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EMERGENCE OF NARROWBAND HIGH FREQUENCY OSCILLATIONS FROM ASYNCHRONOUS, UNCOUPLED NEURAL FIRING

Stephen V. Gliske*,

Department of Neurology, University of Michigan, 500 S. State St., Ann Arbor, MI 48109, USA, sgliske@umich.edu

William C. Stacey*,

Departments of Biomedical Engineering and Neurology, University of Michigan, 500 S. State St., Ann Arbor, MI 48109, USA, wstacey@med.umich.edu

Eugene Lim,

Department of Physics, Ohio Wesleyan University, 61 S. Sandusky St., Delaware, OH 43015, USA

Katherine A. Holman, and

Department of Physics, Towson University, 8000 York Road, Towson, MD 21252, USA

Christian G. Fink

Department of Physics and Neuroscience Program, Ohio Wesleyan University, 61 S. Sandusky St., Delaware, OH 43015, USA, cgfink@owu.edu

Abstract

Previous experimental studies have demonstrated the emergence of narrowband local field potential oscillations during epileptic seizures in which the underlying neural activity appears to be completely asynchronous. We derive a mathematical model explaining how this counterintuitive phenomenon may occur, showing that a population of independent, completely asynchronous neurons may produce narrowband oscillations if each neuron fires quasi-periodically, without requiring any intrinsic oscillatory cells or feedback inhibition. This quasi-periodicity can occur through cells with similar frequency-current (f-I) curves receiving a similar, high amount of uncorrelated synaptic noise. Thus, this source of oscillatory behavior is distinct from the usual cases (pacemaker cells entraining a network, or oscillations being an inherent property of the network structure), as it requires no oscillatory drive nor any specific network or cellular properties other than cells that repetitively fire with continual stimulus. We also deduce bounds on the degree of variability in neural spike-timing which will permit the emergence of such oscillations, both for action potential- and postsynaptic potential-dominated LFPs. These results suggest that even an uncoupled network may generate collective rhythms, implying that the breakdown of inhibition and high synaptic input often observed during epileptic seizures may generate narrowband oscillations. We propose that this mechanism may explain why so many disparate epileptic and normal brain mechanisms can produce similar high frequency oscillations.

*These authors contributed equally to this work.

Keywords

HFO; epilepsy; synchronization; rhythmogenesis

1. Introduction

Recent experimental studies have demonstrated examples of epileptic seizures which feature coherent LFP oscillations in the absence of population synchrony.^{1, 2} These coherent oscillations form a narrowband peak in the power spectrum, which is somewhat unexpected since most asynchronous networks form a broad-band peak produced by the heterogeneity of their firing rates. One paper² in particular found essentially no spike-timing synchrony after performing an exhaustive search over multiple time scales in human neocortical seizures featuring gamma band oscillations (peak power of 40–80 Hz). While previous theoretical work has explained how *irregular* neuronal firing may produce LFP oscillations,³ the aperiodic spiking of individual cells in that model still generated synchronous bursting on the network level. Other proposed mechanisms, such as stochastic resonance,⁴ coherence resonance,⁵ or correlations in stochastic input,⁶ likewise feature irregular spiking but still incorporate non-trivial levels of spike-timing synchrony, network coupling, and/or underlying rhythms that drive the network.

High-frequency oscillations (HFOs) are another enigmatic brain rhythm. They feature peak power at > 80 Hz and, although they are not always pathological, have been shown to occur more frequently in the seizure onset zone in patients with epilepsy.^{7, 8} HFOs are therefore a promising biomarker for improving surgical outcomes in patients with epilepsy,⁹ and understanding HFO rhythmogenesis may shed light on mechanisms underpinning ictogenesis.¹⁰ Several studies have suggested that ripples (80–250 Hz) are generated by synchronous spiking of pyramidal cells, and that fast ripples (> 250 Hz) emerge due to desynchronization of such spiking.^{11, 12} The proposed mechanisms for epileptic HFOs range from axo-axonic gap junctions¹³ to ephaptic connections¹⁴ to recurrent axons¹⁵ to disrupted network synchrony.¹¹ HFOs were actually first characterized in normal tissue, and there has been considerable study into their role in normal brain processes.¹⁶ These “normal” HFOs appear to be produced by rhythmic inhibitory postsynaptic potentials with sparse pyramidal cell firing.¹⁷ Thus there has been much interest in distinguishing which HFOs are indicative of epilepsy versus normal brain function.¹⁸ One potential difference between the normal and epileptic HFOs is that fast ripples appear to be more specific to epileptic tissue.¹⁹ However, fast ripples are also present in normal tissue, even in patients without epilepsy,²⁰ and it is still unknown how to distinguish normal from epileptic HFOs. Thus while there is tremendous interest in identifying and understanding HFOs as a new epilepsy biomarker, it remains a large challenge.^{21, 22}

Surprisingly, despite so many potential mechanisms and underlying physiology/pathology, HFOs tend to have similar appearance across different patients and even species: to date there has been no reliable feature discovered that distinguishes any of these underlying pathologies. This suggests that HFOs are a generic phenomenon of active networks, and further implies that they should be formed by generic processes that are independent of the

underlying network structure. The question then becomes: what basic network effects are necessary and sufficient to produce HFOs? We previously used a biophysical model to explore the underlying mechanisms of physiological and pathological HFOs²³ and describe how they can recruit neighboring tissue.²⁴ We then modified that model to be able to generate an LFP signal, in order to distinguish the difference between AP-generated and PSP-generated HFOs.²⁵ We used that model to explore the basic parameters necessary to produce HFOs, and surprisingly found that narrowband ripple oscillations may be generated by completely *asynchronous*, stochastic spiking of pyramidal cells, and that fast ripples transiently emerge from this asynchronous activity.²⁵ This finding has important implications, suggesting that HFOs may simply be a sign of a highly-active neural network, not dependent upon any particular network connectivity.

In the present work we provide a firm theoretical foundation for the hypothesis that narrowband oscillations may emerge from a population of neurons that fire asynchronously, independently, and stochastically. This may be accomplished if the neurons naturally fire with some rhythmicity and with similar average frequencies, conditions which may plausibly be met if a population of neurons receives similar intensity of input and shares similar biophysical parameters. This may occur, for example, when inhibition breaks down during an epileptic seizure and an unrestrained pyramidal cell population receives intense synaptic input. This work therefore proposes a novel and general mechanism for the generation of brain rhythms during pathological conditions such as epileptic seizures, in which rhythms may emerge in the absence of any interactions between neurons (other than noisy excitatory input to a population of neurons). We propose that pathological HFOs resulting from cellular action potentials²⁶ may be generated by this mechanism as well. Note that this work deals with only the primary effects of neuronal current producing either action potential or postsynaptic potential waveforms; other effects such as spreading depression and glial cells are not accounted for by our model. Using these results, we derive bounds on the levels of spike-timing heterogeneity which allow for the emergence of such rhythms, both for action potential- and postsynaptic potential-dominated LFPs.

2. Basic Model

As a simple example, consider a situation in which a population of N neurons fire with the same frequency f_0 , but with uniformly random phase. The contribution to the LFP by any one neuron, $g(t)$, is well approximated as the convolution of a periodic train of delta functions with a kernel waveform (representing the voltage trace of an individual action potential, for example). The Fourier transform of this signal, $G(f)$, will feature peaks at f_0 and its harmonics, with an amplitude of zero at all other frequencies. The LFP, $g_N(t)$, will then be the superposition of N randomly-shifted versions of $g(t)$, $g_N(t) = \sum_{j=1}^N g(t - t_{0,j})$, with $t_{0,j} \sim \text{unif}(0, \frac{1}{f_0})$ (with probability density $P(t_{0,j}) = f_0$ for $0 \leq t_{0,j} < \frac{1}{f_0}$). The Fourier transform of the LFP is then $G_N(f) = \left[\sum_{j=1}^N e^{i\theta_j} \right] G(f)$, where $\theta_j = -2\pi f t_{0,j}$. The energy

spectral density can be determined by defining $A = \sum_{j=1}^N e^{i\theta_j}$ and computing its expected squared amplitude:

$$\begin{aligned} E\{|A(f)|^2\} &= \int_0^{1/f_0} \left(\prod_{j=1}^N dt_{0,j} p(t_{0,j}) \right) |A(f)|^2 \\ &= \left(\frac{-f_0}{2\pi f} \right)^N \int_0^{2\pi f/f_0} \left(\prod_{j=1}^N d\theta_j \right) \left(\sum_{k=1}^N e^{i\theta_k} \right) \left(\sum_{\ell=1}^N e^{-i\theta_\ell} \right) = N + N(N-1) \text{sinc}^2 \left(\frac{\pi f}{f_0} \right) \end{aligned}$$

Combining this result with the fact that $G_M(f) = 0$ for all non-harmonic frequencies, the energy spectral density is

$$E\{|G_N(f)|^2\} = \begin{cases} N|G(f)|^2, & f = nf_0 (n=1, 2, 3 \dots) \\ 0, & \text{otherwise} \end{cases} \quad (1)$$

This toy model therefore suggests the possibility of narrowband collective oscillations emerging from asynchronous neural activity. This example is analogous to the fact that incoherent light waves do not produce completely destructive interference, but superimpose with an intensity that scales linearly with the number of waves. Put another way, the *amplitude* of a completely incoherent superposition scales with $\sqrt{N}$, while the amplitude of a perfectly coherent superposition scales with N .²⁷

3. Energy spectral density of an asynchronous population of quasi-periodic neurons

Of course, individual neurons do not spike perfectly periodically, nor do they share the same intrinsic frequency across a population. We therefore introduce a general model of asynchronous, independent, and stochastic neural activity which takes both of these sources of spike-time variability into account. Specifically, we consider a superposition of renewal processes (which is not itself a renewal process²⁸) in which the inter-event interval (IEI) density of neuron i is given by

$$p_0(\tau^{(i)} | \mu_i, \sigma_{\text{jit}}) = \frac{1}{\sigma_{\text{jit}} \sqrt{2\pi}} \exp \left(-\frac{(\tau^{(i)} - \mu_i)^2}{2\sigma_{\text{jit}}^2} \right), \quad (2)$$

with the parameter μ_i also being normally distributed, drawn from $\mathcal{N}(\mu_0, \sigma_\mu)$, and σ_{jit} being a fixed model parameter.

Therefore σ_μ determines the variability in intrinsic frequency among all cells within the entire population, and σ_{jit} quantifies the degree of “jitter” from one event to the next for a single neuron (see Fig. 1). The mean population frequency is set by μ_0 . (Note that while this

technically permits negative IEI values, this will occur very rarely as long as σ_μ and σ_{jit} are kept sufficiently small with respect to μ_0 , as is the case in all these simulations.)

We assume all events generate either an action potential (AP) or post-synaptic potential (PSP) voltage waveform, so that the overall LFP is computed as the convolution of the waveform with the event trains generated by Eq. 2, summed over all neurons. Our goal is to compute the expected energy spectral density of this model LFP. Since the energy spectrum of such a convolution is the product of the energy spectra of the fixed waveform and the event train, we initially focus on just the spectrum of the event train.

Methods from renewal process theory^{29, 30} may be used to derive the following expression for this spectrum (see Appendix):

$$\begin{aligned} \mathbb{E}_{p(f)} \left[|\mathcal{F}[f_T]|^2 \right] = & \frac{1}{2\pi} \frac{N_C}{N_S} \left(1 + \sum_{k=1}^{N_S-1} 2 \left(\frac{N_S - k}{N_S} \right) \cos(k\mu_0\omega) e^{-(k\sigma_{jit}^2 + k^2\sigma_\mu^2)\omega^2/2} \right) \\ & + \frac{1}{2\pi} \frac{N_C(N_C - 1)}{N_S^2} \text{sinc}^2\left(\frac{\mu_0\omega}{2}\right) \sum_{k=1}^{N_S} \left(e^{-(k\sigma_{jit}^2 + k^2\sigma_\mu^2)\omega^2} + 2 \sum_{\ell=k+1}^{N_S} \cos((\ell - k)\mu_0\omega) e^{-((k+\ell)\sigma_{jit}^2 + (k^2 + \ell^2)\sigma_\mu^2)\omega^2/2} \right). \end{aligned} \quad (3)$$

Eq. 3 is therefore the expected value of the energy spectral density of the train of delta functions whose event times are specified by Eq. 2. Note that this result depends on five model parameters: N_S , the number of spikes per cell (which we assume to be fixed, for simplicity); N_C , the number of cells in the population; μ_0 and σ_μ , which together determine μ for each cell; and σ_{jit} , which introduces variability from event to event (i.e., “jitter”). Fig. 2 shows an excellent match between this analytical result and numerical simulations of the event train for several parameter combinations.

4. AP versus PSP contributions to the LFP

To make comparisons with experimental LFP recordings, the event train must be convolved with a realistic voltage waveform, resulting in the model LFP spectrum being the product of the event train spectrum and the waveform spectrum. Fig. 3 shows the results of convolving with a typical action potential (AP) waveform, for μ_0 corresponding to both 100 Hz and 200 Hz, which is roughly the maximum frequency of pyramidal cell firing during HFOs.^{31, 32}

The model LFPs feature strong peaks in their spectra at both frequencies, and voltage traces from numerical simulations show a clear rhythm in the 200 Hz signal, demonstrating our primary point: completely asynchronous spiking may produce narrowband LFP rhythms when neural activity is quasi-periodic. The 100 Hz oscillation is not as obvious in the time domain because the noise > 300 Hz dominates over the harmonics of the signal.

Fig. 4 shows results from convolving the event train with a typical PSP waveform (from the same simulations as the AP waveform). Note how the energy of the PSP waveform is

concentrated at much lower frequency than that of the AP waveform (gray dashed lines in Figs. 3 and 4), resulting in the 200 Hz PSP signal being severely attenuated compared to the 100 Hz PSP signal. This provides a simple explanation for the conventional wisdom that PSPs tend to dominate the LFP at lower frequencies than APs.³³ However, this conventional wisdom has now been called into question, as recent computational work suggests that low frequency LFPs may have strong involvement of APs intermixed with PSPs.³⁴ Our model did not include this complex low frequency effect, most likely because we assumed a 1–2 ms width for the AP waveform, whereas Reimann et. al. incorporated slow spiking currents which broadened spike duration.³⁴ Both simulations agreed, however, that APs are better suited to generate higher frequencies. In our simulations of clinically-recorded HFOs, the shape of the PSP is better suited to producing lower frequencies (~100 Hz and lower) in a noisy network, while APs are better suited to producing higher frequencies (over 150 Hz). As we described in our prior physiological model, these findings agree with prior experimental findings of HFOs.²⁵

Note that these frequency values are only approximate, as the waveforms presented here are the particular result of a biophysically detailed simulation. Our prior work explored how the PSP rise and decay times affect these results.²⁵ A PSP waveform that was temporally narrower would have its power spectrum shifted to higher frequencies, so that a point process convolved with the waveform would accommodate higher frequency oscillations. Likewise, an AP waveform that was temporally wider would accommodate lower frequency oscillations.

To characterize the strength of rhythms emerging from asynchronous neural activity, in Fig. 5 we plot the signal-to-noise ratio (SNR) as a function of σ_μ and σ_{jit} for 200 Hz AP-convolved LFPs and 100 Hz PSP-convolved LFPs. We define the SNR as the ratio of the

LFP energy spectral density to the waveform energy spectral density at $f = \frac{1}{\mu_0}$. The waveform energy spectral density is considered the noise spectrum since it is what would result from a Poisson event train (white noise) convolved with the waveform.

Note how σ_μ (population heterogeneity) and σ_{jit} (IEI heterogeneity) do not have the same effect on SNR—increasing σ_μ degrades SNR more quickly than increasing σ_{jit} , as a result of its being attached to a factor of k^2 rather than k in Eq. 3. Our model therefore predicts that heterogeneity in mean firing frequency across a neural population will degrade asynchronous rhythms more than an equivalent degree of spike-time jitter. The results in Fig. 5 also suggest bounds on these two sources of spike-time variability for facilitating the emergence of LFP rhythms from asynchronous neural activity. For both AP events at 200 Hz and PSP events at 100 Hz, σ_μ and σ_{jit} can each reach as high as about 20% of μ_0 before the primary spectral peak is washed out by noise.

Fig. 6 shows the evolution of the model LFP generated by an asynchronous population of 500 neurons, firing with a mean frequency of 200 Hz, as spike-time heterogeneity is progressively reduced from $\sigma_\mu/\mu_0 = \sigma_{jit}/\mu_0 = 0.175$ to $\sigma_\mu/\mu_0 = \sigma_{jit}/\mu_0 = 0.025$. Strong oscillations emerge as spike-time heterogeneity goes down, even though throughout the simulation neurons spike independently and therefore asynchronously. It is therefore

possible that HFOs may emerge through some process by which neural populations fire asynchronously but with similar, regular firing rates. This could happen, for example, if inhibition breaks down and pyramidal cells receive excitatory input that drives them toward depolarization block. The subset of cells that does *not* enter depolarization block will then have a smaller variance in firing rate than that of the entire population before the disjoint set of neurons enters depolarization block.

5. Discussion

There is great interest in identifying new biomarkers of epilepsy, and HFOs have risen as one of the most intriguing.^{21, 22} There is much clinical evidence of their utility,^{19, 35} and a clinical trial has begun,³⁶ making HFOs one of the most important potential biomarkers of epilepsy. They have been shown to delineate abnormal tissue,^{20, 37–40} and thus have clear potential as a clinical tool to localize epileptic tissue spatially. In addition, there is evidence that they may help localize seizures temporally as well. Early work¹⁵ showed that HFOs change in the seconds preceding ictal events in animals; later work in humans demonstrated that HFO features vary up to 30 minutes before seizures, sometimes in a stereotypical fashion that could be used to predict seizure onset.⁴¹ Mechanistically, it is well recognized that their potential pathological mechanisms mirror those of epilepsy, further indicating their worth as a biomarker.³⁵ Yet despite nearly 20 years of research, relatively little is understood about the mechanisms and features that distinguish a normal from an epileptic HFO.¹⁸ In large part, this is because the spatiotemporal resolution necessary to resolve these events at the cellular level is still not available in modern research equipment, a limitation that also besets the search for other preictal biomarkers.⁴² Thus in this work we have focused on identifying some of the basic mechanisms underlying their formation, in the hopes of guiding future research.

Our model makes three main predictions. First, completely asynchronous and independent neural activity may produce robust, narrowband LFP oscillations, so long as individual neural activity is quasi-periodic. (Note that quasi-periodicity is essential—independent Poisson processes, for example, result in a flat power spectrum,⁴³ but in many cases do not accurately describe neural activity.^{44–47}) This quasi-periodicity can be obtained with minimal requirements on the type of cells involved, as long as the cells have similar f-I curves and receive sufficient (but still asynchronous) synaptic input. Previous computational work supports this hypothesis, suggesting that pathological HFOs may be generated by a completely asynchronous, uncoupled network of hippocampal pyramidal cells receiving intense synaptic input, with no inhibitory feedback.²⁵ We suggest that a similar mechanism may be responsible for gamma oscillations observed in the absence of spike-timing synchrony described in recent work,² and may also help to explain earlier reports of asynchronous dynamics during seizures.^{48, 49} Second, rhythms generated by asynchronous activity are degraded more by heterogeneity in intrinsic neuronal frequency than by neuronal jitter. And third, we have derived bounds on these two sources of heterogeneity for experimentally detecting oscillations from asynchronous neural activity.

The model presented in this paper is of course highly simplified, as our results do not consider variation in AP/PSP waveforms, nor did we explore mixtures of AP and PSP

waveforms simultaneously contributing to the LFP. Nonetheless, our model provides a simple mathematical explanation for why PSP waveforms tend to dominate the LFP at the lower end of the HFO spectrum, while APs dominate at the upper end: the spectrum of a typical AP waveform is concentrated at higher frequencies than the spectrum of a typical PSP waveform, so that convolution with the same event train will inevitably lead to higher frequency content in an AP-dominated LFP.

In practical terms, these findings mean that HFOs are a generic network phenomenon that can be produced under any condition in which a large number of neurons receive similar, near-maximal inputs. Obviously, such conditions would be common in epilepsy, in which the excitation/inhibition balance is disrupted. But it is important to note that such conditions are not necessarily epileptic: high synaptic input conditions are actually quite common in the brain, even under normal conditions, such as the physiological UP state.⁵⁰ Thus it is important to investigate not only the underlying cells involved in producing an HFO, but also the force that drives them, in order to determine whether it is epileptic. These results should spur future experimental studies which investigate the possibility of neural oscillations emerging from asynchronous neural activity, especially under pathological conditions related to epilepsy.

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Appendix A

Derivation of energy spectral density

To derive the energy spectral density resulting from the superposition of renewal processes described by Eq. 2, let each neuron have event times given by $f^{(k)}(t)$, with the population

level spike train being $f_T(t) = \sum_{j=1}^{N_C} f^{(j)}(t)$ and N_C being the number of cells. The energy spectral density of this aggregate event train is then given by the functional integral

$$\mathbb{E}_{p(f)}[|\mathcal{F}[f_T]|^2] = \int df_T p(f_T) |\mathcal{F}[f_T]|^2, = \int \left[\prod_j df^{(j)} p(f^{(j)}) \right] \left| \sum_{k=1}^{N_C} \mathcal{F}[f^{(k)}] \right|^2. \quad (\text{A.1})$$

Assuming event trains are independent from cell to cell, and that all cells' event trains are drawn from the same family of distributions, this simplifies to

$$\mathbb{E}_{p(f)}[|\mathcal{F}[f_T]|^2] = N_C \int df p(f) |\mathcal{F}[f]|^2 + N_C(N_C - 1) \left| \int df p(f) \mathcal{F}[f] \right|^2. \quad (\text{A.2})$$

In general, since each event train is parameterized by a discrete set of event times t_k , the integration measures are $\int df p(f) = \int d\boldsymbol{\theta} p(\boldsymbol{\theta}) \prod_k dt_k p_k(t_k|\boldsymbol{\theta})$, where $\boldsymbol{\theta}$ represents any additional model parameters on which the pdfs are conditioned. The Fourier transform of f and its magnitude are then

$$\mathcal{F}[f] = \frac{1}{2\sqrt{\pi}} \frac{1}{N_S} \sum_k e^{-i\omega t_k}, \quad (\text{A.3})$$

$$|\mathcal{F}[f]|^2 = \frac{1}{2\pi} \frac{1}{N_S^2} \sum_{k,\ell} e^{-i\omega(t_k - t_\ell)}. \quad (\text{A.4})$$

Applying the change of variables, $\tau_k = t_k - t_{k-1}$, and making the standard renewal process assumption of IEI independence enables the application of an IEI density function, such as that defined in Eq. 2. Recalling the assumption that events occur independently from cell to cell, we may formally state that $p_k^{(i)}(\tau_k^{(i)} | \boldsymbol{\theta}_k^{(i)}) = p_0(\tau^{(i)} | \boldsymbol{\theta}^{(i)})$, for the k th event on the i th neuron.

In order to model asynchronous neural activity from the outset, we introduce a randomly distributed initial temporal offset, $t_0^{(i)}$, as one of the model parameters included in $\boldsymbol{\theta}^{(i)}$. Our model also assumes that inter-event intervals are centered around some value μ , unique for each neuron, so that $\mathcal{F}[p_0]$ can best be expressed as $\mathcal{F}[p_0] = e^{-i\mu\omega} \mathcal{F}[p_0']$. The quantity $\boldsymbol{\theta}$ is thus the n -tuple $[t_0, \mu]$, with $p(\boldsymbol{\theta}) = p_{t_0}(t_0) p_\mu(\mu)$.

The above assumptions imply that in general

$$\int df p(f) \mathcal{F}[f] = \frac{1}{N_S} \mathcal{F}[p_{t_0}] \sum_{k=1}^{N_S} \left\{ \left(\mathcal{F}[\sqrt{2\pi} p_0'] \right)^k \times \mathcal{F}[\sqrt{2\pi} p_\mu](k\omega) \right\}, \quad (\text{A.5})$$

$$\int df p(f) |\mathcal{F}[f]|^2 = \frac{1}{2\pi} \frac{1}{N_S} \left(1 + \sum_{k=1}^{N_S-1} \left[2 \left(\frac{N_S - k}{N_S} \right) \times \text{Re} \left\{ \left(\mathcal{F}[\sqrt{2\pi} p_0'] \right)^k \mathcal{F}[\sqrt{2\pi} p_\mu](k\omega) \right\} \right] \right).$$

(A.6)

In our specific model, Eq. 2 implies $p_0'(\tau) \sim \mathcal{N}(0, \sigma_{\text{jit}})$ and $p_\mu(\mu) \sim \mathcal{N}(\mu_0, \sigma_\mu)$. If we draw the initial temporal offsets from $p_{t_0}(t_0) \sim \text{unif}(-\mu_0/2, \mu_0/2)$, this yields

$$\int df p(f) \mathcal{F}[f] = \frac{1}{\sqrt{2\pi}} \frac{1}{N_s} \operatorname{sinc} \left(\frac{\mu_0 \omega}{2} \right) \sum_{k=1}^{N_s} e^{-(k\sigma_{jit}^2 + k^2\sigma_\mu^2)\omega^2/2} e^{-ik\mu_0\omega}, \quad (7)$$

$$\int df p(f) |\mathcal{F}[f]|^2 = \frac{1}{2\pi} \frac{1}{N_s} \left(1 + \sum_{k=1}^{N_s-1} 2 \left(\frac{N_s - k}{N_s} \right) e^{-(k\sigma_{jit}^2 + k^2\sigma_\mu^2)\omega^2/2} \cos(k\mu_0\omega) \right). \quad (8)$$

Note,

$$\left| \int df p(f) \mathcal{F}[f] \right|^2 = \frac{1}{N_s^2} \operatorname{sinc}^2 \left(\frac{\mu_0 \omega}{2} \right) \sum_{k=1}^{N_s} \left(e^{-(k\sigma_{jit}^2 + k^2\sigma_\mu^2)\omega^2/2} + 2 \sum_{\ell=k+1}^{N_s} \cos((\ell - k)\mu_0\omega) e^{-((k+\ell)\sigma_{jit}^2 + (k^2 + \ell^2)\sigma_\mu^2)\omega^2/2} \right).$$

Putting this together yields Eq. 3,

$$\begin{aligned} \mathbb{E}_p(f) \left[|\mathcal{F}[f_T]|^2 \right] &= \frac{1}{2\pi} \frac{N_c}{N_s} \left(1 + \sum_{k=1}^{N_s-1} 2 \left(\frac{N_s - k}{N_s} \right) \cos(k\mu_0\omega) e^{-(k\sigma_{jit}^2 + k^2\sigma_\mu^2)\omega^2/2} \right) \\ &+ \frac{1}{2\pi} \frac{N_c(N_c - 1)}{N_s^2} \operatorname{sinc}^2 \left(\frac{\mu_0 \omega}{2} \right) \sum_{k=1}^{N_s} \left(e^{-(k\sigma_{jit}^2 + k^2\sigma_\mu^2)\omega^2/2} + 2 \sum_{\ell=k+1}^{N_s} \cos((\ell - k)\mu_0\omega) e^{-((k+\ell)\sigma_{jit}^2 + (k^2 + \ell^2)\sigma_\mu^2)\omega^2/2} \right). \end{aligned}$$

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Figure 1.

Illustration of modeled stochastic events for one neuron. (a) Example event train generated by Eq. 2 with $\mu_i = 10.0$ ms and $\sigma_{jit} = 2.0$ ms. In the model, events may correspond to either action potentials (APs) or postsynaptic potentials (PSPs). (b) Inter-event interval density for a simulation of 10,000 events generated by Eq. 2, with the same parameters as in (a).

Figure 2.

Comparisons of analytically derived energy spectral density of superposition of delta function events, Eq. 3 (black line), against numerically computed energy spectral density (average over 500 simulations, red line). Note the excellent match between these results. Energy spectra are normalized over the range 50 Hz to 1000 Hz. Each plot shown reflects the fixed parameters $\mu_0 = 5$ ms, $N_C = 500$ cells, and $N_S = 500$ delta function events (*without* convolution with any waveform).

Figure 3.

Energy spectra (top) and example time-domain waveforms (bottom) for action potential (AP)-convolved model LFP signals. Spike time variability parameters were set to $\sigma_{\mu}/\mu_0 = 0.1$ and $\sigma_{jit}/\mu_0 = 0.1$, with (a) $\mu_0 = 10$ ms and (b) $\mu_0 = 5$ ms. Normalized LFP energy spectra described by Eq. 3 (solid; black) were compared against the energy spectrum of the AP waveform (dashed; gray), which is also the energy spectrum of an AP-convolved Poisson process (white noise). Simulated time-domain AP waveform²⁵ shown in inset to (a). Energy spectra were normalized to the range of 50 Hz to 1000 Hz. Note stronger emergent rhythms with smaller μ_0 (higher frequency), a phenomenon which was consistent across all simulations.

Figure 4. Example energy spectra (top) and time-domain waveforms (bottom) for postsynaptic potential (PSP)-convolved model LFP signals. Parameters and normalization were set as in Fig. 3 ($\mu_0 = 10$ ms in (a) and $\mu_0 = 5$ ms in (b)), with spectra of Eq. 3 (solid; black) compared against the spectrum of the PSP waveform (dashed; gray), which is also the energy spectrum of a PSP-convolved Poisson process (white noise). Simulated time-domain PSP waveform²⁵ shown in inset to (a). Note stronger emergent rhythms with larger μ_0 (lower frequency), a phenomenon which was consistent across all simulations.

Figure 5.

Signal-to-noise ratio as function of spike time variability. (a) AP-convolved signal with $\mu_0 = 5$ ms (corresponding to a 200 Hz rhythm). (b) PSP-convolved signal with $\mu_0 = 10$ ms (corresponding to a 100 Hz rhythm). Note signal degradation is greater with increasing σ_μ/μ_0 against σ_{jit}/μ_0 . Emergent rhythms depreciate beyond noticeable detection when spike time variability ratios are each ≥ 0.20 .

Figure 6.

Transition to narrowband oscillations in a 200 Hz spiking network. (a) Model LFP was generated by progressively stepping down the parameters σ_μ and σ_{jit} over time. Both parameters were kept equal to one another, μ_0 was set to 5 ms, and event trains were convolved with AP waveforms to simulate a 200 Hz spiking network. (b) Evolution of model LFP as spike-time parameters from (a) are changed (LFP color indicates corresponding values of spike-time parameters). Note the transition from weak to strong

oscillations as σ_{μ} and σ_{jit} decrease. (c) Spectrogram of LFP clearly shows the emergence of stronger oscillations as σ_{μ} and σ_{jit} decrease.

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