding) difficult to see, even though it is present.

In summary, our analysis shows that it is possible to understand the ISIH structure from the distribution of the input signal, using the map from samples to ISIs and a weighting function proportional to the instantaneous firing frequency.

8. Discussion

8.1. Summary

We have examined the conditions under which the attractor of a chaotic input to a neuron model can be reconstructed from ISIs generated by that model. For the simple IF models, the attractor can be reconstructed if the sampling rate is high, i.e., if many firings occur during a characteristic cycle of the input. The IF dynamics then simply map samples of the input signal into ISIs (Section 4). This sampling is non-uniform in time, and non-uniform over the distribution of the input signal values as well (Section 7). For the generic and leaky IF models, more firings occur when the input is high, resulting in shorter ISIs; consequently, higher inputs are sampled more often. As the mean sampling rate of the input decreases, the resulting longer ISIs correspond to input signal averages over longer periods of time. Consequently, the deterministic relation between successive ISIs, due to the short-term forecastability of the chaotic input, decreases. This leads to bad delay embeddings in which points in a neighborhood evolve very differently in time. The quality of the attractor reconstruction deteriorates, and estimates of dynamical invariants such as normalized prediction error diverge from those for the input.

For the generic IF model, reconstruction quality and ISI forecastability decrease as the threshold increases or the signal offset decreases. In the GM model, they decrease as the pacemaker rate decreases, or the threshold (equivalent to a signal offset) increases. For the leaky IF, they decrease as leakiness or threshold increase, or as the signal strength decreases. Also, for all these models, reconstruction quality and forecastability decrease as the range of signal values (samples) in which firings occur shrinks.
Our study makes an interesting prediction concerning the so-called "rate-coder" neurons, i.e. neurons whose mean firing rate varies in some proportion to an input signal. If the dynamics and parameters of a neuron allow it to behave as a rate-coder that can fire at high rates, as the IF models studied here, reconstruction of the input may be possible. This should be true even if the rate-coding is not obvious from visual inspection, as in Fig. 2. However, if firings are often separated by long periods of time (longer e.g. than the Lyapunov time of the input), degradation of the reconstruction will result. A major unknown is the influence of noise, which tends to accompany neurons that act as rate-coders. Understanding the influence of noise will be crucial for making precise statements about real neurons.

For the FHN model with realistic parameters, the ISI attractors are very different from the input attractor (Fig. 9), due to the more complex dynamics of this model. In fact, the sampling rate could not be made high, with firings distributed over the full range of the input, as for the IF models. Explorations of parameter space to uncover ranges where reconstruction occurs were unsuccessful. One reason for this may be that FHN shows little variation in firing frequency for different suprathreshold biases, i.e. for constant signals that lead to periodic firing. In other words, this model does not exhibit sufficient rate-coding. Our findings thus suggest that, a priori, one should not expect real neurons to reconstruct attractors of their inputs, a conclusion compatible with the observed complex behavior of many excitable cells, even with simple inputs [19,27,28].

While input attractor reconstruction from ISIs may not be adequate visually, the ISIs can still be predictable, even for the smallest sampling rate studied here (0.15 Hz for the GM model). The surrogate data analysis in Section 5 further establishes the nonlinear nature of the ISI correlations responsible for this predictability. Also, application of the method in [31,34] to the ISI sequences from the IF models (Section 6) further reveals that evidence for chaos is clear only in the good ISI sequences.

If ISIs are longer than the time over which the input itself can be predicted, they lose their causal relationship to one another. The dependence of dynamical invariants on the sampling rate found here is similar to that for the Rössler x-component itself. This similarity could be made even stronger by using randomly rather than evenly spaced sampling times. In any case, if this x-component is sampled at a sufficiently high rate, all useful dynamical information is present, and can be retrieved for a fairly large range of embedding delays. If it is sampled at a low mean rate, the minimal embedding delay in real time units will be too large, much larger than e.g. the autocorrelation time or the Lyapunov time. Points in a given neighborhood in the embedding space will map to very different parts of this space, destroying the flow lines. Our simulations confirm that the NPE of the x-component decreases with sampling rate (not shown).

For ISIs, the problem of bad neighborhoods at low sampling rates is compounded by the fact that certain portions of the signal may not be sampled at all (Section 7), leading to even higher NPEs. The problems caused by low sampling rates probably account for much of the disparity, found e.g. in [20], between the correlation dimension of the Lorenz attractor and that of attractors constructed from ISIs between threshold crossings of the Lorenz variables themselves.

8.2. Outlook

Our study suggests a number of directions of research into the properties of ISI attractors. In Section 4, we determined maps between successive ISIs and input values at which firings occur in the IF models, in the high firing rate limit. This result provides the connection between the dynamical properties of the input and those of the ISIs. It would be interesting to extend this result to arbitrary rates, and also to more complicated models such as FHN. As pointed out above, the influence of noise on this mapping is certainly an issue deserving attention.

A related question is whether there is a diffeomorphism between the Rössler attractor and the ISI attractor, i.e. a smooth mapping (with a smooth inverse) between the x-time series and the ISI sequence. An answer to this question probably requires a more
rigorous approach using embedding theory [12]. In a general mathematical sense, an infinite number of possible x-time series can yield identical interval sequences, since the dynamics between events can be arbitrary. We are not aware of results indicating that this mapping is injective (as required for a diffeomorphism) if all x-time series are constrained to originate from the same deterministic dynamical system. In other words, we do not know if two different x-time series from the same Rössler attractor must yield different ISI sequences.

Another question is the precise sense in which the thresholding process is similar to taking a Poincaré section on the flow of the combined "neuron + chaotic input" system. We argued in Section 4 that ISI generation in the generic IF model (and similarly for the other two models) is similar to, but dimensionally different from the action of a Poincaré section on the combined flow. It is similar to a stroboscopic Poincaré section for periodically forced systems, except that the intervals between the samples vary chaotically, following the threshold crossings of the voltage variable. However, each sampling yields one measurement on the input x-component (which is converted by a map into an ISI), but does not reveal the other components of the Rössler system. The result is a greater reduction in dimension than that achieved by a Poincaré section. Nevertheless, information about the Rössler attractor can still be obtained through delay embedding. This reasoning could perhaps be extended to the more challenging FHN and other realistic models.

The FHN model studied here does not have a real threshold, but rather a pseudo-threshold [16]. This means that the height of neural firing responses are graded over a very narrow range of input amplitudes. Other more realistic neuron models such as the Hodgkin–Huxley equations can also have either real or pseudo-thresholds, depending on parameters [35]. It would be interesting then to study how our conclusions depend on the type of threshold. Finally, it would be worthwhile to investigate ISI attractors using correlation dimension, and also dynamical information measures such as the KS entropy; results could then cast a different light on studies of neural coding based solely on information theory.

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