



## Spike-time reliability of periodically driven integrate-and-fire neurons<sup>☆</sup>

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### Abstract

The response of model neurons driven by a periodic current converges onto mode-locked attractors. Reliability, defined as the noise stability of the attractor, was studied as a function of the drive frequency and noise strength. For weak noise, the neuron remained on one attractor and reliability was high. For intermediate noise strength, transitions between attractors occurred. For strong noise, mode locking became unstable. The attractor was most stable for frequencies for which the neuron produced one spike on each cycle. The prediction of a reliability resonance as a function of drive frequency has been observed in vitro in cortical neurons. © 2002 Published by Elsevier Science B.V.

*Keywords:* Neural code; Oscillation; Phase locking; Precision

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### 1. Introduction

Although spike trains in the cerebral cortex are highly variable (for a review see [10]), neurons can fire with high temporal precision and reliability in vitro [1,5,8]. Precision is defined here as the inverse of the temporal jitter in the spike time and reliability as the reproducibility of spikes across trials. Information-theoretical analyses of the neuronal spike trains in the lateral geniculate nucleus indicate that precise spike times contain more information about the input than firing rate alone [9]. It is unknown how these precise spike times are used in the cortex.

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If a feature is present in the spike train response to one stimulus across multiple trials it can form the basis of a neuronal code. Spike-time reliability is a measure for the reproducibility of individual spike times [6]. Neurons produce a reliable sequence of spike times in response to some inputs and respond unreliably to others. In vitro, neurons fire reliably when injected with a random current containing high-frequency components, but they fire unreliably when driven with a low-pass or constant current [2,6]. Sinusoidally driven neurons show resonances in reliability as a function of drive frequency [3,4]. Our aim is to understand these experimental results within the framework of noise stability of attractors.

## 2. Methods

The membrane potential  $V$  of an integrate-and-fire neuron driven by a fluctuating current satisfied  $dV/dt = -V + I + f(t) + \xi(t)$ , where  $I$  was the time-independent driving current,  $f(t)$  the fluctuating current and  $\xi$  was a white noise current, with zero mean and variance  $D$ , that represented the effects of intrinsic noise. When the voltage  $V$  reached threshold,  $V(t) = 1$ , a spike was emitted and the voltage was reset to zero. Dimensionless units were used: 1 voltage unit was the distance between resting membrane potential and action potential threshold, approximately 20 mV; one time unit corresponded to the membrane time constant, approximately 10–40 ms. The periodic current was either sinusoidal,  $f(t) = A \sin \omega t$ , or a periodic piecewise constant current equal to  $f(t) = -A$  when  $0 \leq \text{mod}(t, T) < T/2$  and  $f(t) = A$  otherwise. Here,  $A$  was the amplitude of the drive,  $T$  the period, and the frequency  $\omega = 2\pi/T$ . For the sinusoidal current, the differential equation was integrated directly using the fourth-order Runge–Kutta algorithm [7] with step size  $dt = 0.01$ . For the piecewise constant current an analytical spike-time map,  $t' = M(t)$ , was derived [11], here  $t$  and  $t'$  were the previous and new spike time, respectively. Spike times were generated by iterating this map.

The spike phase of the  $n$ th spike time  $t_n$  was  $\psi_n = \text{mod}(t_n, T)/T$ . The mean phase,  $\Psi_m = (p/N_s) \sum_{n=0}^{N_s/p-1} \psi_{m+np}$ , was determined for periodic  $\psi_n$  time series, here  $p$  was the period,  $m = 1, \dots, p$ , and  $N_s$  was the total number of spikes.

## 3. Results

The parameters of an integrate-and-fire neuron driven by a sinusoidal current were chosen such that the neuron produced on average one spike per two cycles of the driving current (Fig. 1). From different initial voltages the neuron converged to one of the two different voltage trajectories (Fig. 1A and B), yielding two different sequences of spike times (not shown). The two solutions are related: when one solution is shifted by one cycle, the other solution is obtained. There were two attractors. Attractor 1, when the neuron spikes on odd cycles, was obtained starting from  $0.78 \leq V_{\text{init}} < 0.98$ , here  $V_{\text{init}}$  was the voltage at the start of the simulation. Attractor 2, when the neuron spikes on even cycles, was obtained starting from  $0.0 \leq V_{\text{init}} < 0.78$  and  $0.98 \leq V_{\text{init}} < 1.0$ .

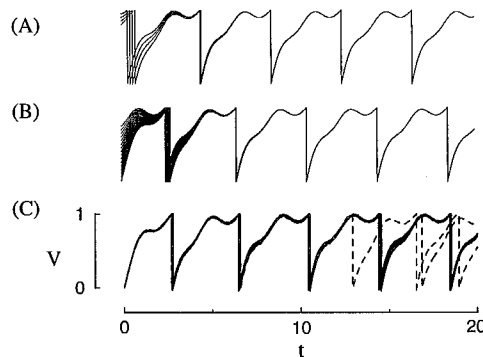


Fig. 1. Integrate-and-fire neuron driven by a sinusoidal current. (A,B) Voltage traces  $V(t)$  converged to one of the two attractors starting from 20 different initial voltages. (C) Voltage traces for 10 different realizations of intrinsic noise. Neuron remained on the attractor for 8 out of 10 trials (solid lines) and on 2 trials it made a transition to another attractor (dashed lines). Parameters were  $A = 0.21$ ,  $T = 2$ ,  $I = 1.0$ , (A,B)  $D = 0$  and (C)  $D = 10^{-4}$ .

The attractor dynamics in the presence of noise was studied starting from  $V_{\text{init}} = 0$  with a different realization of the intrinsic noise on each trial. Ten voltage curves are shown in Fig. 1C, 8 out of 10 curves remained close to the attractor, whereas on 2 trials the voltage deviated from the attractor.

Next, the dynamics of an integrate-and-fire neuron driven by a piecewise constant periodic current was studied (Fig. 2). For a given frequency  $\omega$  the neuron converged, after a brief transient, onto a periodic attractor and was then mode locked to the drive. The resulting spike train was periodic with a period equal to  $q$  drive cycles, during which  $p$  spikes were emitted. The average interspike interval was  $qT/p$ . The winding number  $\langle N \rangle$  is the average number of spikes per drive cycle, during mode locking it was rational and equal to  $p/q$ , where  $p$  and  $q$  were positive integers. For  $A = 0.4$ , the neuron was 1:1 mode locked when the period was close to the average interspike interval obtained without the periodic drive ( $A = 0$ ). This led to a step of constant winding number  $p/q = 1$  in the  $\langle N \rangle$  versus  $\omega$  characteristic (Fig. 2A(a)). There were also steps for other rational winding numbers and the  $\langle N \rangle$ - $\omega$  graph had the appearance of a staircase. For low  $q$  values, the steps were wide, with the  $\frac{1}{1}$  step being the widest.

During  $p:q$  mode locking, the neuron fired at  $p$  different phases  $\Psi_m$  (see Section 2). The winding number was constant on the mode locking step, whereas the spike phase increased with  $\omega$ . For instance, during 1:1 entrainment  $\Psi_1$  was equal to  $\frac{1}{2}$  on the left-hand side of the step and increased to 1 on the right-hand side of the step.

There were  $q$  different attractors of the dynamics for  $p:q$  mode locking. The other attractors were obtained from a given attractor by shifting over multiples of the drive cycle (data not shown).

The attractors were not equally stable for all parameter values corresponding to the same winding number. Two frequency values for which 1:1 entrainment was obtained were considered as an example: (1)  $\omega/2\pi = 0.87$  with  $\Psi_1 = 0.64$  in the middle of the

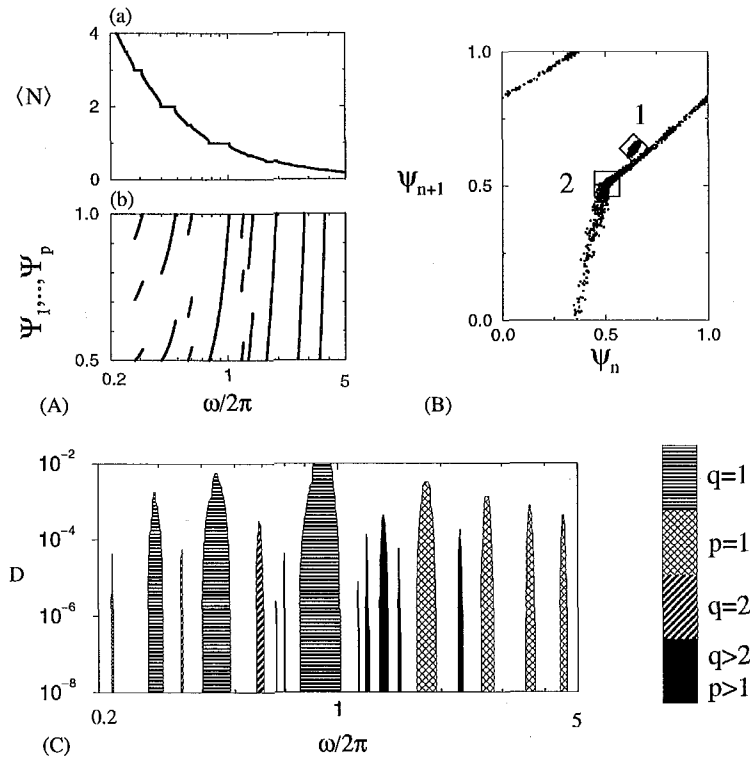


Fig. 2. The integrate-and-fire neuron was mode locked to a periodic piecewise constant current. (A) (a) The average number of spikes per cycle,  $\langle N \rangle$  and (b) spike phases  $\Psi_1, \dots, \Psi_p$  for steps with  $p < 4$  were plotted versus frequency  $\omega$ . (B) Spike-phase return map, the next phase  $\psi_{n+1}$  versus the previous phase  $\psi_n$ , during 1:1 mode locking. The zero-noise return map was plotted for  $\omega/2\pi = 0.87$  (1, open diamond) and for  $\omega/2\pi = 0.78$  (2, open square). The dots form the corresponding return maps in the presence of noise with  $D = 10^{-4}$ . See text for description. (C) An Arnold Tongue was formed by the set of points with the same winding number  $p/q$  and it was coded for its  $p/q$  value (legend is to the right of (C)). For clarity only a few Arnold tongues were shown:  $q = 1, p = 1$  (with  $q > 1$ ),  $q = 2$  (with  $p > 1$ ), and  $q > 2$  (with  $p > 1$ ); the maximum value of  $p$  was 4 and for  $q$  it was 5. Parameters were  $I = 1.5$  and  $A = 0.4$ .

step and (2)  $\omega/2\pi = 0.78$  with  $\Psi_1 = 0.51$  near the left-hand side of the step. The return map, where the next phase  $\psi_{n+1}$  was plotted versus the previous phase  $\psi_n$ , was a single point  $(\Psi_1, \Psi_1)$  in the absence of noise (Fig. 2B). This point was the fixed point of the map. For  $D = 10^{-4}$ , and  $\omega/2\pi = 0.87$ , the return map consisted of a cloud of points distributed around the fixed point. However, for  $\omega/2\pi = 0.78$ , the phase took any value between 0 and 1. Noise induced an extra spike on some cycles at a phase that was far from the fixed point of the dynamics, this resulted in large deviations of the spike phase. It took a number of cycles for the neuron to return to the attractor. In general, the closer the neuron was to the edge of a step—a bifurcation point—the less stable the attractor was against intrinsic noise. Attractors for mode locking at higher  $q$  values were less stable since the step width was smaller. For the piecewise constant periodic current considered in Fig. 2, the fixed point phases only took values between  $\frac{1}{2}$  and 1.

The unstable edges of the step corresponded to the phases  $\frac{1}{2}$  and 1. For  $p > 1$ , multiple phases had to fit in this interval. Hence, for higher  $p$  there was at least one phase  $\Psi_m$  close to the edge—the resulting attractor was less stable against noise.

The mode locking regions (Arnold Tongues) were also determined as a function of noise strength for a fixed amplitude  $A = 0.4$  (Fig. 2C). The width of the tongue (step width) decreased as a function of  $D$ , since more and more points close to the edge became unstable. 1:1 mode locking was most stable; for  $D = 10^{-2}$ , the 1:1 step was still present, whereas other steps had become unstable or could not be resolved on the parameter grid used for the simulations.

#### 4. Discussion

The dynamics of a periodically driven model neuron was studied as a function of drive frequency and noise strength. The model neuron was mode locked to the periodic drive and the winding number  $p/q$  was constant for a range of frequency values. The dynamics changed qualitatively at frequency values for which the winding number changed: the periodicity of the spike train, the number of attractors, and the spike times all changed discontinuously. Close to these bifurcation points the dynamics was sensitive to noise. The attractor was less stable against noise and noise could induce transitions between different attractors, missing or extra spikes. Hence, the reliability of the discharge was reduced.

The key observation is that in the presence of noise reliable discharge is only obtained far from bifurcation points, for frequencies in the middle of the mode locking steps. The 1:1 step is the widest, and the frequency values in the middle are the most stable. Hence, the discharge is more reliable for frequency values during which the neuron is 1:1 mode locked compared with outside 1:1 mode locking. The reliability of pyramidal cells and interneurons in rat prefrontal cortical slices was studied with sinusoidal current injection over a range of frequencies [3]. Pyramidal cells mode locked in the 5–20 Hz range, whereas interneurons mode locked in the 5–50 Hz range [3]. Spike-time reliability was always highest during 1:1 mode locking [3].

The location and density of bifurcation points also determine the reliability for a neuron driven by arbitrary fluctuating currents. These and other results will be presented elsewhere [12].

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