Synchronization in Distributed Neural Systems

Vinod Menon[1] and D.S. Tang[2]

[1] Department of Computer Sciences,
University of Texas at Austin,
Austin, Texas 78712

[2] MCC
3500 West Balcones Center Drive
Austin, Texas 78759

Abstract

Localized populations of neurons (neuronal groups) can synchronize their oscillatory activity by the nonlinear interaction of reentrant (reciprocal) signals with the ongoing oscillatory activity within a group. Some of the characteristics of this process are explored using an extended Wilson-Cowan model. For a wide range of parameters, the introduction of reentrant connections induces phase locked oscillations with a concomitant large cross correlation between the activities of the groups. Nonlinear summation of the excitatory and inhibitory signals mediated by reciprocal connections between the groups establishes synchrony. The synchronization is input driven: when one of the groups receives subthreshold excitation, no oscillations are induced in this group. The frequency-amplitude-phase relations derived show that the frequency, phase and correlation of the synchronized response depends critically on the phases of the interacting signals. Reentrant signaling reduces the frequency of oscillation when the reentry delay is small. This decrease is proportional to the mean reentrant connection strength. However, as the reentry delay increases, the reentrant signal arrives out of phase with the inhibitory signal and the frequency and phase difference between the activity of the two groups undergo a jump bifurcation. At the transition region, phase coherence is lost thereby reducing the cross correlation. The phase difference between groups increases with increasing mismatch in the intrinsic frequencies of the groups and can be exactly zero when the intrinsic frequencies of the groups are the same. The phases of interacting signals influence the oscillations and are in turn influenced by the global activity, emphasizing the phasic nature of signaling in neural systems.

1 Introduction

Recent experiments indicate that spatially separated localized populations of neurons can synchronize their oscillatory activity and the degree of synchronization reflects global stimulus properties (Gray et al. 1989, Eckhorn et al. 1988). These experiments directly bear on the following question: how does a distributed neural system synchronize its activity across spatially separated regions in the absence of 'clocks' and algorithms such as those needed in a distributed computer (Edelman 1987)? An understanding of the underlying mechanisms is important in order to gain insight into the complex functions performed by neural systems.

In the first place, it is important to understand the origin and characteristics of the oscillations generated by a localized population of neurons. The detailed computer simulations and

experimental work of Traub, Miles and Wong (1988, 1989) on the CA3 slice of the hippocampus indicate that the temporal activity consists of rhythmic population oscillations in which the number of cells firing per unit time oscillates synchronously even though single neurons may fire asynchronously. A clear indication of the population nature of the activity is that the population firing rate 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. These results indicate that a possible source of oscillations could be the interactions of excitatory and inhibitory neurons in localized populations of neurons called neuronal groups (Edelman 1987) since it could provide a locus for temporal interaction. The computer simulations of Sporns et al. (1989) suggest that the synchronization of the oscillatory activity in neuronal groups can be achieved by reentrant (reciprocal) signaling. The signature of phase locked oscillations is found, not in the activity of individual cells, which can fire asynchronously, but in the cross correlation (between groups) of the number of cells firing per unit time which is proportional to the experimentally observed local field potential.

In an earlier paper (Menon and Tang, 1989), the authors studied some of the characteristics of population oscillations generated by interacting excitatory and inhibitory subpopulations of neurons in a neuronal group. The redundant and the quasi-random nature of the circuitry in a neuronal group allows us to represent the mean temporal activity by renormalized variables for the fraction of excitatory and inhibitory neurons firing per unit time (Wilson and Cowan, 1972). It is found that in the presence of delay in the inhibitory feedback or a slowly decaying inhibitory signal, which causes a phase shift between the excitatory and inhibitory components, robust limit cycle oscillations are generated. The frequency-amplitude-phase relations derived indicate that the frequency of oscillation of the number of neurons firing per unit time depends on several parameters- the delay in inhibition, the decay time periods of excitatory and inhibitory activity, the refractory period, the connection strengths and the input. The oscillations are input driven, due to the dissipative nature of the activity in an unexcited group (or one excited subthreshold). Due to variations in virtually all parameters, (Edelman, 1987), no two groups are likely to have exactly the same frequency of oscillation. This paper is concerned with the nonlinear interaction of the excitatory and inhibitory components from two groups in order to elucidate the origins and characteristics of synchronization of oscillatory activity in distributed neural systems.

2 Mathematical Model, Illustrative Results

In the mathematical model we consider, the nonlinear summation of voltages at the membrane of a neuron is renormalized to represent the population response of excitatory and inhibitory subpopulations in a neuronal group (Cowan 1971). Fig. 1 is a schematic illustration of the inter and intra group interactions between two neuronal groups G and G' where E, and I represent the excitatory and inhibitory subpopulations of G and E', and I' the corresponding subpopulations of G'. (*Notation:* Throughout this paper, the unprimed variables refer to the group G, and the primed ones to G'.) Following Wilson and Cowan (1972), the fraction of excitatory and inhibitory cells firing per unit time, $f_e(t)$, and $f_i(t)$ for the group G, and $f'_e(t)$, and $f'_i(t)$, for the group G', at time t are given by the following time coarse grained and spatially averaged nonlinear differential equations,

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

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

$$T'_e \dot{f}'_e(t) = \quad -f'_e(t) + (1 - \int_{t-r_e}^{t} f'_e(t')dt')\sigma'_e(x'_e) \tag{2.3}$$

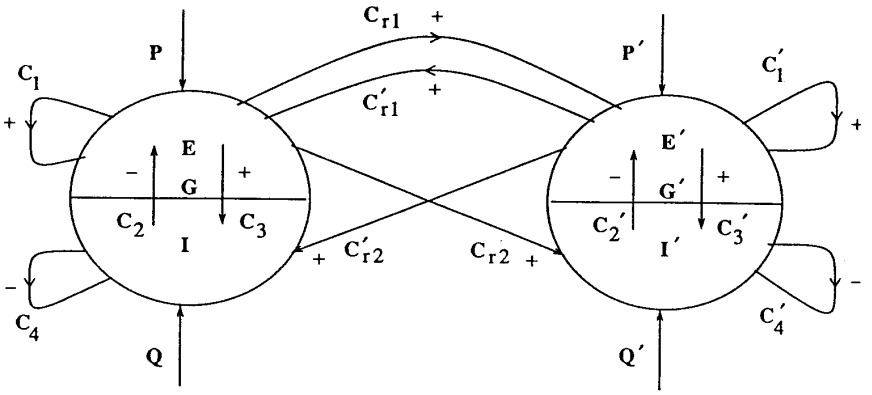

Figure 1: A schematic of two interacting neuronal groups G and G' each consisting of excitatory and inhibitory subpopulations, E, I and E' and I' respectively. External inputs P and Q and P' and Q' activate the neurons. The mean synaptic strengths for the intra group interactions of the excitatory and inhibitory subpopulations are C_1, C_2, C_3, C_4 for the group G, and C_1', C_2', C_3', C_4' for the group G'. Reciprocal excitatory connections C_{r1}, C_{r1}', C_{r2} and C_{r2}' mediate the signaling between the groups and are referred throughout the paper as reentrant connections. The sign and arrow indicate the excitatory or inhibitory effects of one subpopulation on the other or itself.

$$T_i' \dot{f}_i'(t) = -f_i'(t) + (1 - \int_{t-r_i}^{t} f_i'(t')dt')\sigma_i'(x_i') \tag{2.4}$$

$$x_e(t) = C_1 f_e(t) + C_{r1}' f_e'(t - t_r') - C_2 f_i(t - t_d) + P \tag{2.5}$$

$$x_i(t) = C_3 f_e(t) + C_{r2}' f_e'(t - t_r') - C_4 f_i(t - t_d) + Q \tag{2.6}$$

$$x_e'(t) = C_1' f_e'(t) + C_{r1} f_e(t - t_r) - C_2' f_i'(t - t_d') + P' \tag{2.7}$$

$$x_i'(t) = C_3' f_e'(t) + C_{r2} f_e(t - t_r) - C_4' f_i'(t - t_d') + Q' \tag{2.8}$$

where x_e, x_i, x_e', and x_i' are the activities and $\sigma_e(x_e)$, $\sigma_i(x_i)$, $\sigma_e'(x_e')$, and $\sigma_i'(x_i')$ are the responses (outputs) of the respective subpopulations. The sigmoids have the standard form, $\sigma(x) = \frac{1}{1+\exp(-\beta(x-\chi))}$ where β and χ are respectively the sigmoid nonlinearity and threshold. Consider, for example, the equation for the fraction of excitatory cells firing per unit time, $f_e(t)$ (Eqn. 2.1) for the subpopulation represented by E- T_e is the time scale of the decay of activity, r_e is the absolute refractory period of the excitatory cells, t_d is the delay in the inhibitory signal (typically due to latency in chemical activation), t_r' is the delay in the reentrant signal arriving from group G', (typically due to the transmission time), and P is the (constant) external input which drives the activity. Similar considerations hold for each of the other subpopulations. Although synchronization of the activities of the groups is observed for a wide range of parameters, in order to keep the model analytically tractable, the following approximations are made: $C_1 = C_2 = C_3 = C_4 = C_1' = C_2' = C_3' = C_4' = C$, $C_{r1}' = C_{r2}' = C_{r1} = C_{r2} = C_r$, $r_i = 0$. *Notation:* In the following discussion, the intrinsic frequencies of the two groups (without reentry) will be denoted by Ω and Ω' and the synchronized frequency of two groups by ω.

Numerical simulations of Eqns. 2.1 - 2.8 illustrate the theoretical problem we wish to study. The two neuronal groups discussed above have, in general, different frequencies of oscillation. For a wide range of parameters, with the introduction of reciprocal signaling, the oscillatory activity of the two groups are phase locked (Fig. 2) with a concomitant increase in cross correlation (Fig. 3).

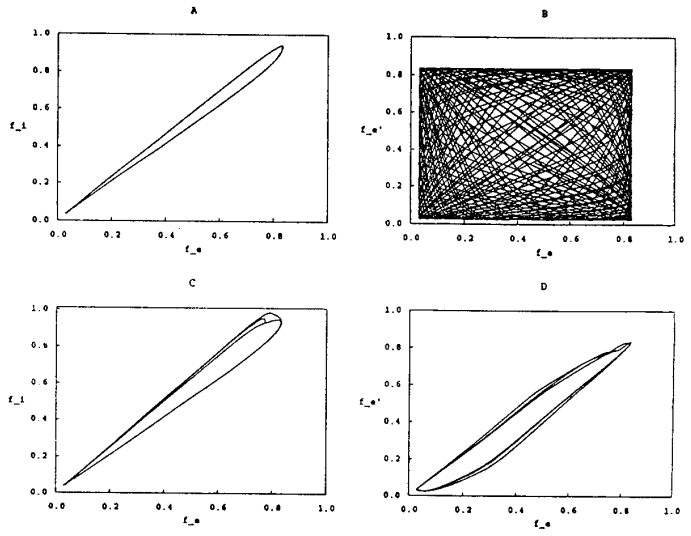

Figure 2: The phase portraits before and after the introduction of reentry indicate that reentrant signaling induces phase coherence in the inter group excitatory components. Without reentry, the excitatory, f_e, and inhibitory, f_i, components within a group are correlated **(A)**, but the cross components f_e and f'_e are uncorrelated, **(B)**. After the introduction of reentry, both the intra group **(C)**, and the inter group components are correlated **(D)**.

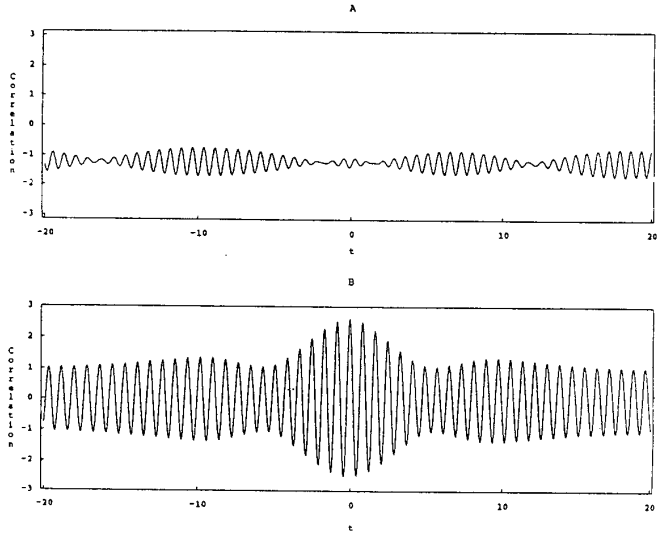

Figure 3: The cross correlation between the excitatory components, $f'_e(t)$ and $f_e(t)$ of the two groups **(A)** before and **(B)** after the introduction of reentry. The intrinsic frequencies of the groups are $\Omega = 8.90$ and $\Omega' = 8.28$. The frequency of the synchronized oscillation drops to $\omega = 7.67$. Similar reductions in the frequency have been reported by Sporns et al. (1989). The cross correlations are normalized with respect to the mean and standard deviation of the activity after introduction of reentry **(B)**.

3 Nonlinear Theory

In this section, a nonlinear theory using the method of harmonic balance, (Bogoliubov and Mitropolsky, 1961) is discussed. Neglecting the higher harmonics, solutions to Eqns. 2.1 - 2.8 may be approximated by,

$$f_e(t) = \bar{f}_e + f_{i0}\sin(\omega t) \tag{3.1}$$

$$f_i(t) = \bar{f}_i + f_{i0}\sin(\omega t - \theta_i) \tag{3.2}$$

$$f'_e(t) = \bar{f}'_e + f'_{i0}\sin(\omega t - \theta'_e) \tag{3.3}$$

$$f'_i(t) = \bar{f}'_i + f'_{i0}\sin(\omega t - \theta'_i) \tag{3.4}$$

where θ_i, θ'_e and θ'_i are the phase differences (assumed to be constant) between f_e and f_i, f_e and f'_e, and, f_e and f'_i respectively. The sigmoid is approximated by a piece-wise linear function, and using the averaging technique of Bogoliubov-Krylov-Mitropolsky (Bogoliubov and Mitropolsky, 1961), the nonlinear differential equations Eqns. 2.1 - 2.8 are reduced to algebraic equations when the amplitude of the input to the sigmoid is large compared to the bias (this requires excitation of the subpopulations at the threshold, i.e., $P \sim \chi_e$, $Q \sim \chi_i$, $P' \sim \chi'_e$ and $Q' \sim \chi'_i$) but the harmonics are still weak (Menon and Tang, 1990). For $T_e = T_i = T$, and $\bar{f}_e \sim f_{e0}$ the frequency-amplitude-phase relations simplify to,

$$\omega T = -\frac{\frac{C_r f_{e0}}{C f_{i0}}\sin(\theta'_e+\omega t'_r)-\sin(\omega t_d)}{\frac{f_{e0}}{f_{i0}}+\frac{C_r f_{e0}}{C f_{i0}}\cos(\theta'_e+\omega t'_r)-\cos(\omega t_d)} \tag{3.5}$$

$$\frac{\omega T - \tan(\theta'_e)}{1+\omega T\tan(\theta'_e)} = -\frac{\frac{f_{e0}}{f_{i0}}\sin(\theta'_e)+\frac{C_r}{C}\frac{f_{e0}}{f_{i0}}\sin(\omega t_r)-\sin(\theta'_e+\omega t'_d)}{\frac{f_{e0}}{f_{i0}}\cos(\theta'_e)+\frac{C_r f_{e0}}{C f_{i0}}\cos(\omega t_r)-\cos(\theta'_e+\omega t'_d)} \tag{3.6}$$

$$\frac{f_{e0}}{f_{i0}} \sim \frac{1}{1+\frac{2r_e}{\pi\sqrt{1+\omega^2T^2}}} \tag{3.7}$$

where the frequency, ω and the phase difference between the two excitatory components, θ'_e are the unknown variables.

Using these relations, the following results may be shown: Refractoriness in the excitatory neurons is important for generating oscillations when reentry is introduced. The suppression of the number of excitatory neurons firing per unit time makes this possible. Synchronization is achieved by adjusting the amplitudes and phases of the various excitatory and inhibitory components as well as the frequency of the coherent response. The (relative) phase of an interacting signal has two components, one due to synaptic coupling (the 'phase difference'), for example, θ'_e above, and the other explicitly due to delay in activation of the signal, for example, $\omega t'_r$. The phase difference between the excitatory components of the groups, θ'_e is strictly zero only when there is a certain symmetry: if the frequencies of oscillation are exactly the same and the synaptic coupling is symmetric both in strength and delay. Arbitrarily small phase differences are possible when $\Omega \rightarrow \Omega'$. For small reentry delays, the phase difference between the groups increases with increasing mismatch in the intrinsic frequencies of the groups. Reentrant signaling reduces the frequency of oscillation when the reentry delay is small compared to the delay in the inhibition, in agreement with the detailed simulations of Sporns et al. (1989). This decrease is proportional to the mean reentrant connection strength. However, as the reentry delay increases, the reentrant signal arrives out of phase with the inhibitory signal and the frequency and phase difference between the activity of the two groups undergo a jump bifurcation. At the transition region, phase coherence is lost thereby reducing the cross correlation. Similar phenomena occur when

the reentry delay times are asymmetric, $t_r \neq t'_r$, even if the intrinsic frequencies of the groups are exactly the same.

Numerical simulations with other models suggest that nonlinear summation of excitatory and inhibitory signals is critical for establishing synchrony between groups. The locus of such interaction may be the inhibitory interneurons whose firing is much better correlated with the population activity (Traub et al. 1989).

Thus, the phase of a signal arriving from a neuronal group depends on the time delay, the synaptic coupling and frequency of the ongoing oscillation. The interaction of signals with different phases in turn influences the characteristics of the ongoing oscillations. The frequency of the underlying activity itself is a signature of the global activity of (possibly) several groups acting coherently. In this manner, neural systems build up global cooperative activity. Such cooperative interactions are likely to be important in higher brain functions (Edelman, 1987).

References

[1] Bogoliubov, N.N. and Y.A. Mitropolsky (1961), Asymptotic methods in the Theory of Nonlinear Oscillations, Hindustan Publishing Corp., New Delhi.

[2] Cowan, J.D. (1971), Stochastic Models of Neuroelectric Activity, in Proc. I.U.P.A.P. Conf. Stat. Mech., eds. S. Rice, J.Light and K. Freed, Univ. of Chicago Press, Chicago.

[3] Eckhorn, R., R. Bauer, W. Jordan, M. Brosch, W. Kruse, M. Munk, and H.J. Reitboeck (1988), Coherent Oscillations: A Mechanism of Feature Linking in the Visual Cortex ?, Biological Cybernetics, 60, 121-130.

[4] Edelman, G.M. (1987), Neural Darwinism, The Theory of Neuronal Group Selection, Basic Books, New York.

[5] Gray, C.M., P. Konig, A.K. Engel and W. Singer (1989), Oscillatory Responses in Cat Visual Cortex Exhibit Inter-columnar Synchronization which Reflects Global Stimulus Properties, Nature vol. 338, 334-337.

[6] Menon, V. and D.S. Tang (1989), Inhibition Delay Induced Nonlinear Oscillations in Neural Systems, MCC Tech. Rep. ACT-HI-353-89, submitted for publication.

[7] Menon, V. and D.S. Tang (1990), Synchronization by Nonlinear Interaction of Reentrant Signals, MCC Tech. Rep. ACT-HI-466-89, submitted for publication.

[8] Traub, R.D., R. Miles and R.K.S. Wong (1988), Large Scale Simulations of the Hippocampus, IEEE Eng. Med. Biol. Mag., 7, 31.

[9] Traub, R.D., R. Miles and R.K.S. Wong (1989), Model of the Origin of Rhythmic Population Oscillations in the Hippocampal Slice, Science Vol. 243, 1319 - 1325.

[10] Sporns O., J.A. Gally, G.N. Reeke and G.M. Edelman (1989), Reentrant Signaling among Simulated Neuronal Groups leads to Coherency in their Oscillatory Activity, Proc. Natl. Acad. Sci. USA, Vol. 86, 7265-7269.

[11] Wilson, H.R. and J.D. Cowan (1972), Excitatory and Inhibitory Interactions in Localized Populations of Model Neurons, Biophys. J. Vol. 12, 1-24, 1972.