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Title: Spontaneous Spiking Is Governed By Broadband Fluctuations

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Abstract

Populations of cortical neurons generate rhythmic fluctuations in their ongoing spontaneous activity. These fluctuations can be seen in the local field potential (LFP), which reflects summed return currents from synaptic activity in the local population near a recording electrode. The LFP is spectrally broad and many researchers view this breadth as containing many narrowband oscillatory components which may have distinct functional roles. This view is supported by the observation that the phase of narrowband oscillations are often correlated with cortical excitability and can relate to the timing of spiking activity and the fidelity of sensory evoked responses. Accordingly, researchers commonly “tune in" to these channels by narrowband filtering the LFP. Alternatively, neural activity may be fundamentally broadband and composed of transient, non-stationary rhythms that are difficult to approximate as oscillations. In this view, the instantaneous state of the broad ensemble relates directly to the excitability of the local population with no particular allegiance to any frequency band. To test between these alternatives, we asked whether the spiking activity of neocortical neurons in marmoset of either sex is better aligned with the phase of the LFP within narrow frequency bands, or with a broadband measure. We find that the phase of broadband LFP fluctuations provides a better predictor of spike timing than the phase after filtering in narrow bands. These results challenge the view of the neocortex as a system composed of narrow-band oscillators, and supports a view in which neural activity fluctuations are intrinsically broadband.

Significance Statement: Research into the dynamical state of neural populations often attribute unique significance to the state of narrowband oscillatory components. However, rhythmic fluctuations in cortical activity are non-stationary and broad spectrum. We find that the timing of spontaneous spiking activity is better captured by the state of broadband fluctuations over any latent oscillatory component. These results suggest narrowband interpretations of rhythmic population activity may be limited, and broader representations may provide higher fidelity in describing moment-to-moment fluctuations in cortical activity.

Introduction

Since the first human electroencephalogram (EEG) recordings by Hans Berger(Berger, 1929), neuroscientists have inferred cortical function from the state of rhythmic fluctuations in neural population activity(Buzsaki, 2004; Wang, 2010). These brain rhythms are believed to arise from return currents generated by large scale spiking activity in cortical neural populations(Logothetis, 2003; Katzner et al., 2009; Buzsáki et al., 2012). When recorded intracranially with penetrating electrodes, rhythmic activity can be measured in the local field potential (LFP), which typically reflects neural signals arising within ~250 μM of the electrode tip(Katzner et al., 2009; Lindén et al., 2011). LFP fluctuations are spectrally broad, but are often thought to be composed of activity in narrow frequency bands correlated with distinct neural functions(Canolty et al., 2010; Einevoll et al., 2013; Friston et al., 2015). For example, in the visual cortex, alpha band rhythms (8-15 Hz) are thought to reflect feedback processes of suppression(Jensen and Mazaheri, 2010; van Kerkoerle et al., 2014) and have been shown to be attenuated with or modulated by attention(Worden et al., 2000),(Busch and VanRullen, 2010). Beta band rhythms (15-30 Hz) have been linked to motor planning(Sanes and Donoghue, 1993; Rubino et al., 2006) and feedback regulation of excitability(Bastos et al., 2015; Friston et al., 2015). Theta band (4-8 Hz) activity has been related to attention(Fiebelkorn and Kastner, 2019), working memory load(Jensen and Tesche, 2002) and hippocampal function(Buzsáki, 2002). Delta band (< 4 Hz) activity has been related to sleep and states of arousal(Sanes and Donoghue, 1993; Steriade et al., 2001; McGinley et al., 2015). Higher frequency gamma activity (30-90 Hz) has been linked to local coordination in excitation and inhibition(Brunel and Wang, 2003; Bartos et al., 2007; Buzsáki and Wang, 2012), attention(Fries et al., 2001, 2008; Gregoriou et al., 2009), memory(Pesaran et al., 2002; Colgin et al., 2009; van Vugt et al., 2010; Lundqvist et al., 2018), and perception(Singer and Gray, 1995; Panagiotaropoulos et al., 2012; Misselhorn et al., 2019), and has been used as a surrogate for measuring cortical activation(Crone et al., 2006; Ray et al., 2008a; Anon, 2013).

Oscillatory activity can be induced under certain conditions, such as the increased low frequency power that is observed in the EEG when eyes are closed(Berger, 1929; Geller et al., 2014), optogenetically(Lu et al., 2015; Bitzenhofer et al., 2017; Zutshi et al., 2018), electrically(Contreras et al., 1997; Kirov et al., 2009; Escobar Sanabria et al., 2020), or pharmacologically as in the alpha oscillations that occur in medial prefrontal cortex under propofol induced anesthesia(Purdon et al., 2013; Flores et al., 2017; Bastos et al., 2021).

It has been proposed that certain frequency bands play a privileged role in routing information among brain areas(Akam and Kullmann, 2010; Bonnefond et al., 2017; Khamechian et al., 2019). The idea that communication between brain areas occurs through oscillatory processes within narrow frequency bands bears similarity to a radio, where signals are broadcast within different frequency bands and a receiver can be tuned to receive them(Hoppensteadt and Izhikevich, 1998). For example, the idea of cross-cortical communication through coherence views synchrony in gamma oscillations as periods of coordination between pre- and postsynaptic groups so as to transmit signals about, for example, an attended stimulus while blocking competing inputs(Fries, 2015). These patterns of gamma-band synchronization are proposed to be regulated across cortical areas by top-down signals within a slower (8-20 Hz) frequency band(Bastos et al., 2015). Other theories posit that the LFP is composed of multiplexed oscillatory neural signals that are separate streams of information processing(Lisman and Idiart, 1995; Panzeri et al., 2010; Akam and Kullmann, 2014; Tingley et al., 2018). If oscillatory activity in separate frequencies encodes distinct information channels, and the spiking activity of neurons are the fundamental units of information transmission in the nervous system, then the spiking activity of individual neurons should show preferential alignment of their spiking activity to oscillatory rhythms in order to "tune in" to a channel of information(Canolty et al., 2010; Belluscio et al., 2012). There is evidence to suggest this can occur, as spikes have been found to preferentially align with the

96 phase of theta(Takahashi et al., 2014; Souza and Tort, 2017; Strüber et al., 2022),
97 alpha(Haegens et al., 2011), gamma(Fries et al., 2001; Womelsdorf et al., 2007; Ray et al.,
98 2008b), and beta(Donoghue et al., 1998; Canolty et al., 2010) frequencies.

99 An alternative view is that neurons spike with no preference for any particular
100 narrowband frequency. Rather, spiking is modulated by the instantaneous state of fluctuations
101 in the local population, which varies from moment to moment across a broad range of
102 frequencies. Supporting this view is the observation that balanced excitation and inhibition
103 creates fluctuating neural activity patterns in the awake state, which often exhibit $1/f^{\alpha}$ power
104 spectra across a broad range of frequencies(Destexhe et al., 2001; Gao et al., 2017). Studies
105 in humans have found that changes in cognitive state are associated with broad spectral
106 changes in the EEG(Voytek et al., 2015). The membrane potential of individual neurons is
107 correlated with the population fluctuations measured in the instantaneous LFP(Haider et al.,
108 2016), as opposed to any narrowband component, which suggests the broadband LFP is
109 therefore informative about the instantaneous excitability of neurons in the population(Davis et
110 al., 2020). Accordingly, previous work has found that spikes are weakly coupled to all
111 frequencies of the broadband LFP(Martin and Schröder, 2016), and specific interactions in
112 narrowband frequencies may at times be due to spurious artifacts from narrowband
113 filtering(Scheffer-Teixeira and Tort, 2016).

114 Even when approximately oscillatory activity may be transiently apparent in LFP
115 recordings, it is difficult to describe the phase of neural fluctuations within a narrow range of
116 frequencies because of their non-stationarity(Pesaran et al., 2018). LFP phase is a useful
117 measure for tracking the state of neural fluctuations because it is indicative of the relative
118 transition in the balance of excitation and inhibition with, for example, the falling phase
119 reflecting a transition from inhibition to excitation, and the rising phase transitioning from
120 excitation to inhibition(Atallah and Scanziani, 2009; Poo and Isaacson, 2009; Isaacson and

121 Scanziani, 2011; Teleńczuk et al., 2017). This is in contrast to amplitude measures, which can
122 be ambiguous as the same negative voltage value could reflect neurons becoming more
123 depolarized or more hyperpolarized depending on the signal history. Under this view, one can
124 better characterize the state of neural populations from the phase of broadband fluctuations in
125 LFP activity and neurons will show preferential alignment of their spiking activity to the
126 broadband signal phase, not to any narrowband oscillatory phase.

127 In order to ask whether neuronal spiking is better coupled to narrowband oscillations or
128 broadband fluctuations during waking visual function, we compared spike-phase coupling after
129 filtering the LFP in various filter bands. If the spiking probability of a neuron is phase-locked
130 with the LFP within some frequency band, this is evidence that the neuron in question
131 participates, to some degree, in oscillatory activity of the larger ensemble of neurons whose
132 transmembrane currents give rise to that rhythm. If narrowband rhythms do reflect distinct
133 information channels, then the phase of these oscillations should be particularly informative
134 about the excitability of neurons participating in that oscillatory rhythm, and therefore the timing
135 of their spontaneous spiking activity. Alternatively, if the excitability of the population is
136 reflected in the phase of the broad spectrum fluctuations, then the spiking activity of neurons
137 should be more poorly predicted by any individual oscillatory component and better predicted
138 by the phase of the broadband LFP. Therefore, in this work we take the magnitude of spike-
139 phase coupling as a direct measure of the degree to which oscillatory activity reflects a discrete
140 information channel.

141 The ability to test between these alternatives has been limited, however, because the
142 calculation of phase using the Hilbert Transform breaks down when the frequency content of a
143 signal is too broad(Le Van Quyen et al., 2001). It had been infeasible to directly compare the
144 relative phase-coupling of spiking activity to narrow- or broadband LFP signals without
145 consideration of this potential confound. To overcome this technical limitation, we have

developed a measure of phase (Generalized Phase, GP)(Davis et al., 2020), a generalization of the Hilbert Transform that can be applied to spectrally broad signals, allowing us to directly compare narrow- and broadband phase estimates of cortical excitability. This enabled us to test whether the timing of spontaneous spiking activity in cortical populations is better aligned with the phase of classically defined narrowband oscillations, similar to channels on a radio, or is more tightly coupled to the phase of the broad ensemble of non-stationary components. In recordings made from the marmoset middle temporal (MT) extrastriate visual cortex, we find that spontaneous spiking is more strongly phase-coupled to the broadband LFP than to any individual narrow band. Thus, fluctuations in spontaneous neuronal spiking are not coupled preferentially to individual narrowband oscillations, but rather track with the instantaneous fluctuations of neural activity as they change from moment to moment.

Materials and Methods

Electrophysiology Recordings

One male (monkey W) and one female (monkey T) marmoset monkey *(Callithrix jacchus)* was surgically implanted with a headpost for head stabilization and eye tracking. The headpost contained a hollow chamber housing an Omnetics connector for a Utah array (Blackrock Microsystems), which was implanted in a 7x10 mm craniotomy over area MT (stereotaxic coordinates 2 mm anterior, 12 mm dorsal). An 8x8 (64 channel, monkey W) and 9x9 with alternating channels removed (40 channel, monkey T) Utah array was chronically implanted over area MT using a pneumatic inserter wand. The electrode spacing was 400 μM with a pitch depth of 1.5 mm. The craniotomy was closed with Duraseal (Integra Life Sciences, monkey W) or Duragen (Integra Life Sciences, monkey T), and covered with a titanium mesh embedded in dental acrylic. All surgical procedures were performed with the monkeys under general anesthesia in an aseptic environment in compliance with NIH guidelines. All

experimental methods were approved by the Institutional Animal Care and Use Committee (IACUC) of the Salk Institute for Biological Studies and conformed with NIH guidelines. Data used in this study was previously used in Davis et al., 2020.

Marmosets were trained to enter a custom-built marmoset chair that was placed inside a faraday box with an LCD monitor (ASUS VG248QE) at a distance of 40 cm. The monitor was set to a refresh rate of 100 Hz and gamma corrected with a mean gray luminance of 75 candelas/m^2. Electrode voltages were recorded from the Utah arrays using two Intan RHD2132 amplifiers connected to an Intan RHD2000 USB interface board. Data were sampled at 30 kHz from all channels. The marmosets were headfixed by a headpost for all recordings. Eye position was measured with an IScan CCD infrared camera sampling eye position at 500 Hz. Stimulus presentation and behavioral control was managed through MonkeyLogic(Asaad et al., 2013) in Matlab. Digital and analog signals were coordinated through National Instrument DAQ cards (NI PCI6621) and BNC breakout boxes (NI BNC2090A). Neural data was broken into two streams for offline processing of spikes (single-unit and multi-unit activity) and LFPs. Spike data was high-pass filtered at 500 Hz and candidate spike waveforms were defined as exceeding 4 standard deviations of a sliding 1 second window of ongoing voltage fluctuations. Artifacts were rejected if appearing synchronously (within 0.5 ms) on over a quarter of all recorded channels. Segments of data (1.5 ms) around the time of candidate spikes were selected for spike sorting using principal component analysis through the open source spike sorting software MClust in Matlab (A. David Redish, University of Minnesota). Sorted units were classified as single- or multi-units and single units were validated by the presence of a clear refractory period in the autocorrelogram. LFP data was low-pass filtered at 300 Hz and down-sampled to 1000 Hz.

Fixation Behavior

The marmosets were trained to saccade to a marmoset face to initiate each trial. Upon the gaze arriving at the face, it disappeared and was replaced with a white fixation point (0.15 DVA). The marmosets held fixation on the fixation point (1.5 visual degree tolerance) for a minimum duration (400 ms monkey W, 300 ms monkey T) awaiting the appearance of a drifting Gabor target (4 DVA diameter; appearing 6-7 DVA eccentricity at 1 of 2 equally eccentric locations in the visual field contralateral to the recording array). Spontaneous data were analyzed from the period of fixation preceding the appearance of a target and excluding the initial 100 ms following fixation initiation. Early fixation breaks (defined by the excursion of the eye position from the fixation window) were excluded from analysis.

Free-viewing Natural Scenes

Marmosets were headfixed and their gaze monitored as in the previous task. Grayscale versions of naturalistic images (spanning 20-30 DVA) were randomly interleaved and presented to the monkey. The monkey was free to look at the images, and after 10 seconds was given a juice reward. Visual activity was analyzed as in the spontaneous fixation data excluding a 250 msec window around the times of saccades. Saccades were defined as velocity peaks exceeding 25 degrees per second. The time of saccade was taken from the peak velocity after threshold crossing. Velocity was calculated from the absolute value of the first numerical derivative of the smoothed vertical and horizontal eye traces (5 ms sliding Gaussian). We excluded from our analysis spikes that occurred from 50 ms before to 200 ms after detected saccades. Multi-unit spiking activity from two recording sessions in Monkey T and one session in Monkey W (N = 142 units) were combined and analyzed as there was no significant difference in SPI effects between the monkeys ($p = 0.10$; Wilcoxon rank-sum test).

Spike Artifact Elimination

In order to eliminate spike artifacts from the LFP, we applied a de-spiking algorithm first described in Zanos et al. 2011(Zanos et al., 2011). The goal of the algorithm is to eliminate the contribution of spike waveforms to the signal that, after being down-sampled and low-pass filtered, constitutes the LFP. The algorithm assumes the LFP is based on the measured wideband voltage trace recorded from the electrode (y) which is composed of a low-frequency signal (the LFP, w), high-frequency spike components η^k, an offset μ, and white noise ε.

Eq. 1:

$$y = w + \sum_{k=1}^{m} \eta^k + \mu + \varepsilon$$

Here, m is the number of spikes for kth neuron k. The high-frequency component of k is the convolution of the spike train s^k and the spike waveform ϕ^k

Eq. 2:

$$\eta^k = \phi^k * s^k$$

Rather than using a spike-triggered average (STA) approach to generate a mean template of the spike waveform which is subtracted at the time of each spike, the algorithm optimally estimates the local field potential w, each spike waveform ϕ^k, and the offset μ which adjusts for the fact that spike waveforms tend to be negative.

The first assumption is that the LFP is smooth with most of its power in the lower frequencies

Eq. 3:

$$p(w) = \mathrm{N}(0, \gamma^2 \Gamma)$$

$N(a, \Sigma)$ represents a multivariate Gaussian with mean a and covariance Σ. Γ is a matrix representing the assumption of smoothness. Multiplying with some vector x (i.e. Γx) produces

a low-pass filtered version of x. γ controls the strength of the prior. The second assumption is that ε is generated by a white noise process $p(\varepsilon) = \mathrm{N}(0,2\mathrm{I})$. The final assumption is that the spike waveforms ϕ^k lie in a subspace B where $\varphi^k = B\phi^k$ and the spike waveforms are described in a 1.5 ms interval around the peak depolarization. Bayesian inference was used to obtain maximum a posteriori (MAP) model parameters for the LFP w, the spike waveforms ϕ^k, and the offset μ. By Bayes' theorem, the log-posterior model is

Eq. 4:

$$p(w, \phi^k, \mu|y) \propto \mathrm{p}(\mathrm{y}|\mathrm{w}, \phi^k, \mu)\, p(w) = kexp\left[-\frac{1}{2\sigma^2}\sum_i\left(y - w - \sum_{k=1}^{m}\eta^k - \mu\right)_i^2 - \frac{1}{2\gamma^2}w\Gamma^{-1}w\right]$$

where k is a constant factor. The partial derivatives with respect to the parameters are set to 0 and the log of this expression provides the MAP estimates of the parameters $\bar{w}$, $\bar{\varphi}^k$, and $\bar{\mu}$.

Eq. 5:

$$\bar{w} = (\gamma^2\Gamma + \sigma^2 I)^{-1}\gamma^2\Gamma\left[y - \sum_k s^k * \left(B\bar{\varphi}^k\right) - \bar{\mu}\right]$$

$$\bar{\varphi}^k = \left(s^k * B\right) + \left[y - \bar{w} - \sum_{j\neq k} s^j * \left(B\bar{\varphi}^j\right) - \bar{\mu}\right]$$

$$\bar{\mu} = \frac{1}{n}\sum_k\left[y - \bar{w} - \sum_k s^k * \left(B\bar{\varphi}^k\right)\right]$$

An implementation of this algorithm in MATLAB is available from the original authors' website (http://apps.mni.mcgill.ca/research/cpack/lfpcode.zip).

Generalized Phase

We calculated Generalized Phase (GP) as described previously(Davis et al., 2020). The purpose of GP is to mitigate the breakdown of the analytic signal representation for spectrally broad signals. As an initial step in the GP representation, then, we filter the signal within a wide bandpass (i. e. 5-50 Hz; 4th-order zero-phase Butterworth filter), excluding low-frequency

content that contributes to origin offsets in the complex plane that distort the estimate of phase angles for higher frequency signals. We then use the single-sided Fourier transform approach(Johansson, 1999; Marple, 1999) on the wideband signal and compute phase derivatives as finite differences, which are calculated by multiplications in the complex plane(Feldman, 2011/4; Muller et al., 2014, 2016). High-frequency intrusions appear in the analytic signal representation as complex riding cycles(Feldman, 2011/4), which manifest as periods of negative frequencies in the analytic signal representation. As a secondary step we then numerically detect these complex riding cycles (N_c points of negative frequency) and utilize shape-preserving piecewise cubic interpolation on the next $2N_c$ points following the detected negative frequency epoch. The resulting representation captures the phase of the largest fluctuation on the recording electrode at any moment in time (Fig. 1f), without the distortions due to the large, low-frequency intrusions or the smaller, high-frequency intrusions characteristic of the *1/f*-type fluctuations in cortical LFP(Pereda et al., 1998; Linkenkaer-Hansen et al., 2001; Milstein et al., 2009). All phase estimates of filtered LFP segments were calculated using the GP algorithm.

Spike-phase coupling

3 second LFP epochs centered on the period of fixation were analyzed during the fixational behavioral task. The LFP segments were filtered (4^{th}-order zero-phase Butterworth filter with varying filter bandwidths depending on the analysis condition) and spike-phase coupling was calculated over epochs of fixation excluding the initial 100 ms following fixation initiation. The degree of spike-phase coupling was measured as the mean resultant vector length for the LFP phase distribution collected at the time of observed spikes. This measure was calculated using the circ_r function in the Circular Statistics Toolbox for Matlab(Berens, 2009). The mean resultant vector r of the spike phase distribution is the normalized sum over complex exponentials of the phase angles ϕ

Eq. 6:

$$r = \frac{1}{M}\sum_{j}^{N} e^{i\Phi j}$$

where M is the number of spikes, and the modulus of r ($|r| \in [0, 1]$) represents the degree of spike phase modulation. The closer the value is to 0, the more uniform the phase distribution. The closer the value is to 1, the more concentrated the phases.

Filtered-Raw LFP Signal to Noise Ratio (SNR)

We calculated the signal to noise ratio (SNR) in dB by computing the ratio of the summed squared magnitude of the filtered LFP (in either theta (4-8 Hz), alpha (8-15 Hz), beta (15-30 Hz) low gamma (30-50 Hz) or the wideband (5-50 Hz) filter) to the summed squared magnitude of the broadband 1-100 Hz LFP. The SNR was calculated over a window corresponding to approximately a single cycle of the mean frequency of each filter band (150 ms, 75 ms, 50 ms, 25 ms, and 50 ms respectively). The tested window was slid by 1/5th the window width over the entire fixation period. Only spike times that occurred in a window that exceeded -5 dB SNR was included in the SPI calculation for that narrowband filter.

Generalized Linear Model (GLM) Analysis

In order to compare the relative predictive power of spike timing between multiple narrow and a single wideband measure of LFP phase (GP), we tested GLMs trained to predict the likelihood of spiking activity. In particular, both GLMs were trained using LFP phases recorded at points in time when spikes occurred and an equal size sample of LFP phases, selected at random, when no spike occurred. The first model used as predictors the phase at the time of each spike or non-spike for (1) theta (4-8 Hz), alpha (8-15 Hz), beta (15-30 Hz), and low gamma (30-50 Hz) narrowband filtered LFP. The second model used a single predictor: the narrowband beta phase (15-30 Hz), and the third model also used a single predictor: the

wideband (4-50 Hz) LFP GP computed on the same training set. In order to linearize the circular phase variables we used the sine and cosine of each phase value as separate predictors(Cremers and Klugkist, 2018), resulting in 8 predictors for the narrowband model and 2 predictors for the single narrow and wideband models.

Eq. 7:

$$Y_i = \kappa_0 + \kappa_1 \sin(\varphi_\theta) + \kappa_2 \cos(\varphi_\theta) + \kappa_3 \sin(\varphi_\alpha) + \kappa_4 \cos(\varphi_\alpha) + \kappa_5 \sin(\varphi_\beta) + \kappa_6 \cos(\varphi_\beta) + \kappa_7 \sin(\varphi_\gamma) + \kappa_8 \cos(\varphi_\gamma)$$

Single narrowband GLM:

Eq. 8:

$$Y_i = \kappa_0 + \kappa_1 \sin(\varphi_\beta) + \kappa_2 \cos(\varphi_\beta)$$

Single wideband GLM:

Eq. 9:

$$Y_i = \kappa_0 + \kappa_1 \sin(\varphi_{WB}) + \kappa_2 \cos(\varphi_{WB})$$

Where the model output Yi for the phases at time sample i is determined by the coefficients on the sine and cosine of the filtered LFP phase. The GLM was fitted using a binominal logit link function to relate changes in the phase predictor variables to the binary output variable at each time sample (spike or no spike). GLMs were fit to half the data in each data set (N = 20 across 2 monkeys) and the predictor coefficients were tested on the other half of the data. The predictive power of each GLM was evaluated by measuring the area under the curve (AUC) for the receiver-operator characteristic (ROC) curve generated by comparing each model output's true spike hit rate to the spike false alarm rate given the model output.

Simulated spike and LFP generation

In order to generate surrogate spiking and LFP data, we first generated a normal distribution of random frequency values with a mean of 10 Hz and a standard distribution of 1 Hz. We then generated a 100 second sinusoidal signal whose frequency drifted with random draws from the frequency distribution. In the case where spikes were generated from the phase of this narrowband signal, we first filtered this signal between 8-15 Hz and used the phase to generate spike times. We also generated a broadband noise signal generated from a Gaussian distribution with mean of 0 and a standard deviation of 1 whose power spectrum followed a 1/f power-law(Kasdin, 1995). In the case where spikes were generated from the phase of the broadband signal, the drifting sinusoidal and pink noise signals were summed in the frequency domain and transformed back into the temporal domain and filtered between 1-100 Hz. The combination of the sinusoidal signal and the noise signal made up our surrogate LFP signal, which was identical between the alternative spike generating conditions.

Spike times were generated using a phase-dependent Poisson spike generator. The phase-dependent spiking probability was defined with a circular-linear function across 21 phase bins with a 0% spiking probability at 0 rad phases and a 1% spiking probability at $\pm\pi$ rad phases. At each millisecond in time, a random value was drawn from a Poisson distribution whose lambda corresponded to the probability of a spike occurring at the phase of either the sinusoidal (narrowband hypothesis) or surrogate LFP (broadband hypothesis) signal at that millisecond. Any drawn value that exceeded 0 produced a single spike time. The relative phase-dependent spike probabilities produced irregular spike trains with mean firing rates roughly between 5-6 Hz in both conditions. The calculation of spike-phase coupling was performed identically as to that in the recorded data. The surrogate LFP was filtered in either narrow or wide filters and the GP was drawn at the time of each spike to generate spike-phase distributions.

Statistical Analysis

Statistical tests used in this study include the parametric pair-wise student's t test, the non-parametric Wilcoxon signed-rank test, and Wilcoxon rank sum test. Two monkeys were used in this work. No power analyses were performed as the number of monkeys used followed with standard conventions to reduce the number of primates required for neuroscience research. All results were consistent across both monkeys and were therefore collapsed for analysis. Individual measurements within N = 20 recording session were averaged and statistical tests were performed on the averages across recording sessions.

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Materials & Correspondence: Correspondence and requests for material should be addressed to J.R and Z.W.D.

Data Availability: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Code Availability: An open-source code repository for the Generalized Phase algorithm is available on http://mullerlab.github.io.

Results

We measured spike-phase coupling for single- and multi-unit spiking activity across traditional narrowband and broadband filtered LFP signals. Spiking activity and LFP data were previously recorded from chronically implanted multielectrode arrays (Utah array, Blackrock Microsystems) in Area MT of two common marmosets (*Callithrix jacchus*; 10 recording sessions in each monkey) as they fixated a point on an otherwise blank screen (gray background, 75 candela/m^2; Figure 1a), awaiting the appearance of a faint visual target during a challenging visual detection task(Davis et al., 2020). Similar experimental paradigms have been used to study the relationship between pre-stimulus oscillatory phase and sensory

375 processing and behavioral performance(Busch et al., 2009; Balasubramanian et al., 2020;
376 Zareian et al., 2020). The raw LFP (filtered from 1-100 Hz) sporadically exhibited rhythmic
377 fluctuations across a range of timescales, but there was not a clear peak in the power spectral
378 density that would be consistent with a clear and consistent oscillatory component (Figure 1b).

379 The LFP during periods of fixation was filtered in classically defined frequency bands—
380 theta (4-8 Hz), alpha (8-15 Hz), beta (15-30 Hz), and low gamma (30-50 Hz)—or in a wideband
381 filter that spanned all of these narrow bands from 5-50 Hz (Figure 1c-g). The bounds of the
382 wideband filter were selected to exclude low frequency fluctuations (< 5 Hz) that are
383 associated with slow changes in arousal(Steriade et al., 2001; Petersen et al., 2003), and high
384 frequency components that may be contaminated by spiking artifacts and could, therefore,
385 induce spurious spike-LFP correlations(Ray et al., 2008a; Zanos et al., 2011). However, it
386 could be possible spiking artifacts exist at sub-50 Hz frequencies, which could, in principle,
387 bias our estimate of the relationship between spiking activity and LFP phase in our broadband
388 representation. To mitigate this potential confound, we performed a “de-spiking” procedure on
389 the data as described in Zanos et al. 2011(Zanos et al., 2011). This removes spike waveforms
390 from the raw (30 KHz) recorded electrode data signals through spike-waveform subtraction and
391 interpolation before downsampling and filtering into the LFP. Any remaining relationship
392 between the phases of sub-50 Hz activity in any frequency band must therefore be due to an
393 indirect relationship between the population currents that give rise to the LFP and individual
394 neuronal spiking, and not the direct contribution of that spike occurring itself.

395 If spiking activity is either organized into oscillations, giving rise to narrowband
396 fluctuations in the LFP, or if LFP oscillations reflect population-wide subthreshold fluctuations
397 that modulate the probability of spiking within a particular band, then spikes should tend to be
398 aligned in phase with the LFP, within these frequency ranges. Alternatively, if no individual
399 rhythmic component of the LFP dictates the excitability of neurons, but rather the precise,

400 moment-by-moment fluctuations of the LFP reflect the state of the population, we would expect
401 spikes to occur more often at phases of the broadband LFP that correspond to states of
402 depolarization across the local population, regardless of frequency.

403 To test these competing hypotheses, we measured the phase of each filtered LFP
404 signal at the times of multi-unit spiking activity. Phase is conventionally measured for
405 oscillatory or spectrally narrow signals by calculating the analytic signal(Feldman, 2011/4;
406 Marple, 1999), where instantaneous amplitude and phase can be expressed in polar
407 coordinates and whose real and imaginary parts are related to each other by the Hilbert
408 Transform. However, for spectrally broad signals, the standard computational implementations
409 break down(Le Van Quyen et al., 2001). Low frequencies can shift the analytic signal
410 representation by a constant in the complex plane, distorting the estimated phase angle. In
411 addition, high frequency intrusions introduce complex riding cycles that generate phase
412 reversals and appear as negative frequencies which distort the analytic signal. To address
413 these problems, we introduced an updated approach to the analytic signal representation,
414 termed “generalized phase” (GP)(Davis et al., 2020). Briefly, in this approach we first impose a
415 high-pass cutoff on the signal (5 Hz). This step aims to eliminate low-frequency intrusions,
416 while also preserving a significant portion of the signal spectrum and minimizing waveform
417 distortion. Second, we identify negative frequencies, which can arise from high-frequency
418 intrusions, and remove them, replacing the phase values with shape-preserving interpolation.
419 This approximates the continuation of the dominant fluctuation’s trajectory. The result, after
420 filtering, is an estimate of phase that tracks with the dominant frequency component of the LFP
421 as it shifts over time (Figure 2a) while minimizing phase distortions that arise due to
422 narrowband filtering a non-stationary broad spectrum signal such as the raw LFP(Yael et al.,
423 2018). All results reported here, for both broadband and narrowband filtered data, were
424 computed using GP. Low- and high-frequency intrusions are rare in narrowband filtered signals

425 so, for narrowband filtered data, computation of GP should yield very similar phase estimates
426 to those estimated using the Hilbert transform. To confirm this, all analyses were repeated for
427 narrowband filtered signals using the Hilbert Transform. As expected, the results were virtually
428 identical. All future mentions of phase therefore refer to the GP of the signal.

429 The phase of the wideband filtered signal is strongly coupled to the timing of measured
430 multi-unit spiking activity (Figure 2b). We measured an index of the coupling of spikes to each
431 filtered LFP by calculating the mean resultant length of the circular spike-phase distribution.
432 This spike-phase coupling index (SPI) value ranges from 0 (uniform spike-phase distribution) to
433 1 (spikes perfectly coupled to a single phase), and for the 5-50 Hz wideband filtered signal, the
434 average SPI was 0.15 ± 0.009 S.E.M. (N = 20 sessions across 2 monkeys). The wideband
435 filtered SPI was significantly stronger than the coupling observed after filtering in theta (SPI =
436 0.08 ± 0.005; $p < 1x10^{-9}$; two-tailed paired sample t-test), alpha (SPI = 0.07 ± 0.005; $p < 1x10^{-10}$),
437 beta (SPI = 0.11 ± 0.007; $p < 1x10^{-11}$) or gamma (SPI = 0.08 ± 0.009; $p < 1x10^{-9}$) frequency
438 bands (Figure 2c-f). These results suggest that the instantaneous rhythmic state of neuronal
439 excitability is better reflected in the phase of the ensemble LFP activity rather than in the phase
440 of any particular narrowband subcomponent.

441 If oscillations reflect information streams analogous to channels on a radio, then it could
442 be the case that some neurons are more coupled to one embedded oscillation and other
443 neurons are more coupled to a different oscillation, and that by collapsing across multiunit
444 activity the phase-dependence of the spiking activity is diluted for each narrowband filter. If
445 true, we might find stronger spike-phase coupling for the wideband filter across the populations
446 even though individual neurons are best coupled to different narrowband oscillations. To test
447 this, we measured the spike-phase coupling across filters for well-isolated single units in our
448 recordings. We did not find any evidence of differential preference across neurons for
449 narrowband signals. Rather, the majority of neurons had a stronger SPI to the state of the

wideband signal as compared to theta (78.50%, N = 107 single units; Figure 3a), alpha (78.50%, Figure 3b), beta (83.18%, Figure 3c), or gamma (85.98%, Figure 3c) filtered signals. Additionally, for the minority of neurons that did show stronger SPI to a narrowband filtered signal, they were more weakly coupled in general (average SPI = 0.09) and did not show specific preference to any one narrowband frequency. Thus, variable population phase-coupling to narrowband signals could not explain why the wideband filtered signals exhibit stronger spike-phase coupling.

One possibility is that spike timing is only governed by each narrowband oscillation when that oscillation is strongly present in the data, and as each oscillation is only transiently present, it is unfair to expect, for example, gamma to predict spike timing when gamma is not present in the data. To test this we restricted our analysis to only count spikes for each frequency band at times when there is strong oscillatory power in that band. To do this we calculated the signal-to-noise (SNR) ratio between the filtered and raw (1-100 Hz) LFP and identified epochs where the narrowband signal exceeded a -5 dB threshold for at least 1 cycle of the center frequency of the filter bandwidth. Only spikes that occurred during these epochs were included for that narrowband's SPI measure. Despite restricting each filter band to spikes that occur when those oscillations are transiently apparent in the data, the wideband measure still captures the strongest SPI values (Figure 4a; wideband mean SPI = 0.16 ± 0.010 S. E. M. as compared to theta: 0.11 ± 0.010, alpha: 0.08 ± 0.005, beta: 0.12 ± 0.010, and gamma: 0.09 ± 0.005; $p < 0.001$, Wilcoxon signed-rank test), while also describing a majority of the recorded data (approximate fraction above dB threshold; wideband: 92% vs. theta: 16%, alpha: 46%, beta: 42%, and low gamma: 19%).

Thus, spike timing is better predicted by broadband phase than narrowband phase for any of the bands tested. We next asked how well spike timing could be predicted based on the combination of all four narrowband filtered signals. To test this we constructed a generalized

linear model (GLM) that took as its input the phase values measured over the four narrow band frequencies (spanning 4 to 50 Hz) at times when a spike occurred and an equal number of randomly drawn times when no spike occurred. The GLM was trained to predict whether or not a spike occurred, based on the four phases. The model was trained on half the data in each recording session, with the remaining data held out as a test set. The model's ability to predict spiking was measured using Receiver Operator Characteristic (ROC) analysis.

We reasoned that if oscillatory activity across the multiple narrow bands drives spiking activity, the four-factor GLM, which has simultaneous access to the phases of all four oscillatory signals, should predict spiking better than a GLM trained to predict spiking based on the phase computed in an individual band (four-factor GLM AUC = 0.578 ± 0.004 S. E. M.; single narrowband GLM AUC = 0.545 ± 0.003 S. E. M.; $p = 0.00009$. Wilcoxon signed-rank test). This analysis shows that more information about spiking is present across multiple bands. This is consistent with two different hypotheses. The first is that the narrow bands capture the individual contribution of oscillations that fall within each band, and the four factor GLM reflects the joint contributions of these oscillatory drivers. An alternative hypothesis is that the processes that drive spiking activity fluctuate over time in their power spectrum, and spiking activity follows these fluctuations over time, regardless of where they travel in frequency. If the first hypothesis is true, the four-factor GLM, which has access to the phase within each band, should perform better than a single-factor broadband GLM, which is provided with a single measure of phase that is blind to the interactions across the same frequency space. If the second hypothesis is true, the single-factor broadband GLM, which uses a measure of phase that tracks with the dominant LFP frequency as it changes over time, should do as well as the four-factor GLM.

To test this, a GLM was trained on the same data that was used to train the four-factor GLM, but instead of providing it with four phases computed within the four narrow bands, it was

trained using only a unitary measure of phase – GP applied to the wideband (4-50 Hz) signal as its input, and its ability to predict spiking was measured using the same ROC analysis. As shown in Figure 4b, there was no significant difference in the ability of the combined 4 narrowband or one wideband GLM to predict spike times as defined by the area under the curve for each session's ROC (wideband mean AUC = 0.579 ± 0.005 S. E. M.; p = 0.16, Wilcoxon signed-rank test). Thus, even when combining signals across multiple frequency bands, narrowband filtering adds no information beyond what is already present in the phase of the momentarily dominant fluctuation in the LFP preserved in the wideband representation and as measured using generalized phase.

Our results suggest spontaneous neuronal spiking in the neocortex is not organized by oscillatory activity, but rather is modulated by fluctuations in synaptic activity that can be estimated from the instantaneous phase of the broadband LFP. If true, then SPI values should be correlated with how much filtering alters the LFP phase relative to the raw recorded LFP. To test this, we compared the strength of spike-phase coupling to each band pass filtered signal with the degree of correlation between the LFP signal before and after filtering (Figure 4c). There was a significant positive correlation between SPI and the raw-filtered LFP correlation across recording sessions ((Pearson's r = 0.65 ± 0.11 95% CI, $p < 1x10^{-12}$), suggesting a direct relationship between spike-phase coupling and how well the filtered LFP tracked with the raw LFP.

If spikes are more coupled to the broadband LFP than any embedded narrowband oscillation, then the optimal filter band for maximizing SPI should be one that is as broad as possible. To test for an optimal filter band, we scanned across a large parameter space varying the lower and upper bounds of the band pass filter. The lower bound ranged from 1 to 50 Hz and the upper bound ranged from 5 to 125 Hz with a minimum bandwidth of 4 Hz. Consistent with our prior results, the strongest spike-phase coupling was observed for filters that included

525 the largest width of the signal spectrum, with an exception for the lowest frequencies (Figure
526 4d). These results indicate optimal filters for maximizing spike-phase coupling estimates span
527 from 3 Hz in the lower band and as high as we sampled in the upper band (125 Hz), assuming
528 spike-artifacts are effectively removed from high frequency components in the LFP. If not, a
529 cautious step then is maintaining a low-pass filter which serves to help mitigate spurious
530 coupling values due to residual spike artifacts in higher frequencies.

531 Spiking activity can bleed into the LFP, artifactually inflating estimates of spike-phase
532 coupling in high frequency bands. Spike artifacts may be responsible for some gamma phase
533 relationships with spiking activity, as the contribution of spike artifacts in the LFP had been
534 previously observed down to 50 Hz(Ray and Maunsell, 2011; Zanos et al., 2011). To avoid this
535 we performed a de-spiking procedure, and examined the consequence of that de-spiking on
536 SPI estimates. A comparison of SPI values on the same data with and without de-spiking found
537 that the de-spiking procedure significantly reduced SPI values for frequency bands that
538 included frequencies below 50 Hz (but not below 15 Hz) such as low gamma (30-50Hz; not de-
539 spiked SPI = 0.13, $p = 1.65 \times 10^{-7}$ two-tailed Wilcoxon ranked sum test), beta (15-30 Hz; SPI =
540 0.13, p = 0.026) and the wideband (5-50 Hz; SPI = 0.18, p = 0.009). There was no significant
541 reduction in either alpha (8-15 Hz; SPI = 0.08, p = 0.067) or theta (4-8 Hz; SPI = 0.09, p =
542 0.190) when we de-spiked the LFP. These observations are consistent with recent reports of
543 spike-artifacts impacting spike-LFP synchronization at frequencies as low as 20 Hz(Banaie
544 Boroujeni et al., 2020). These results argue either that the artificial coupling of spiking activity
545 to LFP phase may be present at low frequencies, or that de-spiking techniques are overly
546 liberal in the removal of spike waveforms. Regardless, even if we consider the possibility that
547 the de-spiking procedure is introducing more noise than it is eliminating, the main result —that
548 the broadband LFP phase produces the strongest SPI values— holds when this technique is
549 not applied and the raw data is left intact.

The results described so far are limited to spontaneous activity recorded during a period in which animals foveated a fixation point at the center of a blank screen while awaiting the appearance of a faint visual target. Do these findings generalize to more naturalistic viewing conditions? To test this, we calculated SPI for each frequency band in animals as they freely viewed natural scene images. Since the focus here is on intrinsic fluctuations, not the transient responses that are evoked at the time of the saccade, neural activity at the time of the saccade (from 50 ms before and ending 200 ms after saccades) was eliminated from analysis. Consistent with the pattern observed during fixation of a blank screen, the wideband filtered signal produced the strongest SPI values (0.16 ± 0.008; N = 142 multi-units across 2 sessions in Monkey T and 1 session in Monkey W), which was significantly stronger than the SPI values measured for theta (0.14 ± 0.007; $p < 1x10^{-7}$ Wilcoxon signed rank test), alpha (0.13 ± 0.007; $p < 1x10^{-16}$), beta (0.10 ± 0.006; $p < 1x10^{-14}$), and low gamma (0.11 ± 0.006; $p < 1x10^{-12}$). Thus the spontaneous coupling of spiking activity to broadband fluctuations is not limited to fixating a blank screen, but is apparent during more dynamic active vision.

While our experimental results suggest spiking activity is better correlated with the instantaneous state of the broadband LFP rather than any individual oscillatory component, the ground truth mechanism relating spiking to rhythmic LFP activity is unknown in our recordings. To explore whether our observations can be explained by the hypothesis that spiking activity is coupled to broadband LFP phase as opposed to a narrowband oscillation, we simulated an LFP signal by combining a narrowband oscillatory fluctuation that consisted of spectral power drifting between 8-15 Hz with broad spectrum noise. The power spectral density of this simulated LFP fluctuation was designed to be consistent with the typical 1/f power-law observed in cortical recordings *in vivo(Miller et al., 2009)* (Figure 5d). We then generated spike times from a Poisson spike generator where the probability was dependent on either the phase of the narrowband 8-15 Hz oscillatory signal (hypothesis A; Figure 5a) or the phase of the

575 combined narrowband and broad spectrum signals (hypothesis B; Figure 5b). Spike probability
576 was phase dependent with spikes most likely to occur near ±π radians and spikes least likely
577 to occur near 0 radians. Importantly, the spectral content of the simulated LFP was identical
578 between the two alternative hypotheses and only the timing of spikes differed between the two
579 conditions (Figure 5c).

580 In order to recover the signal correlated with spike-generation we filtered the simulated
581 LFP in either a narrow bandpass filter from 8-15 Hz, or a wide band pass filter from 5-100 Hz.
582 In the case where spikes were correlated with the phase of the narrowband oscillatory
583 component (hypothesis A, blue), the narrowband filtered LFP signal was relatively weakly
584 correlated with the raw simulated LFP (Pearson's r = 0.49, Figure 6a). However, spike timing
585 was strongly coupled to the phase of the narrowband filtered LFP signal (SPI = 0.34 ± 0.002
586 S.E.M; N = 20 simulations). This coupling was significantly stronger than when using the
587 wideband filter to recover spike phases (SPI = 0.16 ± 0.002 S.E.M; p = < 0.0001 two-tailed
588 Wilcoxon signed-rank test; Figure 6b). In the case where the spikes were generated from the
589 phase of the broad spectral content of the simulated LFP (hypothesis B, orange), the wideband
590 filtered LFP was strongly correlated with the raw simulated LFP (Pearson's r = 0.84, Figure 6c)
591 and the spike-phase relationship was significantly stronger after filtering in the wideband (SPI =
592 0.29 ± 0.002 S.E.M.) as compared to the spike-phase coupling to the narrowband filtered LFP
593 (SPI = 0.14 ± 0.002 S.E.M.; p = < 0.0001 two-tailed Wilcoxon signed-rank test; Figure 6d).
594 These results indicate that, in principle, if neurons were coupled to an oscillatory component,
595 then narrowband filtering to extract that oscillation would indeed yield stronger spike-phase
596 coupling than the broadband signal.

597 We next asked whether a narrowband or broadband spike-correlated signal could
598 reproduce the observed relationship of increasing spike-phase coupling with increasing
599 correlation between the filtered and raw LFP signal. We filtered the signal under various filters

(theta (4-8 Hz), alpha (8-15 Hz), beta (15-30 Hz), wideband (5-50 Hz)) as in the cortical recordings, as well as a broad band pass from 1-100 Hz, and measured both the spike-phase coupling for narrowband and broadband correlated spike generation and the correlation between the filtered and raw LFP signal. In the case where spikes were correlated with the narrowband signal, the best filter was the 8-15 Hz filter (matching the source of the spike generating signal), followed by the wideband and broadband filters which each included the spike generating signal band within its bandwidth, but also included a smaller and larger part of the "noise" spectrum respectively (Figure 7a). In the case where spikes were correlated with the broadband signal, the best filter was the broadband filter, and decreased as the filters became narrower (Figure 7b). The narrowband spike source had a weak correlation between the SPI (Pearson's r = 0.27), and the degree of filter-raw signal similarity as the optimal filter was one that eliminated the broadband noise from the simulated LFP. In contrast, the broadband spike source reproduced the strong positive correlation between SPI and filtered-raw LFP similarity observed in our recordings (Pearson's r = 0.92; Figure 7c). Our results indicate a model where spikes are coupled to the state of fluctuations in the broad spectral content of the LFP is sufficient to account for our observations *in vivo*, and suggest neuronal spiking is not preferentially coupled to narrowband oscillations.

Discussion

A central goal of systems neuroscience is to understand how brain activity underlies information processing and behavior. Ideally, we would like to record every action potential of every neuron and ask how they relate to one another in the service of behavior, but even with the best available neurophysiological tools -- sets of electrode arrays with contacts numbering in the thousands -- we can only sample a tiny fraction of the neurons in the brain. Therefore, neurophysiologists typically rely on indirect measures of the activity to estimate the spiking statistics of larger cortical populations. These include LFP, EEG, or MEG, which provide indirect measures of the activity of larger populations of neurons. Rhythmic patterns of activity

626 are often observed in these measures, and it is common to treat these rhythmic patterns as
627 meaningful computational units, potentially serving as independent channels of information
628 processing, or if not independent in the context of cross-frequency phase-amplitude
629 coupling(Munia and Aviyente, 2019), at least functionally dissociable from the signal in which
630 they are embedded(Thut et al., 2012; Einevoll et al., 2013), similar to turning the dial on a radio
631 to receive different streams of information.

632 One way of thinking about rhythmic dynamics is that the spiking probabilities of the
633 neurons in the larger population co-vary within some frequency band and that this results in an
634 oscillation — for the example studied here, in the LFP. If so, then by filtering the LFP within that
635 oscillatory band and asking how it relates to some measure of either behavior (e.g.
636 performance on a discrimination task), a neural property (such as spike timing or transmission
637 of information across areas), or its covariation with some behavioral manipulation (e.g.
638 directing attention into or away from the retinotopic locus of the electrode), one can identify the
639 contribution of the oscillation to neural computations or behavior. However there are some
640 problems with treating neural fluctuations as oscillations. First, neural fluctuations are often
641 only transiently rhythmic in the awake state(Jones, 2016), and even then they are not purely
642 sinusoidal(Cole and Voytek, 2017) as they drift in frequency content from moment to moment
643 with changes in arousal(Vinck et al., 2015), attention(Fries et al., 2001), or sensory
644 input(Henrie and Shapley, 2005). Even in the case when neural fluctuations are strongly
645 rhythmic, we find narrowband filtering captures less of the spike-phase relationship than when
646 maintaining a wideband representation. This may be because the application of narrowband
647 filters to signals that are non-stationary in their frequency content can result in a loss of timing
648 precision in phase estimates(Yael et al., 2018).

649 The results presented here argue that neurons are not specifically coupled to
650 narrowband oscillatory activity, but rather it is the state of the broadband moment-to-moment

651 fluctuations that are informative of the relative excitability of the local population. This is not to
652 say that rhythms are not apparent in fluctuating dynamics or that they are irrelevant for cortical
653 function. Nor are we suggesting that rhythmic power is limited to what one would expect from
654 stochastic synchronizations in a 1/f noise process. For example, it is not the case that
655 oscillatory rhythms are only as informative as their fraction of the spectral content of broadband
656 fluctuations. We observed that low gamma filtered signals had stronger SPI values than one
657 might expect based on their relative power in the PSD and given how poorly correlated the
658 gamma filtered signals were to the raw LFP. Similarly, the alpha band filtered signals had much
659 more power and were relatively well correlated with the raw LFP, yet had weaker SPI values
660 than the beta band filtered signals, which were more poorly correlated with the raw LFP.
661 Indeed, there is variation in the degree to which spikes couple to LFP phase across the five
662 frequency bands studied here. However, that does not imply those frequency bands are
663 independent information channels, distinct from the rest of the LFP. It is evident that they are
664 not, as we see the strongest SPI values for the broadest frequency bands.

665 In order to test what one would expect to see if it were the case spikes preferentially
666 coupled to a narrow set of frequencies, we simulated spike trains generated from the phase of
667 oscillatory signals embedded in an otherwise 1/*f* noise spectrum (Hypothesis A). Under these
668 conditions, we found stronger SPI to the narrowband filter that best matched the signal
669 underlying spike generation signal. We also found a reduction in SPI values when the
670 broadband filter was used. This matches what one would intuitively expect from a system
671 composed of an oscillatory signal combined additively with a broad noise. This is the intuition
672 that often underlies narrowband filtering approaches in electrophysiological signal analysis.
673 While there may be alternative explanations for why a broadband signal produces stronger SPI
674 values in our cortical recordings, the second model, where spikes are fluctuation driven

675 (Hypothesis B), was sufficient to account for the spike-LFP coupling relationships observed in
676 the data.

677 Since the phase of narrowband oscillatory activity does not predict spiking activity as
678 well as the phase of wideband activity, it raises a question as to whether and when narrowband
679 filtering is appropriate to study rhythmic spiking dynamics. The use of narrowband filters
680 assumes a frequency resolved signal in the brain that is embedded in noise. As shown by
681 hypothesis A and in Figure 5, when neural activity is strongly coupled to latent oscillatory
682 activity, narrowband filtering is effective at recovering the signal. Therefore, in situations with
683 steady, ongoing oscillatory activity that has low variance in frequency, such as sleep spindles,
684 hippocampal theta, or gamma oscillations due to strong feed-forward input, narrowband
685 filtering may better capture spiking. However, if the signal is not known, narrowband filtering
686 imposes an assumption of what is signal and noise that may not be warranted and may yield
687 misleading results. Analytic techniques that allow for the contribution of broader frequency
688 ranges, as used here, may reveal the degree to which results are frequency dependent or filter
689 dependent.

690 It is important to note the limitations of the present findings. First, all analyses here
691 have focused on spontaneous activity. We cannot generalize the present results to neural data
692 collected under other conditions such as data collected during stimulus-evoked responses.
693 Some narrow-band frequency ranges, such as the gamma band, do not exhibit much power in
694 the absence of strong sensory input(Henrie and Shapley, 2005; Ray and Maunsell, 2010).
695 Additional experiments will be needed to determine the degree to which gamma band and
696 generalized phase predict spike timing under these conditions. Further, the majority of the data
697 analyzed here were recorded from the visual cortex in monkeys performing a particular task, in
698 which they foveated a fixation spot at the center of a blank screen, awaiting the appearance of
699 a faint visual target. In our spontaneous cortical recordings, which are largely representative of

700 the aperiodic 1/f power law observed in primate visual cortex(Fries et al., 2001; Henrie and
701 Shapley, 2005; Yu and Ferster, 2010), even when oscillations are transiently present,
702 narrowband filtering produces a weaker estimate of the spike-LFP relationship than a wider
703 representation.

704 The Generalized Phase approach used here provides a meaningful measure of phase
705 for spectrally broad signals(Davis et al., 2020), and reveals a stronger relationship between
706 broadband LFP fluctuations and spiking probability than could be estimated from any individual
707 narrowband filtered signal. The advantage of GP over narrowband signals is that it follows the
708 moment-to-moment fluctuations in the signal and provides a phase value that generalizes
709 across changes in frequency content. This approach can reveal patterns that would not be
710 clear from an analysis of narrowband oscillations. For example, analysis of broadband
711 measures of phase led to the discovery that the alignment of spontaneous traveling waves of
712 cortical activity with the retinotopic locations of faint visual targets was predictive of the
713 magnitude of evoked activity and perceptual sensitivity(Davis et al., 2020). These effects were
714 only apparent in the data when the state of broadband LFP fluctuations was considered. When
715 filtered in narrow bands, the predictive power of wave phase on behavioral performance was
716 abolished. Consistent with those findings, the results presented here show that, at least in the
717 spontaneous waking activity of Area MT, the instantaneous state of cortical populations is
718 better estimated from the GP of broadband LFP fluctuations than from any narrowband
719 oscillatory component. These results suggest that the phase of broadband neural fluctuations,
720 rather than any specific narrowband frequency content, is the main influence on spontaneous
721 spiking activity in the cortex.

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989 **Figures**

990 **Figure 1. Cortical LFP recordings are inherently broad spectrum (a)** Spikes and local field
991 potentials (LFP) were recorded from area MT of common marmosets while they held fixation
992 on a blank screen. 3 seconds of raw LFP (filtered 1-100 Hz) and spike times from a well
993 isolated neuron recorded on the same electrode is plotted on the right. The red box indicates a
994 period of fixation during the recording epoch. **(b)** The power spectrum for the LFP trace in (a) is
995 plotted in black. 10 additional 3 second epochs are plotted in grey. The red dashed line is the
996 mean power spectrum across trials. **(c)** The raw LFP during fixation is plotted in black against
997 the narrowband filtered theta oscillatory component (4-8 Hz, red dotted line). **(d, e, f,** same as
998 c, but for alpha (8-15 Hz), beta (15-30 Hz), and low gamma (30-50 Hz) band pass filters. **(g)**
999 The wideband filtered (5-50 Hz) LFP follows the dominant fluctuation in the raw LFP as it shifts
1000 in temporal frequency.
1001

Figure 2. Spikes are more strongly coupled to the phase of wideband filtered LFP signals than narrowband oscillatory components. (a) The raw (5-200 Hz) filtered LFP trace from Figure 1 is plotted in black. The wideband filtered trace (5-50 Hz) is plotted in pseudocolor corresponding to the generalized phase (GP) of the wideband filtered trace according to the color wheel. GP captures the troughs (blue/purple) and peaks (yellow/green) of the dominant fluctuations while interpolating over the higher frequency, lower amplitude riding cycles. **(b)** Histogram showing the fraction of spikes that occurred during different phases of the wideband filtered LFP (10 phase bins, N = 20 sessions across 2 monkeys; error bars indicate S.E.M.) **(c)** The spike-phase distribution was flatter for theta band (4-8 Hz) filtered LFP. The mean spike-phase index (SPI), which quantifies the mean vector length of the circular distribution of spike phases, is plotted across 20 sessions from 2 monkeys. The wideband filtered LFP (blue) had significantly stronger SPI values than theta filtered LFP (red; $p < 1x10^{-9}$, two-tailed paired sample t-test) **(d-f)** Same as c, but for alpha (green; $p < 1x10^{-10}$), beta (pink, $p < 1x10^{-11}$), and gamma filtered LFP (green; $p < 1x10^{-9}$).

Figure 3. Stronger wideband spike-phase coupling is consistent across the population of recorded single-units. (a) Scatter plot comparing the magnitude of SPI after use of a broadband filter (x-axis) or theta band filter (y-axis) for each identified single unit (N = 107 across 20 recordings sessions). **(b-d)** Same as for (a) but for alpha, beta, and gamma filters. The wideband filter had a consistently stronger SPI than the narrowband filtered oscillatory phases across the population of single-units.

Figure 4. Narrowband signals do not contain more spike-phase information. (a) SPI values after restricting the inclusion of spikes to when significant power is present in each individual filter band (-5 dB SNR threshold, percentages indicate fraction of data above threshold; colored dots are N = 20 sessions from 2 monkeys; black dots are the population

1028 mean). **(b)** Representative ROC curves for GLM analyses comparing model sensitivity for
1029 identifying spike times based on phase, computed in four narrowband frequency ranges that
1030 tile the frequency space from 4-50 Hz (red), a single measure of narrowband oscillatory phase
1031 (blue), or the single wideband GP measure applied to the same frequency range as the 4-
1032 factor GLM (black). There was no significant difference between the 4-factor and wideband
1033 models in identifying spike times based on phase (Wilcoxon signed-rank test, $p = 0.16$),
1034 whereas the single best narrowband model was significantly weaker (beta; $p = 0.00008$). **(c)**
1035 Scatter plot comparing the correlation between the raw LFP and the filtered LFP signal (y-axis)
1036 and the SPI after filtering (x-axis) in each filter band. There was a significant positive
1037 correlation between SPI and how similar the raw LFP was with the signal after filtering
1038 (Pearson's $r = 0.65$, $p < 1x10^{-12}$). **(d)** SPI for a range of band pass filters ranging in high pass
1039 (lower band, 1-50 Hz) and low pass (upper band, 5-125 Hz). Each pixel is color coded with its
1040 average SPI across each recording session (N = 20 sessions from 2 monkeys). White pixels
1041 are filter combinations that have bandwidths less than 4 Hz. Black contour lines denote SPI
1042 intervals (0.02).
1043
1044 **Figure 5. Two alternative hypotheses regarding the relationship between spiking activity**
1045 **and LFP fluctuations. (a)** Signals generated under the hypothesis embedded narrowband
1046 fluctuations drive spiking activity. We generated a narrowband oscillatory fluctuation with power
1047 between 8 and 15 Hz. Spikes were generated with a Poisson spike generator coupled to a
1048 phase-dependent probability distribution with spikes more likely at π/-π phases and less likely
1049 at 0 phases of the narrowband oscillation. This narrowband signal was added to randomly
1050 generated broadband noise to create a simulated LFP. **(b)** Signals generated under the
1051 hypothesis ensemble broadband fluctuations drive spiking activity. We generated the same
1052 narrowband oscillatory fluctuation and added the same randomly generated broadband noise
1053 as in the simulated LFP in a. Spikes were then generated as in (a), but to the phase of the

broadband simulated LFP signal. **(c)** The result of the 2 signal generation paradigms is 2 identical simulated LFP traces, but with different spike trains generated in relation to the state of either the narrow (blue raster) or broadband (red raster) signal. **(d)** The mean power spectrum across 20 simulated LFP signals (error bars are S.E.M).

Figure 6. Spike-phase relationship is best recovered when the filter matches the signal **(a)** The 8-15 Hz narrowband filtered LFP (solid blue line) is the recovered spike-generating signal from the ensemble simulated LFP (dotted blue line) under hypothesis A. **(b)** The SPI from the phase of the narrowband signal is significantly stronger after narrowband filtering as compared to wideband filtering for the simulation where spikes were coupled to the phase of the narrowband component (5-100 Hz; N = 20 simulations; $p < 0.0001$ two-tailed Wilcoxon signed-rank test). **(c)** The wideband filtered LFP (5-100 Hz, red line) is the recovered spike-generating signal from the broadband simulated LFP under hypothesis B (dotted red line). **(d)** The SPI from the phase of the wideband is significantly stronger after wideband filtering as compared to narrowband filtering for the simulation where spikes were coupled to the phase of the broadband LFP ($p < 0.0001$ two-tailed Wilcoxon signed-rank test).

Figure 7. The model with a broadband spike correlation best matches cortical recordings. **(a)** SPI values after filtering simulated LFP in various band passes when spike times are correlated to the phase of 8-15 Hz narrowband component. In this case, the optimal filter is aligned to the signal source (8-15 Hz). **(b)** Same as (a), but when spike times are coupled to the phase of the broadband LFP. The pattern of SPI across filters is well matched to the pattern observed in data (Figure 4c). **(c)** SPI (x-axis) is poorly correlated with the similarity between filtered and raw simulated LFP (y-axis) when spikes are correlated with narrowband signal phase (blue dots, $r^2 = 0.08$). Conversely, the correlation is strong when spikes are correlated

with broad-band signal phase (red dots, r^2 = 0.85). The relationship for a broad-band signal source is well matched to the pattern observed in the cortical recordings (Figure 4c).