Frequency Selectivity of Neural Circuits with Heterogeneous Discrete Transmission Delays

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Neurons are connected to other neurons by axons and dendrites that conduct signals with finite velocities, resulting in delays between the firing of a neuron and the arrival of the resultant impulse at other neurons. Since delays greatly complicate the analytical treatment and interpretation of models, they are usually neglected or taken to be uniform, leading to a lack in the comprehension of the effects of delays in neural systems. This letter shows that heterogeneous transmission delays make small groups of neurons respond selectively to inputs with differing frequency spectra. By studying a single integrate-and-fire neuron receiving correlated time-shifted inputs, it is shown how the frequency response is linked to both the strengths and delay times of the afferent connections. The results show that incorporating delays alters the functioning of neural networks, and changes the effect that neural connections and synaptic strengths have.

1 Introduction

Although the brain is quick to respond, neurons are connected through axons and dendrites that propagate signals with nonnegligible and replicable delays (Swadlow, 1985, 1994). The transmission delay between two neurons depends on the conduction velocity, related to the diameter of the axon or dendrite (Cullheim, 1978; Cullheim & Ulhake, 1979; Gasser & Grundfest, 1939; Lee, Chung, Chung, & Coggeshall, 1986; Waxman, 1980) and the properties of the axon and dendrites (Harper & Lawson, 1985; Waxman, 1980), in combination with the length of the path a pulse travels from one neuron to the other \( \text{time} = \frac{\text{distance}}{\text{speed}} \). Conduction delays have been shown to be plastic (Bakkum, Chao, & Potter, 2008), indicating that conduction delays are tunable to some extent (Hüning, Glünder, & Palm, 1998). On the other hand, conduction velocities have been found to be activity dependent (Swadlow, 1974; Thalhammer, Raymond, Popitz-Bergez, & Strichartz, 1994; De Col, Messlinger, & Carr, 2008). Still, given that the response times of neurons to natural stimuli can be robust (Berry, Warland, & Meister, 1997; Reich, Victor, Knight, Ozaki, & Kaplan, 1997), the transmission delay times should be stable over time (Swadlow, 1985).
Because of the difficulties involved in the analytical treatment of delays, they are often either neglected or taken to be uniform. This has lead to a lack in the comprehension of the effects of (heterogeneous) delays in neural systems and the absence of delays in principal accounts of the working of neural networks. Great insights into the functioning and dynamics have been gained by studying networks without or with homogeneous transmission delays, such as the understanding of the onset and offset of oscillatory activity (Wang & Buzsáki, 1996; Wilson & Cowan, 1972), signal propagation (Mehring, Hehl, Kubo, Diesmann, & Aertsen, 2003; Reyes, 2003; Vogels & Abbott, 2009), activity dynamics (Destexhe, 2009; Renart et al., 2010; Van Vreeswijk & Sompolinsky, 1996), and memory storage (Amit, Gutfreund, & Sompolinsky, 1985; Anderson, 1972; Brunel, 2016; Hopfield, 1982; Klampfl & Maass, 2013).

However, there are cases in which the incorporation of heterogeneous transmission delays can lead to drastically different results. Organisms, and with that their brains, operate in time, and as such it is likely there is an importance in the temporal dimension of the activity of the brain. It has already been advocated that transmission delays endow neural networks with much richer dynamics, increasing their functional capacity and possible dynamics (Chapeau-Blondeau & Chauvet, 1992; Destexhe, 1994a; Izhikevich, 2006; Ostojic, 2014), enabling neural communication based on synchrony or spike ordering (Brette (2012); Gautrais & Thorpe (1998); Thorpe (1990), and allowing oscillations and synchronization (Brunel, 2000; Buzsáki & Draguhn, 2004; Destexhe, 1994b; Ernst, Pawelzik, & Geisel, 1995; Geisler et al., 2010; Maex & De Schutter, 2003; Payeur, Maler, & Longtin, 2015; Van Vreeswijk, Abbott, & Ermentrout, 1994). This letter concerns the connection between transmission delays and the frequencies to which a neuron responds. In particular, it exposes the concerted effect of synaptic strengths and synaptic delays on the frequency selectivity of neurons.

Synaptic connections between (excitatory) neurons are principally understood in light of some variant of a constitutive Hebbian learning process. The resultant view is that for two neurons to be connected by a strong excitatory connection, it means that it is likely to observe a co-occurrence of their spiking activity, and the stronger this connection is, the more likely they will fire together. A synaptic connection can also be understood through the causal effect of a presynaptic neuron on the activity of a postsynaptic cell, determined by the synaptic strength and presynaptic neuron type. Excitatory presynaptic neurons have a depolarizing effect and thus promote the postsynaptic firing, in general leading to higher postsynaptic firing rates. Inhibitory neurons lead to hyperpolarization and thus inhibit or delay postsynaptic firing, leading to reduced postsynaptic firing rates. These effects are more pronounced for stronger connections.

However, by the inclusion of heterogeneous transmission delays, one can conceptualize a small circuit of neurons as a cascade of filters with time-delayed and weighted coupling. Seen in this way, the properties of
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the afferent connections determine the subthreshold frequency response of a neuron, with the synaptic weights functioning as feedforward coefficients in a neural filtering circuit and thus influencing the frequency selectivity of the postsynaptic neuron. This means that the effect of synaptic strengths differs from the one given above and that the effect of a single synapse cannot be completely understood in isolation, but gets a significantly different interpretation when considered in an ensemble of synapses conveying correlated signals.

This letter explores this concept with a single integrate-and-fire neuron receiving correlated and time-shifted inputs. It is shown that the subthreshold frequency response of a neuron is determined by the strengths and relative delay times of the correlated afferent connections. The characteristics of the frequency response for some cases are solved exactly, and qualitative observations are given for more general cases. Subsequently, numerical simulations demonstrate the functional significance of this frequency selectivity and frequency specificity and show that the described effects hold for a range of input correlations.

2 Theory

To show the basic principle, consider a leaky integrate-and-fire (IF) neuron, with a membrane potential governed by

$$\tau \frac{dv}{dt} + v = G \left( I(t) + \sum_{m=1}^{M-1} w_m I^{(m)}(t - d_m) \right), \quad (2.1)$$

in which \( \tau \) is the membrane time constant. This equation is complemented with a spike-and-reset rule: once the membrane potential \( v \) exceeds a threshold \( v_{th} \), the membrane potential is directly reset to a reset value \( v_r \), after which the membrane potential is again directly governed by equation 2.1.

The input is given by the term \( G (I(t) + \sum_{m} w_m I^{(m)}(t - d_m)) \), which denotes the sum of an input \( I \) with correlated and time-shifted inputs \( I^{(m)} \), each of which is multiplied by a weight \( w_m \). The input can be interpreted as the output of \( M \) similar neurons or groups of neurons that receive strongly correlated input and so produce highly correlated outputs, arriving through connections with different delay times due to the different finite conduction velocities of the different axons and dendrites. The term \( G \) is a gain factor that, since the frequency response does not qualitatively depend on the absolute gain but on the relative strengths of the individual inputs, will be set to be unity in the following analysis of this system. Further on, this term will be used as a normalizing factor: \( G = (1 + \sum_{m=1}^{M-1} |w_m|)^{-1} \).

Equation 2.1 without the spiking mechanism (or with \( v_{th} >> M(I) \) for \( M \) inputs identical up to a time-shift) is linear and time invariant; as such,
Figure 1: Subthreshold frequency spectrum of equation 2.1 measured for different time constants $\tau$ (in s $\cdot$ rad$^{-1}$), showing the low-pass filtering effect intrinsic to the membrane equation. Details on the simulation are found in section A.1

The subthreshold frequency spectrum of $v$ is given by the product of the intrinsic frequency response $1/(1 + t\omega)$, with $\omega$ being angular frequency, and the frequency spectrum of the input (Oppenheim, Willsky, & Hamid, 1997; Smith, 2007),

$$\tilde{v}(i\omega) = \frac{1}{1 + \tau i\omega} \left( \tilde{I}(i\omega) + \sum w_m \tilde{I}(m)(i\omega) \right),$$  \hspace{1cm} (2.2)

with $\tilde{I}(i\omega)$ being the spectrum of a single input $I(t)$, from which we see that the membrane equation has a pole on the real axis at $i\omega = -\tau^{-1}$, corresponding to the characteristic decaying response of the leaky IF neuron (Stein, 1965; Gluss, 1967). Thus, the intrinsic frequency response of the membrane acts as a low-pass filter with time constant $\tau$. Figure 1 shows the intrinsic subthreshold frequency response of the membrane equation equation 2.1 for different values of $\tau$.

The frequency transfer function $H(i\omega)$ of linear time-invariant systems can be found by dividing the output spectrum by the input spectrum, $H(i\omega) := \tilde{V}/\tilde{I}$ (Oppenheim et al., 1997). Requiring that all the input spike trains are identical up to differing positive lag times, thus $l^{(m)}(t) := l(t - d_m)$ for all $m$, with $d_m > 0$, and dividing equation 2.2 by $\tilde{I}$, leads to the subthreshold transfer function of the membrane equation 2.1:

$$H(i\omega) = \frac{1 + \sum w_m e^{-d_m i\omega}}{1 + \tau i\omega}.$$  \hspace{1cm} (2.3)

It will be shown later that the requirement for identical but time-shifted inputs can be relaxed and the obtained results will still hold.
2.1 Frequency Response. The frequency response of the neuronal circuit can be understood by finding the roots of the denominator and the numerator of the transfer function, equation 2.3, which will respectively give the positions of the poles and zeros of the frequency response. Since we are not occupied with feedback components other than the intrinsic membrane dynamics, equation 2.3 has just a single pole; its position is, as shown above, determined by the membrane time constant and lies at \( p = -1/\tau \).

The rate of decay of the membrane potential is proportional to the distance of this pole to the origin, which can also be seen from the homogeneous solution to equation 2.1.

The zeros of equation 2.3 correspond to frequencies at which \( H(i\omega) \) vanishes, corresponding to the input frequencies to which the neuron responds minimally, so the roots of the numerator correspond to frequencies that are attenuated by the circuit. Since \( d_m \in \mathbb{R} \), it is difficult to find exact expressions for the roots of equation 2.3. Exact analysis of the roots in general cases is thus beyond the scope of this letter, but it is straightforward to plot equation 2.3 in order to gain qualitative insight into the frequency response.

However, it will be instructive to treat some cases in which the roots can be obtained analytically. For the following, it is assumed that each delay time \( d_m \) is an integer multiple of some basic time unit \( \delta_0 = 1/(2\pi f_{\text{max}}) \) in \( \text{s} \cdot \text{rad}^{-1} \), thus \( d_m = D_m \delta_0 \) with \( D_m \) an integer. The highest frequency to be analyzed is determined by \( f_{\text{max}} \), or, conversely, \( f_{\text{max}} \) can be determined by requirement on \( \delta_0 \) to fit the desired values of \( d_m \). The natural case, which allows a continuous distribution of delays, is recovered by letting \( \delta_0 \to 0 \) (or, equivalently, \( f_{\text{max}} \to \infty \)), and thus an arbitrary precision is obtainable. Notice that this quantization is only a heuristic necessary for the analytical treatment of the frequency response, but this does not restrict the possible delay times that can occur in neural networks or constrain the possible delay times the described frequency filtering effect occurs for.

In the following, a normalized frequency will be used (\( f_{\text{max}} \) will be normalized to unity) such that \( \delta_0 = 1/(2\pi) \text{s} \cdot \text{rad}^{-1} \). Two specific cases will be treated analytically: a neuron receiving one additional input \((M = 2)\) for a delay time \( d_1 > 0 \), resulting in a comb filtering, and the case of a neuron receiving two additional inputs \((M = 3)\) with \( d_2 = 2d_1 \), \( d_1 > 0 \) such that the numerator can be transformed into a quadratic polynomial. Some of the results will be extended to the more general case in which \( d_2 = nd_1 \), for \( n \in \mathbb{N} \). Afterward some qualitative observations about the zeros of equation 2.3 will be made.

In the case of \( M = 2 \), the numerator of equation 2.3 has periodically distributed roots,

\[
z_n = -w_0 \frac{1}{D_1} e^{i\frac{\pi(2n+1)}{D_1}}, \quad \text{for } n = 1, 2, 3, \ldots \text{ and } k = \begin{cases} 
1, & D_1 \text{ even} \\
0, & D_1 \text{ odd}
\end{cases}
\]
Figure 2: Comb filtering. (a) A schematic drawing indicating neuron wiring receiving two inputs with differing delay times $d_0 < d_1$ due to differing path lengths. (b–e) Measured subthreshold frequency spectra for different synaptic weight $w$ values, for two different delay times. Details on the numerical simulations are in section A.1.

from which we immediately see that the attenuated frequencies (given by the angles $\angle z_n$) are determined by the delay time $d_1 = D_1 \delta_0$, and that the weight $w$ only influences the amount of attenuation (given by the magnitudes $|z_n|$). Figure 2 shows the frequency responses for some different values for $d_1$, also demonstrating the reason for the conventionally used name, comb filter.

A more interesting case is to analyze the zeros of the subthreshold transfer function

$$H(i\omega) = \frac{(1 + w_1 e^{-D_1 \delta_0 i\omega} + w_2 e^{-2D_1 \delta_0 i\omega})}{1 + \tau i\omega},$$

(2.5)

describing a neuron receiving $M = 3$ inputs with harmonically related delays (see Figure 3a), which can be obtained exactly by defining $\sigma(i\omega) = e^{D_1 \delta_0 i\omega}$ and multiplying the transfer function by $\frac{\sigma^2}{\sigma^2}$. This allows rewriting the numerator $N(i\omega)$ of the transfer function as

$$N(\sigma) = (\sigma^2 + w_1 \sigma + w_2).$$
Figure 3: Quadratic filters: (a) Schematic of neuron wiring. (b, c) Measured sub-threshold frequency spectra for neurons receiving three inputs with $w_2 = 1$ and different values for $w_1$, for two different delay times $d_1$, and $d_2 = 2d_1$. Details on the numerical simulations are in section A.1.

which is quadratic in $\sigma$. Now any standard strategy to obtain the roots of $N(\sigma)$ can be employed, leading to

$$\sigma = \frac{-w_1 \pm \sqrt{w_1^2 - 4w_2}}{2}.$$ 

Substituting back $e^{D_1 \delta_0 i \omega}$ for $\sigma$, we can use a similar formula as in the case of $M = 2$, giving

$$z_n = -\left(\frac{w_1 \pm \sqrt{w_1^2 - 4w_2}}{2}\right)^{\frac{1}{M_0}} e^{i\frac{\pi n}{D_1 \delta_0}},$$

with $n$ and $k$ the same as in equation 2.4, showing that the zeros of equation 2.5 repeat with a period $1/d_1 = 1/(D_1 \delta_0)$, and that each of these intervals contains two zeros. In this case, the frequencies at which the zeros are positioned are influenced by both the delay times and the connection weights. Notice that since each $w_m$ is required to be real, the complex zeros occur in conjugate pairs. Figures 3b and 3c show the frequency responses for some values for $d_1$ and $w_1$, with $w_2 = 1$.

The periodicity of the zeros also extends to a more general case where $d_2$ is an integer multiple of $d_1$. In this case, the zeros repeat again with period $1/d_1$, but now each interval contains $d_2/d_1$ zeros.

As noted, in general it will be difficult to determine the zeros of equation 2.3 exactly. Still, some of the above observations can be extended by graphing the magnitude of $H(i\omega)$. In summary, the following observations made for the exact cases can be generalized to cases with $M > 3$. The first observation is that the number of zeros in the $[0, \pi)$ interval is determined...
by the longest delay time. More specifically, longer delay times lead to a more rapid succession of zeros. Indeed, this can be inferred from the exact treatment in the previous section, in which higher-order numerators lead to a faster succession of zeros. The second observation is that when the delays have a harmonic relationship, with each \( d_m \) being an integer multiple of \( d_1 \), the pattern of zeros occurs periodically with a period of \( 1/d_1 \). Third, in the case of complex roots, these roots have to occur in conjugate pairs, since the weights are defined to be real. Finally, the period of repetition of zeros is determined by the delay times, but crucially in the case of complex roots, the weights determine the exact attenuated frequency within each interval. This leads to the important observation that synaptic plasticity not only alters the susceptibility and, with that, the frequency, of postsynaptic firing, but alters the frequency selectivity of the neuronal circuit.

3 Discrimination of Inputs

The filtering capabilities endowed by heterogeneous transmission delays are not purely theoretic, but can be shown to have a definite effect for the functioning of neural circuits. Driving two neurons, each with \( M = 3 \) incoming connections and no connections between each other (thus corresponding to two neurons as in Figure 3 in parallel), with differing frequency selectivity with a communal input that consists of white noise during the first 200 ms and subsequently alternates between two filtered white noise signals, each matching the frequency response of one of the neurons, shows that neurons respond selectively to their matched input (see Figure 4; for details on the simulation, refer to section A.2). Whereas both neurons respond with low firing rates during the white-noise input interval, on average 20.26 (sd = 4.92) spikes/second for neuron A and 58.04 (sd = 8.63) spikes/second for neuron B. During the matched input intervals, a clear distinction between the outputs of the two neurons is observed (49.90 (sd = 3.46) spikes/second for neuron A versus 0.02 (sd = 0.16) spikes/second for neuron B during A-matched input (independent \( t \)-test: \( t(998) = 561.51, p = 0.00 \), 2.35 (sd = 1.66) spikes/second for neuron A versus 78.61 (sd = 5.54) spikes/second for neuron B during B-matched input (independent \( t \)-test: \( t(998) = -399.25, p = 0.00 \)).

Thus, neurons are sensitive to their matched spectral input and can selectively respond to differing spectral inputs: each neuron responded less during the other neuron matched input with respect to the white noise input (paired \( t \)-test: \( t(499) = -115.67, p = 0.00 \) for neuron A, paired \( t \)-test: \( t(499) = -45.94, p = 2.13e - 181 \) for neuron B).

In order to visualize the specificity of neuronal filtering circuits, neuronal circuits with subthreshold frequency responses that pass only a narrow band of frequencies are stimulated with narrow band-filtered white noise input with different center band frequencies. Each neuron receives 13
Figure 4: Frequency selectivity. (a) Schematic indicating neuron wiring. Both neurons receive input from a source matched to their own subthreshold frequency selectivity as well as from a source matched to the other neuron. One neuron receives, through an identical set of $M$ input lines, both the matched and unmatched source. In the figure, neuron A receives $M = 3$ inputs (indicated by the solid blue input lines) from source $I_A$ with three different delay times ($d_{a0} = 0 < d_{a1} = 1 < d_{a2} = 2$) and weights ($w_{a0} = G_a, w_{a1} = -2G_a \Re\{e^{i2\pi d_{a1}}\}$ and $w_{a2} = G_a$ with $G_a = 5(2 + 2|\Re\{e^{i2\pi d_{a1}}\}|)^{-1}$), and through the same synapses (same weights and delay times) the input of source $I_B$ (indicated by the solid orange input lines). Neuron B receives input from source $I_A$ (dashed blue input lines) and $I_B$ (dashed orange input lines) with the same connection parameters between sources ($d_{b0} = 0 < d_{b1} = 1 < d_{b2} = 2$, $w_{b0} = G_b, w_{b1} = -2G_b \Re\{e^{i2\pi d_{b1}}\}$, $w_{b2} = G_b$ with $G_b = 0.5(2 + 2|\Re\{e^{i2\pi d_{b1}}\}|)^{-1}$). (b) Box plots indicating difference in firing rates (transformed into $z$-scores) of each neuron during white noise (left two box plots), unmatched (middle box plots) and matched (right-most plots) input. (c) Spike raster and averaged spike rates of neurons A and B in response to a white-noise input (first 400 ms), A-matched input (second and fourth 400 ms blocks) and B-matched input (third and fifth 400 ms blocks). Top plot shows the spike timings of 500 repetitions of the same trial. Bottom plot indicates the average firing rate (transformed to $z$-scores) of the 500 repetitions per neuron. Consult section A.2 for details on the generation of the graphs.

inputs with weights leading to zeros evenly spaced around the unit circle. Details on the numerical simulation are in section A.3. Figure 5 shows that each neuron responds primarily to its matched input, exemplified by the maximal response values in the diagonal entries, and that the responses diminish rapidly with different center frequencies, as shown by a rapid diminishing of activity in the off-diagonal entries. Neuronal circuits with specific wiring are thus capable of responding strongly to matching frequency inputs, while suppressing their output to nonfrequency matched inputs. In order to suppress most of the frequency spectrum and pass only an increasingly narrow band, a neuron needs to receive more and more inputs. However the neurons simulated for Figure 5 received only 13 inputs, many fewer than the estimates of the average number of inputs received by neurons.
Figure 5: Specificity of neuron response. Output firing rate of neurons with narrow bandpass frequency selectivity ($M=13$), with different center-frequencies ($y$-axis), in response to bandpass-filtered white noise input with different center-frequencies ($x$-axis). Diagonal entries correspond to matched input and synaptic-filtering center frequency. Off-diagonal entries correspond to increasing disparity between the synaptic filter and input center frequencies.

4 Robustness for $\rho \neq 1$

Throughout this letter, it has been assumed that the inputs the postsynaptic neuron receives through the different synapses were perfectly correlated $\rho = 1$. Although the intrinsic noise levels of neurons are low (Mainen & Sejnowski, 1995), the great number and diversity of synaptic inputs still likely lead to each neuron being subjected to a “unique” noise source. Indeed correlations in the output of any two neurons are generally weak (Cohen & Kohn, 2011). Perfect correlation is thus in general unlikely. In order to investigate the tolerance to nonperfectly correlated inputs, a neuron is simulated, receiving two additional inputs $M = 3$, with different correlation between the inputs arriving through the different delay lines, thus

$$I^{(m)}(t) = \rho I(t - d_m) + (1 - \rho) \eta_m(t),$$ (4.1)

with $\eta_m$ being a similar noise source as $I$. Fourier-transforming the subthreshold responses shows, as visible in Figure 6a, that with decreasing correlation, the shape of the measured subthreshold frequency spectrum quickly reduces to that of the intrinsic subthreshold response of the membrane equation (equal to the spectrum on the left for $\rho = 0$). This suggests that even relatively small dis-relations between the inputs abolish the frequency selectivity of a neuron described in this letter.
Figure 6: Robustness to decorrelated inputs. (a) Measured subthreshold frequency spectra for decreasing intersynapse input correlation $\rho$, showing fast degradation of frequency selectivity with decreasing correlation. (b) Box plot indicating $z$-scores of firing rate in response to matched (solid boxes) and unmatched (dashed boxes) with different inter-input correlations ($x$-axis). (c) Spike raster and averaged firing rates of 1000 neurons with random synapse parameters (number and position of conjugate zeros), in response to input alternating between matched and unmatched input, repeated for different intersynapse input correlations (indicated with different colors, corresponding to the colors of panel b). Top plot indicates the spike timings of the neurons for six different correlation values (indicated with different colors). Bottom plot indicates the average of the firing rates, transformed into $z$-scores, of all the neurons for each intersynapse correlation value.
However, again simulating different neurons, each adapted to discriminate between spectrally different inputs, but this time with each neuron receiving white noise input with strength \( (1 - \rho) \) in addition to the spectrally shaped input (with strength \( \rho \)), leads to a surprising finding. Figures 4b and 4c show the results similar to figures 4b and 4c, but now for different values of input correlation (refer to section A.4 for details on the simulation and statistics). These results show that functionally the frequency selective effect due to the input parameters is still present for correlations lower \( (\rho = 0.2) \) than for which the frequency response shaping effect is visually prominent from the subthreshold frequency spectrum (see Figure 6a).

Thus importantly, although from the measured frequency spectra the effect of the inputs on the frequency selectivity seemed to be negligible, the frequency selectivity of the neurons is functionally still significantly shaped by the input parameters, and this frequency selectivity is predictable by the theory presented in this letter.

5 Discussion

This letter shows that delays in the transmission of signals between neurons have a determinate effect on the frequency response of individual neurons, making it possible for neural networks to act as finite impulse response filters. It is shown that the length of the delay time, but, importantly, also the strengths of the connections determine the frequency selectivity and that the frequency response of a neuron due to its afferent connections can be characterized by the analysis of the strengths and delay times of the incoming connections. Numerical simulations demonstrated that neural networks can be constructed in which neurons with differing connections from overlapping input sources can differentially respond to spectrally different inputs and can do so with high specificity, thus opening up the frequency domain for usage in neural communication. Finally, it is found that with diminishing input correlation, the measured subthreshold frequency spectra do not show clear signs of the effects of the input parameters, but the frequency selectivity is still functionally present.

The basic setup of the current study is in a way related to that treated in Payeur et al. (2015), where it was shown that a two-layer network with feedforward inhibition shows a power spectral density with a peak at a nonzero frequency. This result is related to the \( M = 2 \) case demonstrated in Figures 2c and 2e, which show the subthreshold frequency response of a neuron receiving two inputs: a direct excitatory and delayed inhibitory copy of a single signal \( I \). Also, the presented theory predicts a peak at a nonzero frequency.

The idea of filtering by neurons is not new: a receptive field is essentially a filter. It is, however, important to note that the frequency filtering as treated in this letter is distinct from a filtering of information (as a receptive field does). The filtering described here is a power filtering; the
attenuation (and accentuation) of the magnitudes of certain frequencies, leading to differential responses to inputs with different frequencies, which does not necessarily alter the signal-to-noise ratio (Lindner, 2014), but alters the dynamics of signal transmission. Thus, unless spectral content directly conveys information, the effect of delays as presented in this letter does not constitute a “neural code” as such. Rather, it plays an indirect role by making it possible to dynamically route signals (e.g., by amplifying certain frequency bands; excitation or inhibition of other neurons by the frequency selective neuron or resetting the phase of oscillatory populations). Through these effects neural codes can be transmitted, so this type of filtering constitutes a medium rather than the message.

5.1 Reinterpretation of Synaptic Strengths. The presented results show that with the inclusion of transmission delays, the effect of synaptic connectivity is different from the generally accepted interpretation: the strength of a synaptic connection determines not merely the frequency of postsynaptic firing, but codetermines the frequencies to which the postsynaptic neuron responds. This subthreshold frequency response is determined by the full ensemble of synapses transmitting correlated inputs to a neuron; thus, the effect of the strength of a single synapse on the activity of the postsynaptic neuron cannot be understood in isolation, only in relation to the other synapses. In the light of this observation, the interpretation of the meaning of synaptic strength and the role of synaptic plasticity might need to be reconsidered. It will be crucial, of course, to test the predictions of the theory presented in this letter experimentally.

5.2 Interpretation of the Inputs. During the theoretical treatment of the frequency selectivity due to synaptic inputs, the time-shifted inputs were taken to be perfectly correlated. Although it was shown that perfect correlation was not needed for neural circuits to retain functionally their frequency selectivity, the correlation levels for which the frequency filtering was qualitatively prominent are higher than reported correlations between pairs of neurons (Cohen & Kohn, 2011). This raises the question how to interpret the inputs used in this study.

A first possibility, which is also the simplest explanation, is to let the different delayed inputs emerge from the same, or largely overlapping, sources through different transmission lines. In this way, the unique noise sources are reduced to that due to synaptic transmission and the propagation of signals along axons and dendrites. It is, so far as I know, not known whether such connection patterns exist in the brain, but in any case, this solution would require a very specific wiring of neural circuits.

Another option arises by observing that the results of the numerical simulations show (see section 3) that switching the input from an unmatched to a matched input elicits a rapid response in the matched neuron, as visible from the switches between the different inputs in Figure 6c. From the
A viewpoint of a neuron, this is equivalent to its input switching from uncorrelated (with arbitrary spectral content) signals, to correlated (and frequency matched) signals. Thus, neurons need only transient presynaptic synchronization to detect their matched spectral input.

As a third explanation, although single cell to single cell correlations are low, and seem to actively be kept low even when driven by the same input (Middleton, Omar, Doirion, & Simons, 2012; Renart et al., 2010; Graupner & Reyes, 2013), collectively coherent activity often co-occurs with irregular firing in single neurons (Buzsáki & Wang, 2012). Network-level oscillatory activity can arise from sparsely interconnected and weakly correlated neurons (Brunel & Hakim, 1999; Brunel, 2000), showing that the correlation between pairs of neurons can be low contemporary with the pooled activation of subsets of a population showing stronger correlations. Thus, the different inputs can be correlated to a high degree if we interpret the input lines of equation 2.1 as each receiving the pooled activity from a population of (sparsely) interconnected and (weakly) correlated neurons.

It is in addition useful to mention that even though in the numerical demonstrations, stochastic inputs are used, the results presented here also hold for deterministic inputs.

Appendix: Suplementary Simulation Details

All simulations carried out in this letter are done with leaky integrate-and-fire neurons (Lapicque, 1907), receiving $M$ correlated, weighted, and time-shifted inputs $w_m I^{(m)}(t - d_m)$. The membrane potential is governed by the equation

$$\tau \frac{dv}{dt} + v = G \left( I(t - d_0) + \sum_{m=1}^{M-1} w_m I^{(m)}(t - d_m) \right),$$

which is supplemented with a spike-and-reset mechanism: each time $v$ surpasses a threshold value $v_c$, it is said to fire a spike and is directly reset to a reset value $v_r$. Throughout, a normalizing gain factor of $G = \left( 1 + \sum_{m=1}^{M-1} |w_m| \right)^{-1}$ is used. In the simulations for the results and figures of this letter, the inputs $I^{(m)}$ to the neuron are either pure white noise or filtered white noise, depending on the particular simulation (see the following sections for the specifics per simulation). In general, for simplicity, the first delay time is set to zero ($d_0 = 0$).

A.1 Measured Subthreshold Frequency Response Spectra. The subthreshold frequency response spectra are measured by driving the neuron with inputs that are time-shifted versions of a single white-noise source with mean $\mu = 0$ and standard deviation $\sigma = 1$. To ignore the fast membrane fluctuation caused by spiking, the spiking threshold was set to
infinity \( (v_c = \infty) \). The simulations were carried out with \( 1 \times 10^4 \) timesteps per spectrum. Each spectrum is the average over the spectra of \( 1 \times 10^4 \) simulated neurons.

**A.2 Frequency Selectivity: Discrimination of Inputs.** The base input both neurons received alternates between two different noise signals with differing spectral content, each of these signals matching the frequency selectivity of either one of the two neurons. In the first 4000 timesteps of each realization, the administered input is an unfiltered white noise signal in order to observe the baseline firing of each neuron. For these simulations, the spike-and-reset mechanism \( v > v_{th} \Rightarrow v \leftarrow v_r \) is used, so it is possible to observe the spiking behavior of the two neurons in response to the different inputs. Simulations were carried out with \( 2 \times 10^4 \) timesteps. Each group consists of 500 neurons, for a total of 1000 neurons. The firing rates are calculated per neuron with a timewindow of 200 timesteps. The rate of each neuron is transformed into \( z \)-scores. The \( z \)-scores are averaged in each condition (white-noise, A-matched, or B-matched) per neuron. Two-sample independent \( t \)-tests are carried out comparing the distribution of average \( z \)-scores of neuron A versus that of neuron B, per condition. Matched sample \( t \)-tests were carried out between the firing \( z \)-scores between the random interval and the unmatched intervals. For plotting purposes, the firing-rate \( z \)-scores are averaged over all neurons per timestep.

**A.3 Frequency Selectivity: Specificity of Responses.** Each neuron receives 13 inputs with weights leading to zeros evenly spaced around the unit circle, with the exception of one conjugate pair. In this way, the neuron is mainly responsive to a small band of frequencies around the angle of the missing pair of zeros. These neurons are subsequently exposed to bandpass-filtered white noise with differing center frequencies. The spike count of each neuron in response to each bandpass-filtered noise stimulus is recorded and normalized per neuron over different inputs such that the maximal count of each neuron equals one. Each pixel corresponds to the average spike count of 500 neurons over \( 2 \times 10^3 \) timesteps. Each spike rate is calculated over the whole time of each trial.

**A.4 Robustness to Nonperfect Correlation.** Each input \( I^{(m)} \) to the synapses of the neurons in these simulations consists of an input consisting of a (delayed) source input \( I \), which is a specifically filtered white-noise signal matched to the preferred spectrum of a neuron. This input is shared by all the synapses. In addition, each synapse receives a unique noise \( \eta_m \), a randomly permuted version of the matched input. This input is unique to each synapse. Thus:

\[
I^{(m)}(t) = \rho I(t - d_m) + (1 - \rho) \eta_m(t). \tag{A.1}
\]
The synapse parameters \((M, w_m, \text{ and } d_m)\) are constructed from \((M - 1)/2\) randomly drawn zeros on the upper half of the unit circle and their conjugates, in addition to the direct input \(m = 0\). This resulted in 1000 neurons with different frequency selectivity. These neurons are then driven in six trials with inputs with differing intersynapse correlations from perfect correlation \(\rho = 1\) to completely uncorrelated \(\rho = 0\), as described above. Each trial consisted of five blocks of equal time: the first 2000 timesteps, all neurons, are driven a random permutation of their matched input (shuffled along the time dimension), resulting in a white-noise input. Following there are four blocks of 2000 time-steps each; during the first and the third blocks, each neuron receives its matched input. In the second and last blocks, each neuron receives the matched input of another neuron, randomly drawn (thus a shuffling of the pairing between neuron and input). The firing rates are calculated over a window of 500 timesteps, for each neuron for each correlation level and transformed into \(z\)-scores. For each correlation level, the mean firing rate \(z\)-score of each neuron during the matched blocks is compared to its firing rate \(z\)-score during the unmatched blocks in a paired \(t\)-test. For plotting of the firing rates, the firing rate \(z\)-scores are averaged across neurons, resulting in a single line per correlation level.

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