POPULATION OSCILLATIONS IN NEURONAL GROUPS

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We study nonlinear oscillations in localized populations (neuronal groups) of excitatory and inhibitory neurons. In particular, we investigate the role of delay in inhibition and slowly decaying inhibition in inducing robust population oscillations. It is found that an arbitrarily small delay in the inhibitory signal can induce oscillations by destroying the stability of the fixed points. A phase shift between the excitatory and inhibitory components underlies the generation of oscillations. Delay in inhibition and slowly decaying inhibitory signals readily result in such phase shift. Linear theory is found to be inadequate to study these oscillations. A nonlinear theory of the relations between the frequency, amplitude, and phase of the oscillations is described. With these relations, some aspects of the origin and characteristics of the oscillations—in particular, the effect of delay in the inhibitory signal, disparate excitatory and inhibitory activity decay time periods, refractoriness in the excitatory neurons, and the mean synaptic strengths between the excitatory and inhibitory subpopulations—are studied. It is suggested that (realistic) excitatory time courses of the form $t \exp^{-t/\tau_e}$, with $\tau_e < \tau_i$, can generate robust oscillations. The generation of harmonics, which can be strong when the frequency is low, the refractory period is large, or the net population activity is high, is analyzed.

1. Introduction

The organization of the brain reflects the tendency of most complex nonlinear systems to organize into coherent structures. A growing wealth of experimental data suggests that the brain is a distributed system with functionally segregated units.1–4 Each module in this system is a localized population of tightly connected neurons termed neuronal group.5 The neuronal group serves as the fundamental input/output unit imposing transforms on signals that are determined by its circuit properties, as well as its extrinsic connections.1 For example, columns in the visual cortex serve as recognizers of elementary properties such as stimulus orientation and ocular dominance.6

In order to understand how complex signals are processed in such a distributed system, it is important to understand the characteristics of the temporal phenomena that results from the interactions within a neuronal group. The nonlinear interaction between the strongly connected neurons in a neuronal group gives rise to a coherent signal. This coherent signal is then mapped to other neuronal groups in the system. Such a mapping subserves the functioning of the distributed system.7,8 In this paper, the temporal characteristics of the coherent signal produced by the nonlinear interaction of neurons in a neuronal group are studied mathematically in some detail. The approach and mathematical formalism developed in this paper may be extended to study the functionally important problem of re-entrant signaling between several groups.9,10

A variety of physiological and psychological experiments and observations suggest the rhythmic organization of temporal phenomena in neural systems. The well known EEG scalp recorded oscillations,11 oscillations in the olfactory bulb and cortex,12 thalamic oscillations,13 oscillations in the central pattern generator in the motor system,14 and the recently observed visual gamma-range cortical oscillations,15–17 all affirm this. The rhythmic organization of temporal phenomena in the brain is also suggested by studies of reaction times to visual stimuli,18 and several neuropsychological experiments on speech production, delivery, and related cognitive phenomena.19 With respect to motor activity Bernstein20 has noted that a diversity of rhythmic human movements may be interpreted to

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a great accuracy with the sum of three or four harmonics in the oscillations.

Since the discovery of the EEG, the role of oscillations has been intensely speculated upon. Wiener noted that oscillations could serve to gate specific inputs—thus, for example, signals arriving within a certain time gap are likely to be combined. Based on several psychological experiments and observations, it has been noted that sensory integration is likely to be aided by oscillations transduced by the different sensory modalities. Integration of new and unexpected signal such as those required to take into account reactive phenomena in motion are likely to be aided by oscillations. Oscillations also serve as the basis for establishing dynamical correlations for sensory segmentation underlying pattern recognition.

Oscillations provide a particularly effective mechanism to create a spatiotemporally continuous representation of objects or events in view of its own cyclic and continuous nature. Globally mapped oscillatory signals may also be involved in neural control of state (in the sleep-wake cycle, for example) as well. Thus, oscillations could serve as the basis of coherent signaling and as autonomous timing mechanisms.

These observations have been given an impetus by recent experiments on the cat visual cortex, indicating that oscillations in the frequency range 20–80 Hz occur in several areas of the neocortex when the animal directs its attention to meaningful stimuli. The oscillations, occurring in spatially separated regions, can be synchronized in a manner that reflects global stimulus properties. These experiments suggest an important role for oscillations in overall integration in distributed systems in order to obtain a coherent reconstruction of visual scenes and more generally in pattern recognition and classification.

While individual neurons can fire rhythmically, it is unlikely that given the massive recurrent connections between neurons this represents the dominant mode of signaling in a distributed neural system. On theoretical grounds, it has been argued that the oscillations must represent collective phenomena. Such oscillations have the advantage of being robust and stable to random fluctuations.

Several recent experimental and computational studies have revealed the origin and critical characteristic of the oscillations, some of which we wish to summarize. Experimental findings indicate that rhythm in the cortex and thalamus may not be due to the 'pacemaker' properties of the thalamic neurons but is an emergent property of the interaction of excitatory and inhibitory neurons. Experimental evidence also suggest that cellular firing is usually less well correlated with the EEG than are synaptic events. Eckhorn et al. have noted the difficulty of detecting rhythmic oscillations in single-unit activity even when the local field potential and multi-unit activity indicate coherent oscillatory activity.

The detailed computer simulations of Traub et al. have recently elucidated the nature of the population oscillations. The work of these scientists on the CA3 slice of the hippocampus indicates that the temporal activity consists of rhythmic population oscillations in which the number of neurons firing per unit time oscillates synchronously, even though single neurons may fire asynchronously. The firing of single neurons is largely stochastic and unpredictable (see also Ref. 35). The amplitude and frequency of this emergent rhythmic activity depend on intrinsic cellular properties, such as refractoriness, delay in the inhibitory feedback, and the mean excitatory and inhibitory synaptic strength. An important indication of the population nature of the activity is that the population firing rate (the fraction of neurons firing per unit time) can be faster than the refractory period of single neurons. Furthermore, when the model slice is cut laterally, it is found that a certain minimum size is needed to sustain coherent oscillations. Variable levels of excitation and inhibition and their relative timings are found to be critical in determining the characteristics (in particular the frequency and amplitude) of the oscillation.

Therefore, it is unlikely that the critical character of the oscillations is likely to be understood by considering the firing of single neurons, or even a few interacting neurons. In short, these results indicate that the most probable source of oscillations could be the interaction of excitatory and inhibitory neurons in localized populations of neurons—neuronal groups. The neurons in a group are tightly coupled, i.e., the synaptic strength within a group is much stronger than that between groups and could provide a locus for temporal interaction.

The model we consider is based on the technique of renormalization, which is widely used to study collective phenomena in the physical sciences (see, for example, Ref. 36). The technique is also closely related to the notion of nonlinear pulse wave transforms. In the present model, the actual renormalization step consists of replacing the summation of excitatory and inhibitory potentials on the membrane of a neuron by the summation of excitatory and inhibitory signals from interacting subpopulations of excitatory and inhibitory neurons. Such an approach
is useful in studying the dynamics of the aggregate, given the complex nonlinear interactions between individual neurons and the fact that cellular refractory periods are not negligible compared to the other time scales in the problem.

In the present work we show that linearized models are inadequate and develop a nonlinear theory of population oscillations. Mathematical work on the oscillations has typically concentrated on stability analysis and linearized models. An important focus here is to analytically underpin the basis of the large dynamic frequency–amplitude–phase range of the oscillations. To this end, it is first shown that a particularly robust method for generating the oscillations is delayed inhibition or slowly decaying inhibition which causes a phase shift between the excitatory and inhibitory components of the interacting intraneuronal-group signals. Theoretical analysis shows that a large range of frequency and amplitude is possible by varying the time course of the inhibitory signal. This is in agreement with the observation that the time courses of the fast and slow GABA_A and GABA_B mediated inhibition play a critical role in regulating the frequency–amplitude characteristics of the oscillations.

The organization of this paper is as follows: in Sec. 2 we describe the mathematical model of Wilson and Cowan and propose a simple extension to study temporal activity due to delayed inhibitory signals. In Sec. 3 the asymptotic stability of the linearized equations is considered. It is found that for a wide range of parameters, delay in feedback from the inhibitory neurons can destroy stability of the fixed points, thereby inducing limit-cycle oscillations. To study periodic solutions, the method of harmonic balance is briefly described in Sec. 4, and in Sec. 5 this method is used to derive nonlinear algebraic equations governing the frequency, amplitude, and phase of oscillations for the piecewise-linear sigmoid. In Sec. 6 it is shown that a linear approximation is inadequate to study the oscillations. We consider a detailed nonlinear theory in Sec. 7. Section 8 summarizes the main results.

2. Mathematical Model

The aim of the mathematical model we consider is to "give an expression to the statistical nature of the interaction of neurons." The model does not refer to the firing or activity of single neurons but to the collective behavior of localized populations of neurons. Such an approach is consistent with the experimental and computational results summarized above. The main problem that this model addresses is the nonlinear interaction of excitatory and inhibitory signals originating from the more complex spatiotemporal interaction of individual neurons.

Figure 2.1 is a schematic representation of the model. External input and recurrent excitation drive the activity of the excitatory subpopulation. The inhibitory subpopulation is activated by the excitatory subpopulation and possibly by external input. The activated inhibitory subpopulation then inhibits the activity of both inhibitory and excitatory neurons usually with a latency.

The nonlinear summation of voltage at the membrane of a neuron can be renormalized to represent the

Fig. 2.1. A schematic of interacting subpopulations of excitatory E and inhibitory I neurons in a neuronal group. External inputs P and Q drive the activity of the neurons. C_1, C_2, C_3, and C_4 are the mean synaptic strengths mediating the inter- and intra-subpopulation interactions. Filled arrows indicate the excitatory effect, and unfilled arrows, the inhibitory effect of one subpopulation on the other or itself.
response of excitatory and inhibitory subpopulations in a localized population of neurons.\textsuperscript{38} This represents a parsing of the complex circuitry within a neuronal group.\textsuperscript{42} The interactions between the subpopulations may then be modeled by the following time coarse grained and spatially averaged nonlinear differential equations.\textsuperscript{30} \(f_e(t)\) and \(f_i(t)\), the fraction of excitatory and inhibitory neurons firing per unit time at time \(t\),

\[
T_e \dot{f}_e(t) = -f_e(t) + \left[ 1 - \int_{t-r_e}^{t} f_e(t') dt' \right] \sigma_e(x_e) \tag{2.1}
\]

\[
T_i \dot{f}_i(t) = -f_i(t) + \left[ 1 - \int_{t-r_i}^{t} f_i(t') dt' \right] \sigma_i(x_i) \tag{2.2}
\]

\[
x_e = C_1 f_e(t) - C_2 f_i(t) + P
\]

\[
x_i = C_3 f_e(t) - C_4 f_i(t) + Q
\]

where \(x_e\) and \(x_i\) are the activities and \(\sigma_e(x_e)\) and \(\sigma_i(x_i)\) are the responses of excitatory and inhibitory sub-populations. The sigmoid is taken to be of the form

\[
\sigma(x) = \frac{1}{1 + \exp[-\beta(x - \chi)]}
\]

where \(\beta\) and \(\chi\) are respectively the sigmoid nonlinearity and threshold. \(T_e\) and \(T_i\) are the decay periods of excitatory and inhibitory activity, and \(r_e, r_i\) are the absolute refractory periods of the excitatory and inhibitory neurons respectively.

The change in the fraction of neurons firing depends on (1) the decay in activity and (2) the fraction of neurons that are not refractory and is active. The fraction of the neurons that are not refractory is \((1 - \int_{t-r_e}^{t} f_i(t') dt')\), and the fraction of neurons that are active is given by the sigmoid in terms of the average input to the neurons. \(C_1, C_2, C_3, C_4\) are the mean synaptic strengths mediating the E to E, I to E, E to I to I subpopulation interactions, and \(P, Q\) are the external inputs to the E and I subpopulations. The important properties of this model are (1) renormalized nonlinear interaction consisting of summation of excitatory and inhibitory signals with sigmoid saturation, (2) strong linear dissipation, and (3) cellular refractoriness that reduces the pool of neurons available for driving the activity of the subpopulations, thus accounting for temporal redundancy.

Wilson and Cowan have shown that for some class of stimulus \((P, Q)\) values, limit-cycle oscillations will be obtained if the following (sufficient but not necessary) conditions are satisfied (for \(r_e = 1, r_i = 1\)):

1. \(C_1 \beta_e - C_4 \beta_i > 18\)

2. \(\beta_e \beta_i C_2 C_1 > (\beta_i C_1 - 1)(\beta_i C_4 - 9)\) and \(\beta_e C_1 - C_2 < 9\).

Condition 2 ensures that there is only one fixed point, and condition 1 implies that the fixed point is unstable. These conditions require that there be a strong negative feedback \((C_2 C_3 \gg C_1 C_4)\). We will show that limit-cycle oscillations exist for a much wider range of parameters than implied by the above results.

Equations (2.1) and (2.2) ignore delay in the expression of the inhibitory signal at the synapse.\textsuperscript{43} Such delays are a typical feature of inhibitory interneurons and have been shown to be critical for oscillations—blocking slow inhibition can prevent partially synchronized bursts.\textsuperscript{33,34} If we denote the time course of the inhibitory postsynaptic potentials developing onto the excitatory and inhibitory subpopulations by \(\alpha(t)\), Eqs. (2.1) and (2.2) are modified to

\[
T_e \dot{f}_e(t) = -f_e(t) + \left[ 1 - \int_{t-r_e}^{t} f_e(t') dt' \right] \sigma_e(C_1 f_e(t) - C_2 f_i(t) + P)
\]

\[
T_i \dot{f}_i(t) = -f_i(t) + \left[ 1 - \int_{t-r_i}^{t} f_i(t') dt' \right] \sigma_i(C_3 f_e(t) - C_4 f_i(t) + Q)
\]

Approximating the time course by the delta function, \(\alpha(t) = \delta(t - t_d)\), where \(t_d\) is the delay in the inhibitory feedback, the above equations are,

\[
T_e \dot{f}_e(t) = -f_e(t) + \left[ 1 - \int_{t-r_e}^{t} f_e(t') dt' \right] \sigma_e(C_1 f_e(t) - C_2 f_i(t - t_d) + P)
\]

\[
T_i \dot{f}_i(t) = -f_i(t) + \left[ 1 - \int_{t-r_i}^{t} f_i(t') dt' \right] \sigma_i(C_3 f_e(t) - C_4 f_i(t - t_d) + Q)
\]
\[ T_e \tilde{f}_e(t) = -f_e(t) + \left[ 1 - \int_{t-t_d}^{t} f_e(t')dt' \right] \times \sigma_i[C_3 f_i(t) - C_4 f_i(t - t_d) + Q] \quad (2.6) \]

In the next section we show that Eqs. (2.5) and (2.6) display limit-cycle oscillations for a wide range of parameters when the inhibitory signal delay, \( t_d \), is nonzero.

3. Asymptotic Stability of Linearized Equations

Although the role of delay in inducing oscillations has been explored in other neural network models, the specific role of inhibition in models with interacting renormalized excitatory and inhibitory signals has not been explored. In this section, we consider the stability of the fixed points of Eqs. (2.5) and (2.6). It is shown that even small delays in the inhibition can destroy the stability of the fixed points thereby inducing oscillations. A different view of the origin of the oscillations will be described when a nonlinear theory is described.

A necessary condition for the existence of oscillations is that at least one of the fixed points is unstable. Proving existence of limit cycle oscillations for delay differential equations is quite complicated and no attempt is made to do so here. However, for the problem at hand, we will interpret the instability of all the fixed points to mean that oscillations could exist, although this is a much stronger condition than is actually needed. Numerical experiments indicate that the only limit sets that occur are fixed points and periodic orbits.

For the stability of a fixed point of the nonlinear functional differential equations (2.5) and (2.6) a necessary and sufficient condition is the stability of the linearized equations. The fixed points, \( \bar{f}_e \) and \( \bar{f}_i \), are given by

\[ \bar{f}_e = (1 - r_e \bar{f}_e)\sigma_e(C_1 \bar{f}_e - C_2 \bar{f}_i + P) \quad (3.1) \]

\[ \bar{f}_i = (1 - r_i \bar{f}_i)\sigma_i(C_3 \bar{f}_e - C_4 \bar{f}_i + Q) \quad (3.2) \]

Linearizing around the fixed point gives the following characteristics equation for small \( r_e \) and \( r_i \) (see Appendix A.1 for details)

\[ \lambda^2 + G\lambda + H + \lambda J e^{-\tau_e \lambda} + I e^{-\tau_i \lambda} = 0 \quad (3.3) \]

where

\[ G(z_e) = k_e + k_i - \alpha_e \sigma_i(z_e)C_1 \]

\[ H(z_e) = k_e [\kappa_e - \alpha_e \sigma_i(z_e)C_1] \]

\[ I(z_e, z_i) = \alpha_e \sigma_i(z_e) \sigma_i(z_i) \alpha_i(C_2 C_3 - C_1 C_4) \]

\[ J(z_i) = \alpha_i(z_i) \alpha_i C_4 \]

\[ \sigma_i(z_e) = \frac{\beta_e}{\{4 \cosh^2[-\beta_e(z_e - \chi_e)]\}} \quad (3.4) \]

\[ \sigma_i(z_i) = \frac{\beta_i}{\{4 \cosh^2[-\beta_i(z_i - \chi_i)]\}} \]

\[ T_e k_e = 1 + r_e \sigma_e(z_e) \]

\[ T_i k_i = 1 + r_i \sigma_i(z_i) \]

\[ T_e \alpha_e = 1 - r_e \bar{f}_e \]

\[ T_i \alpha_i = 1 - r_i \bar{f}_i \]

\[ \bar{z}_e = C_1 \bar{f}_e - C_2 \bar{f}_i + P \]

\[ \bar{z}_i = C_3 \bar{f}_e - C_4 \bar{f}_i + Q \]

The quasi-polynomial [Eq. (3.3)] has an infinite number of roots. A necessary and sufficient condition for the stability is that \( \text{Re } \lambda < 0 \), for all roots. \( \sigma_i(z_e) \) and \( \sigma_i(z_i) \), are the slopes of the sigmoid at the fixed point. \( \sigma' \) lies between 0 and \( \beta/4 \) and its maximum value is at the threshold.

The following theorems, proven in Appendix A.2, indicate the nature of the solutions to the characteristic equation. Here we will discuss only the implications of the theorems.

**Theorem 3.1.** For sufficiently large delay \( t_d \) the fixed point is unstable if \( H < 0 \).

**Theorem 3.2.** A set of sufficient conditions for stability of a fixed point is:

(i) \( t_d(H + I) > 0 \) and (ii) \( G - J > t_d|I| \).

**Theorem 3.3.** If \( t_d^2(H + I) < 0 \), the fixed point is unstable.

The following results indicate when limit-cycle oscillations could occur and the critical delay for which this happens:

(1) If \( \sigma_i(z_e) = 0 \) and \( \sigma_i(z_i) = 0 \) then the fixed point is stable.
Proof. Let \( \sigma'(\bar{x}_e) = \sigma'(\bar{x}_i) = 0 \). Then \( G = \kappa_e + \kappa_i \), \( H = \kappa_e \kappa_i > 0 \), \( I = 0 \) and \( J = 0 \), from Eqs. (3.4). From Theorem 3.2 it then follows that the fixed point is stable.

Hence, oscillations cannot occur for any value of delay if the slope of the sigmoid at all of the fixed points is zero for both the excitatory and the inhibitory components. Typically, the slope of the sigmoids is zero when either the driving input is too strong or too weak compared to the threshold for excitation.

(2) An interesting case arises when the sigmoid is a step function so that the slope is zero everywhere except the threshold where it is infinite. The result derived in (1) above indicates that no oscillations are possible in such a case since the slope is zero almost everywhere. Thus, variance in the subpopulation, implying a non-step-function sigmoid, may be essential in generating stable oscillations. Numerical experiments indicate this to be true. Note however that this result has not been proved rigorously.

(3) If \( H < 0 \), which necessarily requires \( \sigma'_e(\bar{x}_e) \neq 0 \), there is a time delay, \( \tau \), such that for \( t_d > \tau \), all fixed points are unstable. This follows directly from Theorem 3.1. This result indicates that for a wide range of parameters, all the fixed points are unstable, and therefore limit-cycle oscillations occur for large enough delay. When \( r_e = r_i = 0 \) and \( T_e = T_i \), for \( H < 0 \), it is necessary that \( C_1 > 1/\sigma'_e(\bar{x}_e) \). If the fixed point is near the threshold this simply requires \( C_1 > 4/\beta_e \).

(4) If \( H + I < 0 \) for all fixed points, then from Theorem 3.3, arbitrarily small delays can cause the

Fig. 3.1. The fixed point can become unstable when a small delay is introduced in the inhibitory feedback thereby inducing limit-cycle oscillations. (a) The fraction of excitatory neurons firing per unit time \( f_e(t) \) for inhibitory delay \( t_d = 0 \) illustrates stabilization to a fixed point. (b) \( f_e(t) \) for delay \( t_d = 0.05 \) indicates destabilization of the fixed point leading to robust oscillations. Results are obtained from the numerical simulation of Eqs. (2.5) and (2.6). Similar results hold for the inhibitory component.
fixed points to be unstable. This result is particularly important for \( I \propto C_2 C_3 - C_1 r_2 C_4 = 0 \), i.e., there is no dominant feedback. Hence, if the condition \( C_1 > 4/\beta_e \) derived in (3), above, is satisfied, even an arbitrarily small delay can cause oscillations. An example of this is illustrated in Fig. 3.1.

(5) On the other hand, if \( H + I > 0 \), condition (ii) of Theorem 3.2, \( G - J > |J|/t_d \), gives the delay times for which the fixed point is stable:

\[
t_d = \frac{\left[ \kappa_e + \kappa_i - \alpha_2 \sigma_e(\bar{x}_e)C_1 - \sigma_i(\bar{x}_i)\alpha_2 C_4 \right]}{\left[ \sigma_e(\bar{x}_e)\sigma_i(\bar{x}_i)\alpha_e \alpha_i (C_2 C_3 - C_1 C_4) \right]}
\]

For \( t_d < \max(t_d^*) \), where \( \max \) is the maximum over all fixed points, every fixed point is guaranteed to be stable and no oscillations are possible. For \( r_e = r_i = 0 \), it is easy to see that for a wide range of parameters, stability is difficult to guarantee.

(6) The role of refractoriness in the excitatory neurons in inducing oscillations is indicated by the following argument. Let \( \sigma_e(x_e) = \sigma_i(x_i) = 1 \) [hence \( \sigma'_e(\bar{x}_e) = 0 \) and \( \sigma'_i(\bar{x}_i) = 0 \)], as we have seen, even large delays cannot destabilize the fixed point. Consider parameters such that when \( r_e = r_i = 0 \), \( f_e = 1 \). \( f_e \) decreases when \( r_e \neq 0 \). This follows straightforwardly from Eq. (3.1), \( f_e = \sigma_e(\bar{x}_e)/(1 + r_e \sigma_e(\bar{x}_e)) < 1 \). Now, with a smaller value of \( f_e \), \( \sigma_e(\bar{x}_e) \) can be less than 1 thereby increasing \( \sigma'_e(\bar{x}_e) \) to nonzero values, hence delay can induce oscillations.

(7) Oscillations can occur even if the delay \( t_d \) is zero and there is no dominant feedback, but the inhibitory decay time is greater than the excitatory

Fig. 3.2. Even with zero inhibitory time delay, \( t_d \), low-frequency oscillations can be induced when the activity decay time scales, \( T_e \) and \( T_i \), are disparate: \( T_e < T_i \). (a) The fraction of excitatory neurons firing per unit time \( f_e(t) \). (b) The fraction of inhibitory neurons firing per unit time \( f_i(t) \). (c) The phase portrait showing nonzero phase between the excitatory and inhibitory components. In this example, \( T_e = 0.1 \) and \( T_i = 0.25 \). The other parameters are the same as in Fig. 3.1.
decay time, $T_x > T_e$. From Eq. (3.3), when $t_d = 0$, it is easy to see that if $G + J < 0$, the characteristic equation has a positive real part and hence the fixed point is unstable. From Eqs. (3.4), since $J \sim 1/T_i$ and $G \sim (1/T_e)(1 + (T_e/T_i) - \sigma_i(x)c_i)$, the effect of small excitatory decay time $T_e$ and large inhibitory decay time $T_i$ is to decrease $G + J$, thereby causing the fixed point to be unstable. Figure 3.2 illustrates an example of oscillations when $t_d = 0$ but $T_e < T_i$.

From these results we note that there exist a wide range of parameters for which delay in the inhibitory signal or a slowly decaying inhibitory signal can destabilize the fixed point. In particular, it is not necessary that the coupling be feedback dominated. Arbitrarily small delays can cause instability of the fixed points and hence oscillations.

4. Method of Harmonic Balance

To study periodic solutions of Eqs. (2.5) and (2.6) we apply the method of harmonic balance, which reduces the problem of finding periodic solutions of differential equations to finding solutions of algebraic nonlinear equations. The method is closely related to the averaging technique.

The solution of Eqs. (2.5) and (2.6) is taken to be of the form $f = f + f_0 \sin(\omega t)$. Therefore, the input to the nonlinear sigmoid is of the form $x(t) = B + A \sin(\omega t + \theta)$ where $B$ is the bias, $A$ the amplitude, $\omega$ the frequency, and $\theta$ an appropriately determined phase. The main problem now is to obtain an approximate response of the nonlinear sigmoid. The crucial step here is to approximate the response of the nonlinear sigmoid by the Fourier transform of $\sigma(x)$,

$$\sigma(x) \sim BF_B(\sigma, A, B) + AF_A(\sigma, A, B) \sin(\omega t + \theta) + AF_A^+(\sigma, A, B) \cos(\omega t + \theta)$$

Using these approximations, the differential equations reduce to algebraic ones.

In the present problem, for the general form of the sigmoid, it is hard to evaluate the integrals above. However, the integrals can be easily evaluated by using the piecewise-linear saturation function (Fig. 4.1)

$$F_B(\sigma, A, B) = \frac{m x}{2B} \left[ g\left(\frac{\delta + B}{A}\right) - g\left(\frac{\delta - B}{A}\right) \right]$$

$$F_A(\sigma, A, B) = \frac{m}{2} \left[ f\left(\frac{\delta + B}{A}\right) + f\left(\frac{\delta - B}{A}\right) \right]$$

$$F_A^+(\sigma, A, B) = 0$$

where $\chi + \delta$ is the saturation point, and $m$ is the slope of the sigmoid with $\delta m = \frac{1}{2}$.

The integrals simplify further for the symmetric version of the sigmoid

$$\sigma_s(x) = mx \quad |x| < \delta$$

$$0.5 \quad x > \delta$$

$$-0.5 \quad x < -\delta$$

The gain functions $F_B, F_A$, and $F_A^+$ for inputs of the form $x(t) = B + A \sin(\omega t + \theta)$ to $\sigma_s$ can now be easily evaluated

$$F_B(B, A) = \frac{mA}{2B} \left[ g\left(\frac{\delta + B}{A}\right) - g\left(\frac{\delta - B}{A}\right) \right]$$

$$F_A(B, A) = \frac{m}{2} \left[ f\left(\frac{\delta + B}{A}\right) + f\left(\frac{\delta - B}{A}\right) \right]$$

$$F_A^+(B, A) = 0$$

Fig. 4.1. Piecewise-linear saturation nonlinearity, $\sigma(x)$. $\chi + \delta$ is the saturation point, $m$ is the linear gain with $\delta m = \frac{1}{2}$. 
where \( f \) and \( g \) are given by,

\[
g(x) = \frac{2}{\pi} \left( x \sin^{-1} x + \sqrt{1 - x^2} \right) \quad |x| \leq 1
\]

\[
= |x| \quad |x| > 1 \quad (4.6)
\]

\[
f(x) = -1 \quad x < -1
\]

\[
= \frac{2}{\pi} \left( \sin^{-1} x + x \sqrt{1 - x^2} \right) \quad |x| \leq 1
\]

\[
= 1 \quad x > 1 \quad (4.7)
\]

While in principle higher harmonics can be taken into account, the complexity of the problem has so far prevented us from tackling these. The existence of higher harmonics depends not only on the response of the nonlinear sigmoid but also the linear operator \((d/dt)^{-1} \sim 1/\omega\). Thus if the frequency is low, a pronounced generation of harmonics is possible. Figure 4.2 indicates a general case where the harmonics can be strong. We will discuss the generation of harmonics as particular cases are considered in Sec. 4. For example, when the input to the sigmoid is very large, numerical experiments and theory indicate that the third harmonic can have an amplitude of about \( 1/3 \) of the fundamental. In such cases, the approximation of taking the input to the nonlinear element as a bias plus sinusoid is incorrect.

In the next section, the method of harmonic balance discussed above is used to derive nonlinear algebraic equations governing periodic solutions of Eqs. (2.5) and (2.6).

5. Frequency-Amplitude-Phase Relations

In this section we derive the frequency-amplitude-phase relations between the excitatory and inhibitory components of the following equations using the method of harmonics discussed in Sec. 4. For simplicity, we temporarily ignore cellular refractory periods and set \( r_e = r_i = 0 \).

\[
T_e \ddot{f}_e(t) = -f_e(t) + \sigma_r[C_1 f_e(t) - C_2 f_i(t - t_d) + P]
\]

\[
T_i \ddot{f}_i(t) = -f_i(t) + \sigma_r[C_3 f_e(t) - C_4 f_i(t - t_d) + Q]
\]

Shifting the origin to the threshold \( \chi \), Eqs. (5.1) and (5.2) are modified to

\[
T_e \ddot{f}_e(t) = -f_e(t) + 0.5 + \sigma_r^2[C_1 f_e(t) - C_2 f_i(t - t_d) + P - \chi_e]
\]

\[
T_i \ddot{f}_i(t) = -f_i(t) + 0.5 + \sigma_r^2[C_3 f_e(t) - C_4 f_i(t - t_d) + Q - \chi_i]
\]

Neglecting the higher harmonics, solutions to these equations may be approximated by,

\[
f_e(t) = \bar{f}_e + f_{e0} \sin(\omega t)
\]

\[
f_i(t) = \bar{f}_i + f_{i0} \sin(\omega t - \theta_i)
\]

where \( \theta_i \) is the phase difference between \( f_e \) and \( f_i \), which has to be self-consistently determined from the solution. We assume \( \theta_i \) to be constant.

Inserting Eqs. (5.5) in (5.3) and (5.4) gives

\[
\omega T_e f_{e0} \cos(\omega t) = -\bar{f}_e - f_{e0} \sin(\omega t) + 0.5
\]

\[
+ \sigma_r^2 \{[C_1 \bar{f}_e - C_2 \bar{f}_i + P - \chi_e]
\]

\[
+ [C_1 f_{e0} \sin(\omega t)
\]

\[
- C_2 f_{i0} \sin(\omega t - \theta_i - \omega t_d)]\}
\]

\[
T_i f_{i0} \cos(\omega t - \theta_i) = -\bar{f}_i - f_{i0} \sin(\omega t - \theta_i) + 0.5
\]

\[
+ \sigma_r^2 \{[C_3 \bar{f}_e - C_4 \bar{f}_i + Q - \chi_i]
\]

\[
+ [C_3 f_{e0} \sin(\omega t)
\]

\[
- C_4 f_{i0} \sin(\omega t - \theta_i - \omega t_d)]\}
\]
\[ -C rf_{0} \sin(\omega t - \theta - \omega_{d}) \]\hspace{1cm} (5.6)

The input to the sigmoid \( \sigma^{*} \) can be cast into a more elegant form with a single sinusoidal component. Writing the argument of the excitatory sigmoid \( \sigma^{*} b \) as \( x = B e + A e \sin(\omega t + \theta_{ae}) \) the following can be inferred:

\[ B e = C_{1} \bar{f} e - C_{2} \bar{f} f + P - \chi_{e} \]
\[ A e^{2} = C_{1}^{2} f_{e0}^{2} + C_{2}^{2} f_{f0}^{2} \]
\[ -2C_{1}C_{2} e f_{e0} f_{f0} \cos(\theta + \omega_{d}) \]
\[ A e \sin(\theta_{ae}) = C_{2} f_{e0} \sin(\theta_{f} + \omega_{d}) \]
\[ A e \cos(\theta_{ae}) = C_{1} f_{e0} - C_{2} f_{f0} \cos(\theta_{f} + \omega_{d}) \]
\[ \tan(\theta_{ae}) = \frac{\sin(\theta_{f} + \omega_{d})}{\cos(\theta_{f} + \omega_{d})} \] (5.7)

Similarly, writing the argument of \( \sigma^{*} f \) as \( x = B i + A i \sin(\omega t + \theta_{ai}) \),

\[ B i = C_{3} \bar{f} e - C_{4} \bar{f} f + Q - \chi_{i} \]
\[ A i^{2} = C_{3}^{2} f_{e0}^{2} + C_{4}^{2} f_{f0}^{2} \]
\[ -2C_{3}C_{4} e f_{e0} f_{f0} \cos(\theta_{i} + \omega_{d}) \]
\[ A i \sin(\theta_{ai}) = C_{4} f_{e0} \sin(\theta_{f} + \omega_{d}) \]
\[ A i \cos(\theta_{ai}) = C_{3} f_{e0} - C_{4} f_{f0} \cos(\theta_{f} + \omega_{d}) \]
\[ A i \sin(\theta_{ai} + \theta_{f}) = C_{3} f_{e0} \sin(\theta_{f}) + C_{4} f_{f0} \sin(\omega_{d}) \]
\[ A i \cos(\theta_{ai} + \theta_{f}) = C_{3} f_{e0} \cos(\theta_{f}) - C_{4} f_{f0} \cos(\omega_{d}) \]
\[ \tan(\theta_{ai}) = \frac{\sin(\theta_{f} + \omega_{d})}{\cos(\theta_{f} + \omega_{d})} \] (5.8)

Equations (5.6) can now be written as

\[ \omega T_{i} f_{0} \cos(\omega t + \theta_{e}) = -\bar{f} e \sin(\omega t + \theta_{e}) + 0.5 \]
\[ + \sigma^{*}[B e + A e \sin(\omega t + \theta_{ae})] \]
\[ \omega T_{i} f_{0} \cos(\omega t - \theta_{i}) = -\bar{f} i - f_{i0} \sin(\omega t - \theta_{i}) + 0.5 \]
\[ + \sigma^{*}[B i + A i \sin(\omega t + \theta_{ai})] \] (5.9)

Using the nonlinear gain functions described in Sec. 4, the nonlinear terms in the above equations can be written as

\[ \sigma^{*}(x_e) = B e F_{Be} + A e F_{Ac} \sin(\omega t + \theta_{ae}) \]
\[ \sigma^{*}(x_i) = B i F_{Bi} + A i F_{Ai} \sin(\omega t + \theta_{ai}) \] (5.11)

where the functions \( F_{B}(B, A) \) and \( F_{A}(B, A) \) are as in Eqs. (4.3) and (4.4). Substituting Eqs. (5.11) in (5.9) and (5.10) and equating the bias and coefficients of \( \cos \) and \( \sin \) to zero, we get

\[ \bar{f} e = 0.5 + B e F_{Be} \]
\[ \omega T_{i} f_{e0} = A e F_{Ac} \sin(\theta_{ae}) \]
\[ f_{e0} = A e F_{Ac} \cos(\theta_{ae}) \]
\[ \bar{f} i = 0.5 + B i F_{Bi} \]
\[ \omega T_{i} f_{i0} = A i F_{Ai} \sin(\theta_{ai} + \theta_{f}) \]
\[ f_{i0} = A i F_{Ai} \cos(\theta_{ai} + \theta_{f}) \] (5.12)

(5.13)

(5.14)

(5.15)

(5.16)

(5.17)

The nonlinear differential equations, Eqs. (5.3) and (5.4), have thus been reduced to algebraic equations, Eqs. (5.12)–(5.17). In what follows we attempt to gain some insight into the nonlinear oscillations by studying these equations. Modification of these equations to take into account refractoriness in the excitatory neurons is deferred to the latter part of Sec. 7.

6. Linear Theory

We first seek the solution to small-amplitude oscillations. These oscillations are unstable to small perturbations and almost never exist in real systems; however their study could shed light on the behavior of the nonlinear system. To solve Eqs. (5.12)–(5.17) for the frequency, phase, and ratio of excitatory and inhibitory neurons firing in the linear region, we first approximate the gain functions \( F_B \) and \( F_A \), noting that \((s + B)/A \gg 1\). These approximations hold when \( \delta \) is large and the amplitude and bias components of the input into the sigmoid are small. From Eqs. (4.3)–(4.7), it follows that \( F_B \sim m \) and \( F_A \sim m \) where
\( m = 0.5/\delta \) is the slope of the sigmoid. This result would also follow from straightforward linearization. Equations (5.12)–(5.17) can now be written as

\[
\begin{align*}
\tilde{f}_c &= 0.5 + B_c m_c \\
\omega T_c f_{c0} &= A_c m_c \sin(\theta_{ae}) \\
f_{c0} &= A_c m_c \cos(\theta_{ae}) \\
\tilde{f}_i &= 0.5 + B_i m_i \\
\omega T_i f_{i0} &= A_i m_i \sin(\theta_{ai} + \theta_i) \\
f_{i0} &= A_i m_i \cos(\theta_{ai} + \theta_i).
\end{align*}
\] (6.1)

Substituting for \( A_c \cos(\theta_{ae}), A_c \sin(\theta_{ae}), A_i \cos(\theta_{ae} + \theta_i), A_i \sin(\theta_{ae} + \theta_i) \) from Eqs. (5.7) and (5.8),

\[
\omega T_c f_{c0} = m_c C_2 f_{i0} \sin(\theta_i + \omega t_d) \\
(6.2)
\]

\[
f_{c0} = m_c [C_1 f_{c0} - C_2 f_{i0} \cos(\theta_i + \omega t_d)] \\
(6.3)
\]

\[
\omega T_i f_{i0} = m_i [C_3 f_{c0} \sin(\theta_i) - C_4 f_{i0} \sin(\omega t_d)] \\
(6.4)
\]

\[
f_{i0} = m_i [C_3 f_{c0} \cos(\theta_i) + C_4 f_{i0} \cos(\omega t_d)]. \\
(6.5)
\]

Eliminating \( \theta_i + \omega t_d \) from Eqs. (6.2) and (6.3) and \( \theta_i \) from Eqs. (6.4) and (6.5).

\[
\frac{f_{c0}^2}{f_{i0}^2} = \frac{m_c^2 C_2^2}{T_c^2 \omega^2 + (m_c C_1 - 1)^2} \\
(6.6)
\]

\[
\frac{f_{c0}^2}{f_{i0}^2} m_i^2 C_3^2 = [T_i \omega - m_i C_4 \sin(\omega t_d)]^2 + [m_i C_4 \cos(\omega t_d) + 1]^2. \\
(6.7)
\]

From these equations, the following relation for \( \omega \) may be obtained

\[
[T_i \omega - m_i C_4 \sin(\omega t_d)]^2 + [m_i C_4 \cos(\omega t_d) + 1]^2 = \frac{m_c^2 m_i^2 C_3^2 C_5}{T_c^2 \omega^2 + (m_c C_1 - 1)^2}. \\
(6.8)
\]

Some simple results may be obtained when \( t_d = 0 \). In this limit, the frequency can be solved for

\[
\omega = -\sqrt{(\alpha^2 + \beta^2) + \sqrt{\omega_0^4 + (\alpha^2 + \beta^2)^2}}. \\
(6.9)
\]

\[
T_c \omega_0 = m_c m_i C_2 C_3 \\
(6.9)
\]

\[
T_i \alpha = \frac{1}{\sqrt{2}} (m_c C_1 - 1) \\
(6.9)
\]

\[
T_i \beta = \frac{1}{\sqrt{2}} (m_c C_4 + 1). \\
(6.9)
\]

The phase difference between the excitatory and inhibitory components is found to be \( \tan(\theta_i) = \omega T_i/(m_c C_4 + 1) \). If feedback dominates, \( C_2 C_3 \gg C_1 C_4 \), then

\[
\omega \sim \omega_0 = \sqrt{\frac{m_c m_i C_2 C_3}{T_i T_c}}. \\
\]

The phase difference is

\[
\tan \theta_i = \frac{T_i}{T_c} \sqrt{m_c m_i C_2 C_3} \sim \frac{\pi}{2}. \\
\]

In numerical solution of the differential equations, we tested the theoretical frequency and phase results. It was found that the linear theory predicted much larger frequencies than the correct values. The phase difference between the components was also in disagreement. This leads us to conclude the linear theory is inaccurate and inadequate to study oscillations in the feedback system with delay. Furthermore, as the stability analysis of Sec. 3 has shown, linear oscillations can be unstable to even small time delays in the feedback.

7. Nonlinear Theory

As noted above, linear oscillations are guaranteed only in the low-gain limit and are unstable not only to perturbations but also to delay in feedback. Nonlinear saturation mechanisms then limit the response of the subpopulations. In addition, refractoriness of the neurons limits the number of neurons firing per unit time. Next, we study nonlinear oscillations using the method of harmonic balance discussed in Secs. 4 and 5. The following equations were derived in Sec. 5 [Eqs. (5.12)–(5.17)] neglecting the refractoriness in both excitatory and inhibitory neurons (consideration of the effect of refractoriness in the excitatory neurons is deferred to the latter part of this section, see Case 3).
\[ f_e = 0.5 + B_e F_{Be} \quad (7.1) \]
\[ \omega T_{e,f_{Be}} = A_e F_{Ae} \sin(\theta_{ae}) \quad (7.2) \]
\[ f_{i0} = A_i F_{Ai} \cos(\theta_{ae}) \quad (7.3) \]
\[ \tilde{f}_i = 0.5 + B_i F_{Bi} \quad (7.4) \]
\[ \omega T_{i,f_{Bi}} = A_i F_{Ai} \sin(\theta_{ai} + \theta_i) \quad (7.5) \]
\[ f_{i0} = A_i F_{Ai} \cos(\theta_{ai} + \theta_i) \quad (7.6) \]

Some general observations may be made without explicitly solving the equations above.

(1) If \(|(\delta + B)/A| > 1\) and \(|(\delta - B)/A| > 1\) and these terms have opposite sign, \(F_A = 0\) from Eqs. (4.4) and (4.7). No oscillations occur when \(F_A = 0\). This implies that nonlinear oscillations, if they exist, must be a strong sinusoidal component (compared to the bias) to the input activity.

(2) The phase shift \(\theta_0 = \phi + \omega_d t_d\), between the excitatory and inhibitory signals is critical for the oscillations. It has two components: \(\phi\), originating from the feedback coupling and \(\omega_d t_d\) from the time delay in feedback. The response from the nonlinear sigmoid is proportional to \(A_e \sin(\phi) F_{Ae} = \frac{F_{Ae}}{2} C_{21} f_{i0} \sin(\theta_i)\).

Since \(F_{Ai}\) is bounded by \(m_i\), the slope of the sigmoid, the response is exactly zero when \(\theta_0 = 0\). When \(C_{21} C_{2} = -C_{21} C_{2}\), the phase difference \(\phi\) can be zero (this statement will be proved below) in which case it is necessary that the time delay is not equal to zero. When \(\phi \approx \pi/2\), \(A^2 = C_{1}^2 f_{i0}^2 + C_{2}^2 f_{i0}^2 - 2C_{1} C_{2} f_{i0} \sin(\theta_i) \approx (C_{1}^2 f_{i0}^2 + C_{2}^2 f_{i0})\), hence the sinusoidal component of the input to the nonlinear sigmoid could be large, in which case the corresponding nonlinear response is nonzero.

(3) Inter- and intrasubpopulation asymmetries (for example, \(C_{1} C_{2} = -C_{2} C_{1}\), or \(P - X_i \neq Q - X_i\)) can also result in nonzero phase differences between the excitatory and inhibitory signals. However, the results of Wilson and Cowan (see Sec. 2) show that rather stringent conditions are required on the asymmetry in feedback coupling to cause adequate phase shifts to induce oscillations in the present model.

(4) When the input \(P\) is large, no oscillations occur in the excitatory component because the effective gain from the nonlinear sigmoid for the oscillating component, \(F_{Ae}\), is zero: for example consider \(P\) such that \((\delta - B)/A > 1\) and \((\delta + B)/A > 1\), i.e., the bias is very large, where \(A_{e\text{max}}\) is \(C_{1} + C_{2}\), in which case \(F_{Ae} = 0\). Therefore there exists a \(P = P_{e\text{max}}\) such that for \(P > P_{e\text{max}}\) no oscillations occur. A similar result holds for the inhibitory component.

(5) If the excitatory subpopulation receives subthreshold excitation, i.e., \(P\) is small compared to the threshold, \(X_i\), no oscillations occur. The reason is essentially the same as the one above: the input to the sigmoid has a large bias component compared to the maximum possible oscillating component, thereby reducing the nonlinear gain for the sigmoidal component, \(F_A\), to zero. Thus, the oscillations are input driven underscoring the strongly dissipative nature of the interaction in the absence of external drive.

(6) It is possible for oscillations in the inhibitory component to occur in the absence of oscillations in the excitatory component. This typically occurs when \(P\) is large so that \(F_{Ae} = 0\), as discussed above, but the external input \(Q\) to the inhibitory neurons is close to the threshold and hence \(F_{Ai} \neq 0\).

(7) The frequency of oscillation depends on the connectivities \(C_{1}, C_{2}, C_{3}, C_{4}\) as well as the time scales \(t_d, T_e, T_i\) and the inputs \(P, Q\).

It is extremely difficult to solve Eqs. (7.1)–(7.6) exactly. However, in the large-amplitude limit, \(B/A < 1\), the equations may be simplified as follows.
The nonlinear gain is

\[ F_{d}(B, A) = \frac{mA}{2B} \left[ g\left(\frac{\delta + B}{A}\right) - g\left(\frac{\delta - B}{A}\right) \right] \]

\[ F_{A}(B, A) = \frac{m}{2} \left[ f\left(\frac{\delta + B}{A}\right) + f\left(\frac{\delta - B}{A}\right) \right]. \quad (7.7) \]

Let \(|(\delta + B)/A| < 1\) and \(|(\delta - B)/A| < 1\), then substituting for \(g\) and \(f\) from Eqs. (4.5) and (4.7),

\[ F_{d}(B, A) = \frac{mA}{B\pi} \left[ \frac{\delta + B}{A} \sin^{-1}\left(\frac{\delta + B}{A}\right) \right. \]

\[ + \sqrt{1 - \left(\frac{\delta + B}{A}\right)^2} \]

\[ + \left. \frac{\delta - B}{A} \sin^{-1}\left(\frac{\delta - B}{A}\right) \right] \]

\[ + \sqrt{1 - \left(\frac{\delta - B}{A}\right)^2} \]

\[ F_{A}(B, A) = \frac{m}{2} \left( \sin^{-1}\left(\frac{\delta + B}{A}\right) \right) \]

\[ + \frac{\delta + B}{A} \sqrt{1 - \left(\frac{\delta + B}{A}\right)^2} \]

\[ + \frac{\delta - B}{A} \sqrt{1 - \left(\frac{\delta - B}{A}\right)^2} \]
Approximating \( \sin^{-1}(x) \sim x \) and \( \sqrt{1 - x^2} \sim (1 - x^2/2) \) above,

\[
F_B(B, A) = \frac{2}{\pi A} \quad \text{(7.9)}
\]

\[
F_A(B, A) = \frac{2}{\pi A} - \frac{\delta(\delta^2 - 3B^2)}{2\pi A^3} \quad \text{(7.10)}
\]

In making this approximation we are faced with a dilemma: without this approximation Eqs. (7.1)–(7.6) are very difficult to solve analytically; on the other hand, when the approximation is strictly valid the harmonic feedback is strong and therefore the bias plus sinusoidal input to the nonlinear sigmoid is incorrect. The neglect of harmonics is valid only for the moderately strong inputs into the nonlinear sigmoid, typically \( A + |B| \leq 10\delta \), i.e., the maximum input into the sigmoid is within an order of magnitude of \( \delta \). Also, for \( (\delta + B)/A > 0.6 \), the approximations \( \sin^{-1}(x) \sim x \) and \( \sqrt{1 - x^2} \sim (1 - x^2/2) \) are incorrect. Within the regime suggested above, the approximations used do give correct results.

Neglecting the \( O(1/A^3) \) term in \( F_A \), Eqs. (7.1)–(7.6) can be written as,

\[
\bar{f}_e = 0.5 + B_e \frac{2}{\pi A_e} \quad \text{(7.11)}
\]

\[
\omega T_{ef0} = \frac{2}{\pi} \sin(\theta_{ae}) \quad \text{(7.12)}
\]

\[
f_{e0} = \frac{2}{\pi} \cos(\theta_{ae}) \quad \text{(7.13)}
\]

\[
\bar{f}_i = 0.5 + B_i \frac{2}{\pi A_i} \quad \text{(7.14)}
\]

\[
\omega T_{ifi0} = \frac{2}{\pi} \sin(\theta_{ai} + \theta_i) \quad \text{(7.15)}
\]

\[
f_{i0} = \frac{2}{\pi} \cos(\theta_{ai} + \theta_i) \quad \text{(7.16)}
\]

From the Eqs. (7.11)–(7.16), the following may be easily shown,

\[
T_e \omega = \tan(\theta_{ae})
\]

\[
T_i \omega = \tan(\theta_{ai} + \theta_i)
\]

where, from Eqs. (5.7) and (5.8),

\[
\tan(\theta_{ae}) = \frac{\sin(\theta_i + \omega t_d)}{C_1 f_{e0} - \cos(\theta_i + \omega t_d)}
\]

\[
\tan(\theta_{ai}) = \frac{\sin(\theta_i + \omega t_d)}{C_4 f_{i0} - \cos(\theta_i + \omega t_d)}
\]

We consider here oscillations with \( P \sim \chi_e \) and \( Q \sim \chi_i \). The bias \( B \) then depends on the mismatch of the excitatory and inhibitory decay time and not the actual value of the external input. Below, some of the characteristics of the oscillations for a few different cases are discussed. Except as noted, all the numerical values quoted are for the following default parameters:

\( C_1 = C_2 = C_3 = C_4 = 5.0 \), \( t_d = 0.1 \), \( T_e = T_i = 0.1 \), \( m_e = m_i = 0.5 \), \( P = Q = 4.0 \), \( \chi_e = \chi_i = 4.0 \), \( r_e = r_i = 0.0 \). In Case 3 below, \( r_e \neq 0.0 \).

**Note on Method:** The differential equations were solved by fourth-order Runge–Kutta method with step size 0.005. The numerical values of the theoretical results quoted were obtained by solving the simplified frequency–amplitude–phase relations using the Newton–Raphson method for finding the roots of nonlinear algebraic equations.

**Case I**

Let \( C_1 C_4 = C_2 C_3 \), so that there is no dominant feedback, and let there be similar excitatory and inhibitory decay time scales, \( T_e = T_i = T \). The following results may be shown:

1. The phase difference \( \theta \) between the excitatory and inhibitory components is equal to zero. From Eqs. (7.18), when \( C_2 C_3 = C_1 C_4 \), \( \tan(\theta_{ae}) = \tan(\theta_{ai}) \), and from Eqs. (7.17) if \( T_e = T_i \), \( \tan(\theta_{ae}) = \tan(\theta_{ai} + \theta_i) \). It follows that \( \theta_e = 0 \).

Figures 7.1 and 7.2 illustrate examples of phase-locked oscillations. Note that the zero phase difference is due to the symmetry. In this case, oscillations exist only because of the ‘hidden phase shift,’ \( \omega t_d \), caused by the delay in the inhibitory feedback.
(2) The excitatory and inhibitory components have the same amplitude, i.e., \( f_{e0} / f_{i0} = 1 \). From Eqs. (7.12) and (7.13) eliminating \( \theta_{e0} \), and from Eqs. (7.15) and (7.16) eliminating \( \theta_{i0} + \theta_i \),

\[
f_{e0}^3 (1 + T_0^2 w^2) = \frac{4}{\pi^2} \tag{7.19}
\]

\[
f_{i0}^3 (1 + T_i^2 w^2) = \frac{4}{\pi^2} \tag{7.20}
\]

The two relations above give \( f_{e0} / f_{i0} = 1 \). The amplitudes, \( f_{e0} \) and \( f_{i0} \), decreases with increasing oscillation frequency.

(3) With the above results, Eq. (7.17) may be solved for the frequency of oscillation,

\[
T \omega = \frac{\sin(\omega t_d)}{C_1 / C_2 - \cos(\omega t_d)} \tag{7.21}
\]

For \( C_1 = C_2 \) this is simply \( T \omega = \cot((\omega t_d)/2) \). If this relation is cast in the form \( (2T/t_d)\psi = \cot(\psi) \), where \( \psi = \omega t_d \), it is easy to see that for fixed \( T \) the frequency is a monotonic decreasing function of the delay \( t_d \).

Table 7.1 compares the numerical and theoretical results for the variation of frequency with the inhibitory signal delay. The results are close, particularly for lower frequency. The time period of the oscillation is different from any time scale in the problem. As noted in Sec. 4, the harmonics become important when (1) the input to the nonlinear sigmoid is large and/or (2) the frequency is small. Figure 7.1(a) indicates that the harmonics are small when the frequency is large and the input to the sigmoid is small. Figure 7.1(c) shows that even when the input to the sigmoid is small, harmonics can be generated because the nonlinear gain drops as only \( 1/\omega \). The theory and approximations used, however, do not capture the functional dependence of the frequency on \( C \). This is partly

Fig. 7.1. Oscillations with zero phase difference between the excitatory and inhibitory components can occur under certain symmetry constraints: \( C_1 C_2 = C_3 C_4 \), \( T_e = T_i \), and \( P = \chi_e \), and \( Q = \chi_i \). Such zero phase difference oscillations cannot arise in the absence of delayed feedback. (a) Fraction of excitatory neurons firing per unit time, \( f_e(t) \). (b) Fraction of inhibitory neurons firing per unit time, \( f_i(t) \). (c) Phase portrait of the \( f_e \) and \( f_i \) shows zero phase difference. (d) The frequency spectrum showing a weak third harmonic. The frequency of oscillation is \( \omega = 11.50 \).
Table 7.1. The frequency of oscillation, \( \omega \), monotonically decreases with increasing inhibitory feedback delay \( t_d \) (comparison of theoretical and numerical results).

<table>
<thead>
<tr>
<th>( t_d )</th>
<th>( \omega ) (num.)</th>
<th>( \omega ) (theory)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.05</td>
<td>17.49</td>
<td>19.2</td>
</tr>
<tr>
<td>0.1</td>
<td>11.35</td>
<td>13.06</td>
</tr>
<tr>
<td>0.2</td>
<td>7.67</td>
<td>8.60</td>
</tr>
<tr>
<td>0.3</td>
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<td>1.84</td>
<td>1.85</td>
</tr>
<tr>
<td>2.0</td>
<td>1.38</td>
<td>1.38</td>
</tr>
<tr>
<td>3.0</td>
<td>0.92</td>
<td>0.98</td>
</tr>
</tbody>
</table>

because at larger values of \( C \), the harmonic feedback becomes strong and this variation is not accounted for. The frequency decreases as the mean synaptic strength \( C \) is increased (Table 7.2). For lower frequencies, there is much less variation of frequency with \( C \), presumably because harmonics are present even with small values (of \( C \)). For small \( C \), the approximations \( \sin^{-1} x \sim x \) and \( \sqrt{1 - x^2} \sim 1 \) are no longer valid, and the frequency must be obtained by a detailed numerical solution of the transcendental equations. The frequencies obtained in that case approach the numerical results even more closely and is found to increase as \( C \) decreases. The details of the calculations are

Table 7.2. The frequency of oscillation decreases as the mean synaptic strength \( C \) is increased (numerical results), and its variation is much less when the frequency is small.

<table>
<thead>
<tr>
<th>( C )</th>
<th>( \omega ) (num.) ( t_d = 0.1 )</th>
<th>( \omega ) (num.) ( t_d = 0.5 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>11.35</td>
<td>4.29</td>
</tr>
<tr>
<td>10</td>
<td>9.66</td>
<td>4.14</td>
</tr>
<tr>
<td>20</td>
<td>8.13</td>
<td>3.83</td>
</tr>
<tr>
<td>200</td>
<td>5.21</td>
<td>3.07</td>
</tr>
</tbody>
</table>

Fig. 7.2. When the inhibitory delay is increased, the amplitude and frequency of the oscillations can change significantly. The number of neurons firing per unit time increases and the frequency decreases (compare with Fig. 7.1). (a) Fraction of excitatory neurons firing per unit time, \( f_e(t) \). (b) Fraction of inhibitory neurons firing per unit time, \( f_i(t) \). (c) The phase portrait once again indicates zero phase difference between the excitatory and inhibitory components. (d) The frequency spectrum showing the presence of moderately strong odd harmonics because the frequency of the oscillation is smaller (\( \omega = 4.30 \)). The inhibitory delay is \( t_d = 0.5 \).
tedious, offer no particular insight, and therefore are not presented here.

(4) As shown above, when \( C = C_1 = C_2 = C_3 = C_4 \) and \( T_s = T_r \), \( f_{r0} \) is equal to \( f_{r} \); therefore if \( P = Q = \chi \), the biases \( B_e \) and \( B_i \) are zero. In Appendix A.3 it is shown that the even harmonic feedback is proportional to the bias. Hence the even harmonics are negligible. As the mean connection strength \( C \) is increased, it is the odd harmonics that are important. In particular, the third harmonic can have an amplitude of \( \frac{1}{3} \) of the fundamental [Eqs. (A.8)]. However if, for example, \( P \) is increased beyond the threshold \( \chi \), the bias \( B_e \) will in general be nonzero and the even harmonics, in particular the second harmonic, would be present.

(5) To study how the frequency varies with \( C_1/C_2 = C_3/C_4 \), a general result concerning the frequency of oscillation is proved next (we assume oscillations exist).

**Theorem 7.1.** For \( x > 0 \), frequency of oscillation given by \( T_\omega = \sin(\omega t_d)/(x - \cos(\omega t_d)) \) monotonically decreases as \( x \) increases.

**Proof.** The expression for frequency is first cast into the form:

\[
x(\psi) = \gamma \frac{\sin(\psi)}{\psi} + \cos(\psi)
\]

(7.22)

where \( \gamma = t_d/T \) and \( \psi = \omega t_d \). Let \( \psi_0 \) be the root of the equation above. It is easy to see that \( \psi_0 \) satisfies \( \pi/2 < \psi_0 < \pi \). Now we show that for \( 0 < \psi < \psi_0 \), \( x(\psi) \) is a monotonically decreasing function. The turning point of \( x(\psi) \) occurs when \( x'(\psi) = 0 \). Let this value be \( \psi_1 \). Then, \( \tan(\psi_1) = \gamma \psi_1/(\gamma + \psi_1^2) \). At \( \psi_1 = 0 \), \( x(\psi) \) is its maximum value. This implies that at \( \psi_1 = 0 \), \( x(\psi) \) is a decreasing function. The next turning point occurs at \( \psi_1 \) such that \( \pi < \psi_1 < 2\pi \), which means that \( \psi_1 > \psi_0 \). Hence \( x(\psi) \) is a monotonically decreasing function for \( 0 < \psi < \psi_0 \). This completes the proof.

From this result it follows that as \( C_1/C_2 \) decreases, (maintaining \( C_3/C_4 = C_1/C_4 \) the frequency of oscillation increases. Table 7.3 compares the theoretically derived frequency with numerical results for \( C_1/C_2 = C_3/C_4 = \frac{1}{3} \) and \( C_1/C_2 = C_3/C_4 = 2.5/6 \) as a function of the delay \( t_d \). Comparing Tables 7.1 and 7.3 we find that the frequency of oscillation increases with decreasing \( C_1/C_2 \). When \( C_1/C_2 \neq 1 \), the mismatch between excitatory and inhibitory activity generates a bias, hence the oscillations contain odd as well as even harmonics.

<table>
<thead>
<tr>
<th>( C_1 )</th>
<th>( C_2 )</th>
<th>( t_d )</th>
<th>( \omega ) (num.)</th>
<th>( \omega ) (theory)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>6</td>
<td>0.05</td>
<td>18.87</td>
<td>22.47</td>
</tr>
<tr>
<td>2.5</td>
<td>5</td>
<td>0.1</td>
<td>12.27</td>
<td>14.39</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.2</td>
<td>8.13</td>
<td>9.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.0</td>
<td>2.61</td>
<td>2.66</td>
</tr>
</tbody>
</table>

**Case 2**

Consider next the case of disparate decay time scales, \( T_s > T_r \), again with \( C_3/C_4 = C_1/C_4 \). The phase difference, \( \theta_i \), between the excitatory and inhibitory components is no longer zero, and \( f_e \neq f_i \) as shown below:

1. From \( T_{e0} = \omega(T_{e0}) \) and \( T_{i0} = \omega(T_{i0} + \theta_i) \), of Eq. (7.17) we now have,

\[
\tan(\theta_i) = \frac{\omega(T_{i0} + \theta_i)}{1 + T_{e0}T_{i0}w^2}.
\]

Thus the phase difference is no longer zero (see Fig. 7.3) but is dependent on the mismatch between the excitatory and inhibitory decay time scales as well as the other parameters through the frequency \( \omega \). We noted earlier the importance of the phase shift for oscillations to occur. From the expression for the phase difference, it is therefore possible that when \( T_i > T_r \), oscillations may occur even when there is no time delay. In Sec. 3, we observed that such oscillations do occur (see Fig. 2).

2. Proceeding as before, from Eqs. (7.11)–(7.16), the ratio of the amplitude of the oscillating components may be obtained,

\[
\frac{f_{e0}}{f_{i0}} = \sqrt{1 + T_{e0}^2w^2}.
\]

The amplitude of the excitatory component is thus greater than that of the inhibitory component (Fig. 7.3).

3. With the two results above, we can solve for the frequency,

\[
T_{e0} = \sin\left(\tan^{-1}\left(\frac{\omega(T_{e0} - T_{i0})}{1 + T_{e0}T_{i0}w^2} + \omega t_d\right)\right)
\]


Fig. 7.3. Oscillations with disparate decay time scales $T_r = 0.1$ and $T_i = 0.2$. (a) The fraction of excitatory neurons firing per unit time $f_x(t)$ and (b) the fraction of inhibitory neurons firing per unit time $f_i(t)$ indicate that the amplitude of the inhibitory component is smaller than the excitatory component as predicted theoretically. (c) The phase difference between the two components is no longer zero, the phase difference is about 18°. (d) The frequency spectrum shows the presence of odd harmonics, the third harmonic in particular is moderately strong. The frequency of oscillation is 5.37. The inhibitory delay is $t_d = 0.2$.

\[
\times \left[ \frac{C_1}{C_2} \sqrt{\frac{1 + T_i^2 \omega^2}{1 + T_e^2 \omega^2}} \right. \\
\left. - \cos \left( \tan^{-1} \left( \frac{\omega(T_i - T_e)}{1 + T_e T_i \omega^2} \right) + \omega t_d \right) \right].
\]

(7.24)

Although complicated, this expression for the frequency is a function of only one unknown and can be solved using Newton's method. Table 7.4 compares the numerical and theoretical frequencies for increasing inhibitory decay time $T_i$ as a function of the delay $t_d$. We note (1) the frequencies decrease progressively as the $T_i$ increases and the decay time scales become disparate, (2) the frequency decreases monotonically with the delay, and (3) the frequencies are quite different from any one of the time scales in the system.

<table>
<thead>
<tr>
<th>$T_i$</th>
<th>$t_d$</th>
<th>$\omega$ (num.)</th>
<th>$\omega$ (theory)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2</td>
<td>0.05</td>
<td>7.67</td>
<td>8.72</td>
</tr>
<tr>
<td></td>
<td>0.1</td>
<td>6.60</td>
<td>8.34</td>
</tr>
<tr>
<td></td>
<td>0.2</td>
<td>5.37</td>
<td>6.67</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>3.53</td>
<td>4.01</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>2.30</td>
<td>2.43</td>
</tr>
<tr>
<td>0.5</td>
<td>0.05</td>
<td>3.53</td>
<td>4.70</td>
</tr>
<tr>
<td></td>
<td>0.1</td>
<td>3.22</td>
<td>4.74</td>
</tr>
<tr>
<td></td>
<td>0.2</td>
<td>2.91</td>
<td>4.41</td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>2.30</td>
<td>3.14</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>1.68</td>
<td>2.05</td>
</tr>
</tbody>
</table>
(4) Since \( f_{e0} \neq f_{i0} \), the bias is different from zero and in this case there are even as well as odd harmonics in the oscillation. When \( T_i \gg T_e \), the frequency is small and, as discussed in Sec. 4, harmonic generation can be strong. In this case the bias plus sinusoid approximation is incorrect.

Case 3

The effect of refractoriness in the excitatory neurons on the oscillations is explored next. The refractoriness of the inhibitory interneurons is neglected. Once again we will consider subpopulations with \( C_2C_3 = C_1C_4 \). In Appendix A.4, the method of harmonics is used to obtain the following equations governing the periodic solutions in a manner analogous to the derivation in Sec. 5:

\[
\bar{f}_e = 0.5(1 - \bar{f}_e r_e) + \frac{2B_e}{\pi A_e} (1 - \bar{f}_e r_e) \tag{7.25}
\]

\[
\omega T_e f_{e0} = \frac{2}{\pi} (1 - \bar{f}_e r_e) \sin(\theta_{ae}) \tag{7.26}
\]

\[
f_{e0} = \frac{2}{\pi} (1 - \bar{f}_e r_e) \cos(\theta_{ae}) \tag{7.27}
\]

\[
\bar{f}_i = 0.5 + \frac{2B_e}{\pi A_e} \tag{7.28}
\]

\[
\omega T_i f_{i0} = \frac{2}{\pi} \sin(\theta_{ai} + \theta_i) \tag{7.29}
\]

\[
f_{i0} = \frac{2}{\pi} \cos(\theta_{ai} + \theta_i) \tag{7.30}
\]

These equations are valid if the harmonics, in particular the second and third, are weak. For \( T_i \gg T_e \), this condition is not satisfied as discussed above. Furthermore, in order to concentrate on the critical effects of refractoriness in the excitatory neurons, the discussion here is restricted to the case of identical decay time scales, \( T_e = T_i \). We may now show

(1) The phase difference between the excitatory and inhibitory components is zero; this follows from \( \tan(\theta_{ae}) = \tan(\theta_{ai}) \), and \( \tan(\theta_{ae}) = \tan(\theta_{ai} + \theta_i) \) as shown in Case 1.

(2) The amplitude of the excitatory neurons' firing per unit time is less than the amplitude of the inhibitory neurons' firing per unit time. When \( T_e = T_i = T \), from Eqs. (7.26) and (7.27),

\[
f_{e0} = 2/(\pi \sqrt{1 + \omega^2 T^2}) (1 - r_e \bar{f}_e)
\]

and from Eqs. (7.29) and (7.30),

\[
f_{i0} = 2/(\pi \sqrt{1 + \omega^2 T^2}).
\]

Hence \( f_{e0}/f_{i0} = 1 - r_e \bar{f}_e \). Therefore \( f_{e0}/f_{i0} < 1 \).

(3) The effect of refractoriness is to increase the frequency of oscillation. This result follows from the decreases of \( f_{e0}/f_{i0} \) and Theorem 7.1, since the frequency is given by the same expression as in Case 1,

\[
T \omega = \frac{\sin(\omega t_d)}{C_1 f_{e0} - \cos(\omega t_d)} \tag{7.25}
\]

(4) The amplitudes \( f_{e0}, f_{i0} \), both decrease as a result of refractoriness. This follows straightforwardly from the expressions for \( f_{e0} \) and \( f_{i0} \) derived in (2) and the increase in the frequency \( \omega \) as shown in (3) above.

(5) If we assume that \( \bar{f}_e \sim f_{e0} \), then approximate expressions for the amplitudes and frequency of the oscillation may be derived. With \( \bar{f}_e \sim f_{e0} \), \( f_{e0} \) in (2) can be solved for,

\[
f_{e0} \sim \frac{2}{\pi} \frac{1}{2 r_e \pi + \sqrt{1 + \omega^2 T^2}}.
\]

Therefore,

\[
\frac{f_{e0}}{f_{i0}} \sim \frac{1}{1 + \frac{2r_e}{\pi \sqrt{1 + \omega^2 T^2}}} \tag{7.31}
\]

It can now be shown that the frequency of oscillation is a nondecreasing function of \( r_e \). A proof of this statement follows: consider the frequency of oscillation

\[
T \omega = \frac{\sin(\omega t_d)}{C_1 f_{e0} - \cos(\omega t_d)}
\]

and assume that the frequency decreases with increasing \( r_e \). Then \( f_{e0}/f_{i0} \) as given by Eq. (7.31) decreases. However, by Theorem 7.1, when \( f_{e0}/f_{i0} \) decreases, the frequency increases. This contradicts our assumption that the frequency decreases with \( r_e \). Hence the frequency of oscillation either increases or remains constant as \( r_e \) is increased. This completes the proof.
Consequently, it follows that the amplitudes \( f_{e0} \) and \( f_{i0} \) are nondecreasing functions of \( r_e \). If \( \omega T < 1 \), as is typical in the present discussion, it follows that \( f_{e0}/f_{i0} \sim 1/(1 + \kappa r_e) \), where \( \sqrt{2/\pi} \leq \kappa \leq 2/\pi \). Hence the ratio of the number of excitatory to inhibitory neurons firing per unit time scales inversely with the refractoriness in the excitatory neurons. With the expression for frequency of oscillation given by

\[
T \omega = \frac{\sin(\omega t_d)}{C_1 \frac{1}{C_2} \left[ 1 + \frac{2r_e}{\pi \sqrt{1 + \omega^2 T^2}} \right]} - \cos(\omega t_d)
\]  

(7.32)

we compare the numerical and theoretical results for the change in frequency with increasing \( r_e \) for two different values of delay \( t_d \) (Table 7.5). The frequency of oscillation either increases or is constant as predicted. It is also found that the amplitudes of the oscillation decrease and \( f_{e0}/f_{i0} < 1 \) (Fig. 7.4).

(6) The calculations in Appendix A.3 show that the effect of refractoriness is to introduce a second harmonic, from the product of the integral and the output from the sigmoid term in Eq. 2.5. Additionally, from Appendix A.3, we note that the second harmonic feedback from the nonlinear sigmoid is proportional to the bias [Eq. (a.10)]. With \( f_{e0}/f_{i0} < 1 \) as shown above, the bias due to the mismatch between excitatory and inhibitory activity, \( B \sim C_1 f_{e0} - C_2 f_{i0} \) is nonzero.

We conclude with a brief discussion on the case of strong feedback: \( C_2 C_3 \gg C_1 C_4 \). In this case, it is found that both the second and third harmonics are strong. From Eq. (A.10), the second harmonic is proportional to \( B/A \). When \( C_2 C_3 \gg C_1 C_4 \), at least one of \( B_e = C_1 f_e - C_2 f_i \) and \( B_i = C_3 f_e - C_4 f_i \) is large so that the bias then generates a second strong harmonic. In addition a large sinusoidal input to the sigmoid produces a strong third harmonic as shown in Appendix A.4. In view of the presence of these harmonics, the method used in the section is inappropriate to study the case of dominant feedback.

8. Discussion

The mathematical study of the firing characteristics of a single neuron itself presents enormous difficulties.\(^5\)

In spite of this complexity, the firing pattern of a population of neurons must have a simpler characteristic in order that the signaling be coherent. Nonlinear interactions, between excitatory and inhibitory neurons in a localized population, give rise to collective behavior thereby serving to reduce the extreme variability that is possible in the firing of single neurons. Such population oscillations obviate the need for control and precise timing of individual impulses.

We have studied some characteristics of such population oscillations using a nonlinear theory. It has been shown that a particularly robust mechanism of producing these oscillations is through delay in inhibitory feedback. Delay in the inhibitory feedback induces limit-cycle oscillations by destroying the stability of fixed points. If the slopes of the sigmoids at all the fixed points are zero, stability is guaranteed for all feedback delay times, i.e., oscillations cannot occur. This indicates that for a step function sigmoid oscillations may not occur. This is interpreted to mean that synaptic and/or threshold variability is essential for oscillations. Oscillations can occur even when there is no delay, if the decay time period of the inhibitory activity is greater than that of the excitatory activity. Thus, it is not necessary that the connection strength be feedback dominant as reported in earlier studies.\(^5\)

The frequency-amplitude-phase relations derived shed further light on this. A nonzero phase shift between the excitatory and inhibitory components is essential for the oscillations. The phase shift has two components: one from asymmetry in feedback coupling or slowly decaying inhibitory signals (implying asymmetric decay rates) and the other explicitly due to delay. Only the former contributes to the recorded phase difference between the excitatory and inhibitory components; the latter may therefore be termed a 'hidden phase shift.' Delay and/or slowly decaying inhibitory signals cause a phase shift between the excitatory and inhibitory components; this phase shift underlies the origin of oscillations. Combining these

| Table 7.5. The frequency of oscillation is a non-decreasing function of the refractory period of the excitatory neurons, \( r_e \). Results are shown for two different values of the inhibitory delay, \( t_d = 0.1 \) and \( t_d = 0.5 \). |
|---|---|---|---|
| \( t_d \) | \( r_e \) | \( \omega \) (num.) | \( \omega \) (theory) |
| 0.1 | 0.05 | 11.66 | 13.20 |
| 0.1 | 1.0 | 11.96 | 13.34 |
| 0.1 | 2.0 | 12.73 | 14.20 |
| 0.1 | 5.0 | 13.19 | 14.97 |
| 0.5 | 0.05 | 4.45 | 4.58 |
| 0.5 | 1.0 | 4.45 | 4.60 |
| 0.5 | 2.0 | 4.60 | 4.64 |
| 0.5 | 5.0 | 4.75 | 4.74 |
| 0.5 | 10.0 | 4.75 | 4.82 |
| 0.5 | 15.0 | 4.75 | 4.89 |
| 0.5 | 50.0 | 4.75 | 5.10 |
results, we note that inhibition with time courses such as the alpha functions $-t \exp(-t/\tau)$, used in the simulations of Ref. 33, would be ideally suited to generate oscillatory activity.

The oscillations are input driven and the ideal operating region is excitation close to the threshold. In the present model, too strong or too weak excitation is insufficient to induce oscillations as had already been noted.30 Mathematically, the reason for both of these phenomena is the same; the bias component of the input into the sigmoid is greater than the maximum possible sinusoidal component. Refractoriness in the excitatory neurons is an abetting factor in the existence of oscillations, because it causes suppression of excitatory activity and places the fixed point in a regime wherein the slope of the sigmoid at the fixed point is nonzero so that delayed inhibition can induce oscillations. In agreement with this observation, we have shown that ratio of the excitatory to inhibitory neurons firing per unit time, $f_e/\dot{f}_i$, decreases with increasing excitatory refractory period $r_e$. A detailed simulation of population oscillations35 has noted the importance of refractoriness in suppressing the number of excitatory neurons firing per unit time.

The frequency of oscillation is, in general, different from any time scale in the system and depends on the delay, the time scales of decay of activity, the connection strengths, and the inputs. It is particularly important to note that even in the simplest approximation, it is not the inhibitory time delay that determines the frequency of the oscillation; indeed $\omega t_d \ll 2\pi$ for a wide range of parameters, i.e., the system does not pick up the delay time as the time period of oscillation. The frequency decreases monotonically with (1) the delay in inhibitory feedback and (2) increasing inhibitory decay time.
\[ U(\omega) = -\omega^2 + J_t d_\omega \sin(\omega) + H^2 g_\omega \cos(\omega) + H^2 h_\omega \]  
(A.2.3)

\[ V(\omega) = G_t d_\omega + J_t d_\omega \cos(\omega) - H^2 g_\omega \sin(\omega). \]  
(A.2.4)

For asymptotic stability of the linear \( n \)-th order equation, it is necessary and sufficient that the following condition be satisfied:

\[ \arg \Delta(i\omega) \big|_{\omega=0}^{\infty} = n \frac{\pi}{2}. \]  
(A.2.5)

The coefficients \( G, H, I, J \) depend on the slope of the sigmoid at the fixed point as well as the connectivities and time scales in the problem. No general necessary and sufficient conditions could be derived to show stability or instability of the fixed points. Instead we prove the following theorems which indicate the behavior of the system for particular conditions.

**Theorem 8.2.** A set of sufficient conditions for the stability of a fixed point is:

(i) \( t_d(H + I) > 0 \) and (ii) \( G - J > t_d |I| \).

**Proof.**

\[ V(\omega) = t_d G_\omega + t_d J_\omega \cos \omega - \frac{i^2 |\omega|}{\omega} \sin \omega \]

\[ \geq t_d G_\omega - t_d J_\omega - \frac{i^2 |\omega|}{\omega} \]

\[ \geq t_d \omega (G - J - t_d |I|). \]  
(A.2.6)

Therefore \( V(\omega) > 0 \) if \( G - J - t_d |I| > 0 \). This, together with the condition \( t_d(H + I) > 0 \), implies that \( \arg \Delta(i\omega) \big|_{\omega=0}^{\infty} = \pi \). The proof of this statement follows:

1. There exists \( \omega_1 \) such that \( U(\omega_1) = 0 \) since \( U(\omega = 0) = H + I > 0 \) and \( U(\omega = \infty) = \infty \).

   Now, \( V(\omega) > 0 \) implies \( \arg \Delta(i\omega) \big|_{\omega=0}^{\infty} = \pi/2 \).

2. As \( \omega \to \infty \), \( V/U \to 0 \). Hence, \( \arg \Delta(i\omega) \big|_{\omega=0}^{\infty} = \pi/2 \).

3. Therefore \( \arg \Delta(i\omega) \big|_{\omega=0}^{\infty} = \pi \).

This completes the proof.

**Theorem 8.3.** If \( t_d(H + I) < 0 \), the fixed point is unstable.

**Proof.** From \( U(\omega = 0) = i^2 (H + I) \), \( V(\omega = 0) = 0 \) and \( \omega \to \infty \), \( V/U \to 0 \), it follows that \( \arg \Delta(i\omega) \big|_{\omega=0}^{\infty} = \pm 2n\pi, \quad n = 0, 1, 2, \ldots \). Since \( \arg \Delta(i\omega) \big|_{\omega=0}^{\infty} \neq \pi \), the fixed point is asymptotically unstable.

**A.3.**

We derive the harmonic feedback for the bias plus sinusoid input to the saturation nonlinearity. The main results are summarized at the end of the Appendix. Following the discussion in Sec. 4, the harmonic feedback for the input \( x(t) = B + A \sin(\omega t) \) is

\[ f(x) \sim BF_\theta(f, A, B) + \sum_{k=1}^{\infty} \left[ AF_A(f, A, B, k) \sin(\omega t) \right] \]

\[ + AF^*_A(f, A, B, k) \cos(\omega t) \]  
(A.3.1)

\[ F_A(f, A, B, k) = \frac{1}{\pi A} \int_0^{2\pi} f[B + A \sin(\theta)] \sin(k\theta) d\theta \]

\[ F^*_A(f, A, B, k) = \frac{1}{\pi A} \int_0^{2\pi} f[B + A \sin(\theta)] \cos(k\theta) d\theta \]

We will consider only the case of large amplitude oscillations in which case \((\delta + B)/A < 1\) and \((\delta - B)/A < 1\). For the piecewise-linear sigmoid, \( F_A(f, A, B, k) \) can be evaluated as follows.

\[ \pi A F_A(f, A, B, k) \]

\[ = \int_0^{2\pi} m f[B + A \sin(\theta)] \sin(k\theta) d\theta \]

\[ = \int_{\psi_{10}}^{\psi_{11}} m f[B + A \sin(\theta)] \sin(k\theta) \sin(\theta) d\theta \]

\[ + \int_{\psi_{11}}^{\psi_{20}} m f[B + A \sin(\theta)] \sin(k\theta) \cos(\theta) d\theta \]

\[ + \int_{\psi_{20}}^{\psi_{21}} m f[B + A \sin(\theta)] \cos(k\theta) d\theta \]

\[ + \int_{\psi_{21}}^{2\pi} m f[B + A \sin(\theta)] \sin(k\theta) d\theta \]  
(A.3.2)

where

\[ \psi_{10} = \sin^{-1} \left( \frac{\delta - B}{A} \right) \]
Substituting \( f_e = \tilde{f}_e + e(t) \) and \( f_i = \tilde{f}_i + i(t) \) in Eq. (A.1.1) above, and neglecting second-order terms we get,

\[
T_e e(t) = -e(t)[1 + r_e \sigma_e(\bar{x}_e)] + [1 - r_e \tilde{f}_e] C_1 e(t) \sigma_e'(\bar{x}_e)
- [1 - r_e \tilde{f}_e] C_2 i(t - t_d) \sigma_e'(\bar{x}_e) . \tag{A.1.3}
\]

Similarly for the inhibitory component,

\[
T_i i(t) = -i(t)[1 + r_i \sigma_i(\bar{x}_i)] + [1 - r_i \tilde{f}_i] C_3 e(t) \sigma_i'(\bar{x}_i)
- [1 - r_i \tilde{f}_i] C_4 i(t - t_d) \sigma_i'(\bar{x}_i) . \tag{A.1.4}
\]

These equations can be written in the simplified form:

\[
\dot{e}(t) = -e(t) \kappa_e + C_1 e(t) \sigma_e'(\bar{x}_e) e(t)
- C_2 \alpha_e \sigma_e'(\bar{x}_e) i(t - t_d) \tag{A.1.5}
\]

\[
\dot{i}(t) = -i(t) \kappa_i + C_3 \alpha_i \sigma_i'(\bar{x}_i) e(t)
- C_4 \alpha_i \sigma_i'(\bar{x}_i) i(t - t_d) \tag{A.1.6}
\]

where

\[
T_e \kappa_e = 1 + r_e \sigma_e(\bar{x}_e)
\]

\[
T_i \kappa_i = 1 + r_i \sigma_i(\bar{x}_i)
\]

\[
T_e \alpha_e = 1 - r_e \tilde{f}_e
\]

\[
T_i \alpha_i = 1 - r_i \tilde{f}_i
\]

With \( e(t) \sim e_0 \exp(\lambda t) \) and \( i(t) \sim i_0 \exp(\lambda t) \), the equations can be written as,

\[
\begin{bmatrix}
\lambda + \kappa_e - \alpha_e \sigma_e'(\bar{x}_e) C_1 + \alpha_e \sigma_e'(\bar{x}_e) C_2 \exp(-\lambda t_d) \\
-\alpha_i \sigma_i'(\bar{x}_i) C_3 + \lambda + \kappa_i - \alpha_i \sigma_i'(\bar{x}_i) C_4 \exp(-\lambda t_d)
\end{bmatrix}
\times
\begin{bmatrix}
e_0 \\
i_0
\end{bmatrix} = 0
\]

The characteristic equation, obtained by setting the determinant to zero, is

\[
\Delta(\lambda) = \lambda^2 + G \lambda + H + J \lambda \exp(-\lambda t_d)
+ I \exp(-\lambda t_d) = 0 \tag{A.1.7}
\]

where the coefficients \( G, H, I \) and \( J \) are

\[
G(\bar{x}_e) = [\kappa_e + \kappa_i - \alpha_e \sigma_e'(\bar{x}_e)] C_1
\]

\[
H(\bar{x}_e) = \kappa_i \kappa_e - \alpha_e \sigma_e'(\bar{x}_e) C_1
\]

\[
I(\bar{x}_e, \bar{x}_i) = \sigma_e'(\bar{x}_e) \sigma_i'(\bar{x}_i) \alpha_e \alpha_i (C_2 C_3 - C_1 C_4)
\]

\[
J(\bar{x}_i) = \sigma_i'(\bar{x}_i) \alpha_i C_4
\]

\[
\alpha_e'(\bar{x}_e) = \frac{\beta_e}{\{4 \cosh^2[-\beta_e(\bar{x}_e - \chi_e)]\}}
\]

\[
\alpha_i'(\bar{x}_i) = \frac{\beta_i}{\{4 \cosh^2[-\beta_i(\bar{x}_i - \chi_i)]\}}
\]

\[
\bar{x}_e = C_1 \bar{x}_e - C_2 \tilde{f}_e + P
\]

\[
\bar{x}_i = C_3 \bar{x}_e - C_4 \tilde{f}_i + Q
\]

A.2.

In this Appendix, we prove Theorems 3.1, 3.2, and 3.3 concerning stability of the fixed points.

**Theorem 8.1.** For sufficiently large delay, \( t_d \), if \( H < 0 \), the fixed point is unstable.

**Proof.** Assume that there exists \( \lambda = \lambda_p \) with a positive real part. In the vicinity of \( \lambda_p \), for large delay \( t_d \), Eq. (3.3) can be written as

\[
\lambda^2 + G \lambda + H = 0 . \tag{A.2.1}
\]

The roots of the above equation are \((-G \pm \sqrt{G^2 - 4H})/2\). If \( H < 0 \), one of the roots has a positive real part, which implies that for sufficiently large delay the fixed point is unstable. This root is arbitrarily close to a solution of Eq. (3.3), i.e., there exists a solution with a positive real part. This completes the proof.

We next prove some results concerning stability of the fixed point in the general case. Rewrite Eq. (3.3) by rescaling \( \lambda \rightarrow \lambda/\tau \) (we assume \( t_d \neq 0 \) but may be arbitrarily small):

\[
\Delta = \lambda^2 + G t_d \lambda + H \tau^2 + J t_d \lambda \exp(-\lambda)
+ I \tau^2 \exp(-\lambda) = 0 . \tag{A.2.2}
\]

The stability can be studied by using the Mikhailov criterion. Let \( \Delta(w) = U(w) + iV(w) \), where \( U \) and \( V \) are real. From Eq. (A.2.2),
be the form of the solution of
\begin{equation}
T_j \dot{f}_e(t) = -f_e(t) + I_e(t) + \sigma_e [C_1 f_e(t) - C_2 f_e(t - t_d)] + P
\end{equation}
\begin{equation}
T_j f_j(t) = -f_j(t) + \sigma_j [C_3 f_j(t) - C_4 f_j(t - t_d)]
\end{equation}
\begin{equation}
I_e(t) = 1 - \int_{t-r_e}^{t} f_e(t')dt'
\end{equation}
Then
\begin{equation}
I_e(t) = 1 - \int_{t-r_e}^{t} [f_e + f e_0 \sin(\omega t')]dt'
\end{equation}
\begin{equation}
= (1 - f_e r_e) - 2 f e_0 \frac{\omega r_e}{\omega} \sin\left(\frac{\omega t}{2}\right) \sin\left(\frac{\omega t - \omega r_e}{2}\right).
\end{equation}

The nonlinear response of the sigmoid is $BF_B + AF_A \sin(\omega t + \theta_{ae})$. The averaged response, taking into account the refractoriness, is $\langle I_e(t)[BF_B + AF_A \sin(\omega t + \theta_{ae})]\rangle$, where $\langle \rangle$ denotes the averages as in Eq. (4.1). We now note that the effect of the sinusoidal term in Eq. (4.4) is to introduce a second harmonic proportional to $1/\omega$ when this averaging is carried out. Consistent with the neglect of higher harmonics, we neglect this last term in Eq. (4.4). (It can be shown under very general conditions that this is true. The reason being that when oscillations exist, the ratio of the bias to sinusoidal input to the sigmoid, $B_e/A_e$, is typically less than 1.)

With this approximation, proceeding exactly as in Sec. 5, the following relations may be easily shown:
\begin{equation}
f_e = 0.5(1 - \bar{f}_e r_e) + (1 - \bar{f}_e r_e) B_e F_{Be}
\end{equation}
\begin{equation}
\omega T_e f_{e0} = (1 - \bar{f}_e r_e) \sin(\theta_{ae}) A_e F_{AE}
\end{equation}
\begin{equation}
f_{e0} = (1 - \bar{f}_e r_e) \cos(\theta_{ae}) A_e F_{AE}
\end{equation}
\begin{equation}
\bar{f}_e = 0.5 + B_e F_{Be}
\end{equation}
\begin{equation}
\omega T_e f_{i0} = A_i F_{Ai} \sin(\theta_{ai} + \theta_i)
\end{equation}
\begin{equation}
f_{i0} = A_i F_{Ai} \cos(\theta_{ai} + \theta_i)
\end{equation}
\begin{equation}
\text{References}
\end{equation}
\[ \psi_{11} = \pi - \psi_{10} \]
\[ \psi_{20} = \pi + \sin^{-1}\left(\frac{\delta + B}{A}\right) \]
\[ \psi_{21} = 2\pi - \sin^{-1}\left(\frac{\delta + B}{A}\right). \quad (A.3.3) \]

Equation (A.3.2) evaluates to
\[
\pi A F_A(f, A, B, k) = \frac{-mB}{k} \cos(k\theta) \left| \begin{array}{c} \psi_{00} \\ \psi_{11} \\ \psi_{20} \\ \psi_{21} \\ \psi_{30} \end{array} \right|_0 + \frac{mA}{2} \left[ \frac{1}{k-1} \sin((k-1)\theta) \right] \left| \begin{array}{c} \psi_{00} \\ \psi_{11} \\ \psi_{20} \\ \psi_{21} \\ \psi_{30} \end{array} \right|_0 

- \frac{1}{k+1} \sin((k+1)\theta) \left| \begin{array}{c} \psi_{00} \\ \psi_{11} \\ \psi_{20} \\ \psi_{21} \\ \psi_{30} \end{array} \right|_0 - \frac{m\delta}{k} \cos(k\theta) \left| \begin{array}{c} \psi_{00} \\ \psi_{11} \\ \psi_{20} \\ \psi_{21} \\ \psi_{30} \end{array} \right|_0 

- \frac{mB}{k} \cos(k\theta) \left| \begin{array}{c} \psi_{00} \\ \psi_{11} \\ \psi_{20} \\ \psi_{21} \\ \psi_{30} \end{array} \right|_0 + \frac{mA}{2} \left[ \frac{1}{k-1} \sin((k-1)\theta) \right] \left| \begin{array}{c} \psi_{00} \\ \psi_{11} \\ \psi_{20} \\ \psi_{21} \\ \psi_{30} \end{array} \right|_0 

- \frac{1}{k+1} \sin((k+1)\theta) \left| \begin{array}{c} \psi_{00} \\ \psi_{11} \\ \psi_{20} \\ \psi_{21} \\ \psi_{30} \end{array} \right|_0 + m\delta \cos(k\theta) \left| \begin{array}{c} \psi_{00} \\ \psi_{11} \\ \psi_{20} \\ \psi_{21} \\ \psi_{30} \end{array} \right|_0 

- \frac{mB}{k} \cos(k\theta) \left| \begin{array}{c} \psi_{00} \\ \psi_{11} \\ \psi_{20} \\ \psi_{21} \\ \psi_{30} \end{array} \right|_0 + \frac{mA}{2} \left[ \frac{1}{k-1} \sin((k-1)\theta) \right] \left| \begin{array}{c} \psi_{00} \\ \psi_{11} \\ \psi_{20} \\ \psi_{21} \\ \psi_{30} \end{array} \right|_0 

- \frac{1}{k+1} \sin((k+1)\theta) \left| \begin{array}{c} \psi_{00} \\ \psi_{11} \\ \psi_{20} \\ \psi_{21} \\ \psi_{30} \end{array} \right|_0\right. 

\left. \frac{2\pi}{k} \sin((k-1)\theta) \right|_0 + \frac{mA}{2} \left[ \frac{1}{k-1} \sin((k-1)\theta) \right] \left| \begin{array}{c} \psi_{00} \\ \psi_{11} \\ \psi_{20} \\ \psi_{21} \\ \psi_{30} \end{array} \right|_0 

- \frac{1}{k+1} \sin((k+1)\theta) \right|_0 + \frac{2\pi}{k} \sin((k-1)\theta) \right|_0. \quad (A.3.4)\]

We observe that the harmonics scale as $1/k$. A similar expression is obtained for $F_A(f, A, B, k)$. The calculations are straightforward but tedious; we will therefore simply present the relevant results:
\[
\pi A F_A(f, A, B, k = 3) = \frac{2mB}{3} \left[ \cos(3\delta^+) - \cos(3\delta^-) \right] 

+ \frac{2m\delta}{3} \left[ \cos(3\delta^+) + \cos(3\delta^-) \right] 

+ \frac{mA}{2} \left[ \sin(2\delta^+) + \sin(2\delta^-) \right] 

- \frac{1}{2} \sin(2\delta^+) + \sin(2\delta^-) \right]. 

\pi A F_A(f, A, B, k = 2) = \frac{mB}{2} \sin(2\delta^+) + \sin(2\delta^-) \right] 

+ m\delta \sin(2\delta^+) - \sin(2\delta^-) \right] 

+ mA \left[ \frac{1}{3} \left( \cos(3\delta^+) - \cos(3\delta^-) \right) 

- \cos(2\delta^+) - \cos(2\delta^-) \right]. \quad (A.3.5)\]

where
\[
\delta^+ = \sin^{-1}\left(\frac{\delta + B}{A}\right) \quad \text{and} \quad \delta^- = \sin^{-1}\left(\frac{\delta + B}{A}\right).
\]

For $(\delta + B)/A, (\delta - B)/A \ll 1$, Eqs. (A.3.5) may be simplified by using the approximations $\cos x \sim 1$ and $\sin x \sim x$,
\[
F_A(f, A, B, k = 3) = \frac{2}{\pi A} \frac{1}{3} \quad (A.3.6) 

F_A(f, A, B, k = 2) = 0 \quad (A.3.7) 

F_A^1(f, A, B, k = 2) = \frac{2B}{\pi A} \quad (A.3.8)\]

We summarize the results of this Appendix:
1. The amplitude of the $k$th harmonic is proportional to $1/k$.
2. The second harmonic is proportional to $B/A$ and is phase shifted by $\pi/2$.
3. The amplitude of the third harmonic can be up to a third of that of the fundamental.
4. When the bias $B$ is zero, only the odd harmonics are present. (The calculations for $k = 2, 3$ extend to even and odd harmonics respectively).

\subsection*{A.4.}

The algebraic equations governing the frequency, amplitude and phase of oscillations for $r_e \neq 0, r_i = 0$ are derived. Let
\[
f_e(t) = \bar{f}_e + f_{e0} \sin(\omega t) 

f_i(t) = \bar{f}_i + f_{i0} \sin(\omega t - \theta_i) \quad (A.4.1)\]