CLUSTERING IN INHIBITORY NEURAL NETWORKS WITH NEAREST NEIGHBOR COUPLING

JENNIFER MILLER*, HWAYEON RYU†, ZEYNEP TEYMUROGLU‡,
XUEYING WANG§, VICTORIA BOOTH¶, AND SUE ANN CAMPBELL‖

Abstract. We investigate the clustering dynamics of a network of inhibitory interneurons, where each neuron is connected to some set of its neighbors. We use phase model analysis to study the existence and stability of cluster solutions. In particular, we describe cluster solutions which exist for any type of oscillator, coupling and connectivity. We derive conditions for the stability of these solutions in the case where each neuron is coupled to its two nearest neighbors on each side. We apply our analysis to show that changing the connection weights in the network can change the stability of solutions in the inhibitory network. Numerical simulations of the full network model confirm and supplement our theoretical analysis. Our results support the hypothesis that cluster solutions may be related to the formation of neural assemblies.

1. Introduction.

A neural assembly is a group of neurons which transiently act together, facilitated by strengthened synapses, to achieve a particular purpose. The same neuron may participate in different assemblies. Experimental evidence for the existence of such assemblies lies in measurements of transiently synchronized groups of neurons associated with certain tasks. For example, measurements of neuronal assemblies in the olfactory systems are thought to be associated with encoding sensory information [18], while observation of such assemblies in the hippocampus has been linked to spatial navigation and memory encoding [5, 23]. A key hypothesis about neural assemblies is that they are formed not just due to external inputs to the system, but also due to the intrinsic dynamics of the network [6]. There is experimental evidence in the hippocampus supporting this hypothesis [14, 22]. Mathematically, the intrinsic dynamics of the network should support multiple different groupings of neurons, with different neurons able to participate in multiple groupings and switching between different groupings by changing the connection weights of the network.

Clustering is a type of solution observed in a network of oscillators, where the elements break into subgroups. Elements within a group are synchronized, while elements in different groups are phase-locked with some nonzero phase difference. Studies of large networks of identical (or near-identical), all-to-all coupled oscillators have shown that many possible clus-

---

*DEPARTMENT OF MATHEMATICS, TRINITY COLLEGE
†DEPARTMENT OF MATHEMATICS, DUKE UNIVERSITY
‡DEPARTMENT OF MATHEMATICS AND COMPUTER SCIENCE, ROLLINS COLLEGE
§DEPARTMENT OF MATHEMATICS, WASHINGTON STATE UNIVERSITY
¶DEPARTMENTS OF MATHEMATICS AND ANESTHESIOLOGY, UNIVERSITY OF MICHIGAN
‖DEPARTMENT OF APPLIED MATHEMATICS AND CENTRE FOR THEORETICAL NEUROSCIENCE, UNIVERSITY OF WATERLOO

ter solutions exist and that multistability can occur [3, 13, 21]. Other work on small networks has shown that heterogeneous inputs can cause the network to select particular clustered solutions [19, 20]. Thus clustering in networks of (near-) identical oscillators seems to have the intrinsic dynamics necessary to be associated with the formation of neural assemblies. For this reason these two concepts have been linked [12].

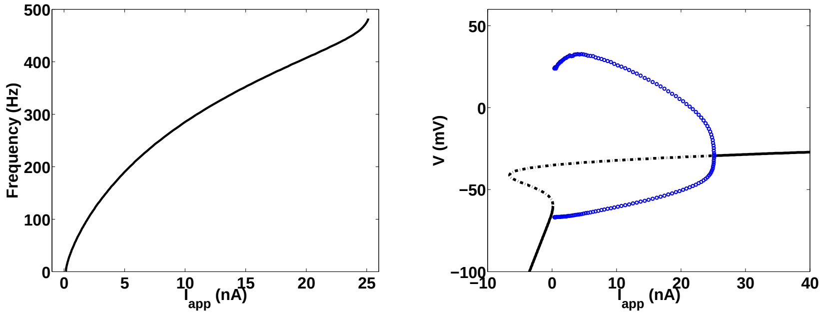
Here we investigate the clustering dynamics of a network of inhibitory interneurons. While all-to-all coupling is appropriate for studying highly connected networks such as the CA3 region of the hippocampus, other brain regions, such as hippocampal area CA1 are more sparsely connected. Thus we focus on coupling structures where each neuron is connected to some set of its neighbors. Details of the model are given in section 2, which also contains a derivation of a phase model reduction of the system. In section 3 we use phase model analysis to study the existence and stability of cluster solutions in the network and apply our analysis to the interneuron model. In section 4 we study the original network model using numerical simulations to support and extend our analysis. In section 5 we summarize our results and draw conclusions.

2. Model.

For our interneuron model we use the single compartment, conductance-based model of Wang and Buzsáki [25]. This model was developed by adjusting the parameters of the Hodgkin-Huxley model [15] to match the action potential shape and spiking properties of fast-spiking interneurons. The equations for the model are

$$\begin{aligned} C\frac{dV}{dt} &= I_{app} - g_{Na} m_\infty^3(V) h (V - V_{Na}) - g_K n^4 (V - V_K) - g_L (V - V_L) \\ &= I_{app} - I_{ion}(V, h, n) \\ \frac{dh}{dt} &= \phi(\alpha_h(V)(1-h) - \beta_h(V)h) = f^h(V,h) \\ \frac{dn}{dt} &= \phi(\alpha_n(V)(1-n) - \beta_n(V)n) = f^n(V,n) \end{aligned} \tag{2.1}$$

where V is the cell membrane voltage in mV and t is time in ms. The variables h and n are dimensionless gating variables representing, respectively, the inactivation of the sodium current and the activation of the potassium current. The activation of the sodium current is assumed to be instantaneous and thus follows the steady state activation function $m_\infty(V) = \alpha_m(V)/(\alpha_m(V) + \beta_m(V))$, where $\alpha_m(V) = -0.1(V+35)/(\exp(-0.1(V+35))-1)$, $\beta_m(V) = 4\exp(-(V+60)/18)$ are the voltage dependent reaction rates associated with the activation gate with units ms^{-1}. Similarly the reaction rates associated with the inactivation of the sodium channel and activation of the potassium channel are $\alpha_h(V) = 0.07\exp(-(V+58)/20)$, $\beta_h(V) = 1/(\exp(-0.1(V+28))+1)$, $\alpha_n(V) = -0.01(V+34)/(\exp(-0.1(V+34))-1)$, $\beta_n(V) = 0.125\exp(-(V+44)/80)$. The constant $\phi = 5$ adjusts the reaction rates for temperature. Maximal sodium, g_{Na}, potassium, g_K, and leak, g_L, conductances are: 35, 9 and 0.1 mS/cm^2 respectively. Rever-



(a) (b)

Fig. 1. *Variation of spiking frequency (a) and amplitude (b) with applied current for the Wang-Buzsáki interneuron model. In (b) solid/dashed lines represent asymptotically stable/unstable equilibrium points, while blue circles represent the maximum and minimum values on the stable limit cycle. Oscillations emerge via a SNIC bifurcation, at* $I_{SNIC} = 0.16$, *and disappear via a Hopf bifurcation, at* $I_{Hopf} = 25.13$.

sal potentials, V_{Na}, V_K, V_L, are 55, -90 and -65 mV respectively, and the capacitance, C, is 1 μF/cm^2.

This model exhibits periodic spiking for $I_{app} \in (0.16, 25.13)$ nA. The variation of the spiking period with I_{app} can be seen in Figure 1. Biologically reasonable intrinsic firing rates are less than 60 Hz [25, 17] which correspond to $I_{app} < 1$. In simulations we use $I_{app} = 0.4$ which corresponds to a spiking frequency of approximately 25 Hz.

The oscillations in this model are created in a saddle node on an invariant circle (SNIC) bifurcation at $I = I_{SNIC} = 0.16$ and are destroyed in a supercritical Hopf at $I = I_{Hopf} = 25.13$. As can be seen in Figure 1, at $I = I_{SNIC}$ the oscillations appear with finite amplitute and frequency 0. Thus close to this point, and in particular at $I = 0.4$, the model may be considered to be a Type I oscillator. See [11, section 3.4] for more dicussion of bifurcations and the emergence of oscillations in neural models.

We consider a network of identical neurons coupled with inhibitory synapses. The synapses are modelled using first order kinetics following [4], giving the model

$$\begin{aligned}
C\frac{dV_i}{dt} &= I_{app} - I_{ion}(V_i, h_i, n_i) - g_{syn}(V_i - V_{syn})\sum_{j=1}^{N} w_{ij}s_{ij} \\
\frac{dh_i}{dt} &= f^h(V_i, h_i) \\
\frac{dn_i}{dt} &= f^n(V_i, n_i) \\
\frac{ds_{ij}}{dt} &= -\frac{s_{ij}}{\tau_{inh}} + \alpha_{inh}(V_j)(1 - s_{ij})
\end{aligned} \tag{2.2}$$

where i is modulo N and

$$\alpha_{inh}(V) = \alpha_0/(1 + \exp(-V/5)).$$

The reversal potential, maximal synaptic conductance and time constant of activation for the synapse are $V_{syn} = -75$ mV, $g_{syn} = -0.2$ mS/cm^2 and $\alpha_0 = 4$ ms^{-1}, respectively, which are appropriate for a GABA synapse [1, 25]. We consider τ_{inh} in the range $1 - 10$ ms, which is consistent with experiments [2, 25]. The coupling matrix $W = [w_{ij}]$ determines if there is a synapse from the j^{th} neuron to the i^{th}. In particular, we will take $w_{ii} = 0$ (no self-coupling), and assume that the neurons are arranged in a 1-dimensional ring with each neuron coupled to r of its nearest neighbors on each side:

$$w_{ij} = \begin{cases} w_1 > 0 & j = i-1, i+1 \\ w_2 > 0, & j = i-2, i+2 \\ \vdots & \\ w_r > 0, & j = i-r, i+r \\ 0, & \text{otherwise} \end{cases} \qquad j \bmod N, \tag{2.3}$$

Thus r will be called the *connectivity radius*. In the analysis we will primarily focus on the cases $r = 1$ (nearest neighbor coupling) and $r = 2$ (two nearest neighbors coupling).

2.1. Reduction to a phase model. Consider a system of ordinary differential equations

$$\frac{d\mathbf{X}}{dt} = \mathbf{F}(\mathbf{X}(t)) \tag{2.4}$$

which has an exponentially asymptotically stable periodic orbit given by $\mathbf{X} = \hat{\mathbf{X}}(t),\ 0 \le t \le T = 2\pi/\Omega$. For example the model (2.4) is in this form with $\mathbf{X} = (V, h, n)$, and has an exponentially asymptotically stable periodic orbit when $I_{SNIC} < I < I_{Hopf}$ as shown in Figure 1. Linearizing (2.4) about this solution gives the periodic system

$$\frac{d\mathbf{X}}{dt} = D\mathbf{F}(\hat{\mathbf{X}}(t))\mathbf{X}.$$

The system adjoint to this is

$$\frac{d\mathbf{Z}}{dt} = -[D\mathbf{F}(\hat{\mathbf{X}}(t))]^T\mathbf{Z}. \tag{2.5}$$

Let $\mathbf{Z} = \hat{\mathbf{Z}}(t),\ 0 \le t \le T$ be the unique periodic solution of (2.5) satisfying the normalization condition

$$\frac{1}{T}\int_0^T \hat{\mathbf{Z}}(t) \cdot F(\hat{\mathbf{X}}(t))\, dt = 1.$$

Now consider a network of identical oscillators given by

$$\frac{d\mathbf{X}_i}{dt} = \mathbf{F}(\mathbf{X}_i(t)) + \epsilon \sum_{j=0}^{N-1} w_{ij}\mathbf{G}(\mathbf{X}_i, \mathbf{X}_j),\ 0 \leq i \leq N-1, \tag{2.6}$$

where ϵ is the coupling strength, G is the coupling function and $W = [w_{ij}]$ is the coupling matrix.

Assuming that ϵ is sufficiently small and the w_{ij} are of order 1 with respect to ϵ, one can apply weakly coupled oscillator theory [9, 10, 11, 16] to show that the phases of the oscillators of (2.2) satisfy

$$\frac{d\theta_i}{dt} = \Omega + \epsilon \sum_{j=0}^{N-1} w_{ij} H(\theta_j - \theta_i) + O(\epsilon^2),\ i \bmod N,$$

where the interaction function, H, is given by

$$H(\theta_j - \theta_i) = \frac{1}{T}\int_0^T \hat{\mathbf{Z}}(t)\mathbf{G}[\hat{\mathbf{X}}(t), \hat{\mathbf{X}}(t + (\theta_j - \theta_i)/\Omega)]\, dt, \tag{2.7}$$

with $\hat{\mathbf{Z}}, \hat{\mathbf{X}}$ as defined above. Note that H is a 2π periodic function of its argument.

Neglecting the higher order terms in ϵ, introducing the phase differences

$$\phi_i = \theta_{i+1} - \theta_i,\ i \bmod N, \tag{2.8}$$

and using coupling described by equation (2.3) gives rise to the following phase difference model

$$\begin{aligned} \frac{d\phi_i}{dt} \quad = \quad & \epsilon \sum_{k=1}^{r} w_k \left[H\left(\sum_{s=0}^{k-1} \phi_{i+s+1}\right) - H\left(\sum_{s=0}^{k-1} \phi_{i+s}\right) \right. \\ & \left. + H\left(-\sum_{s=0}^{k-1} \phi_{i-s}\right) - H\left(-\sum_{s=0}^{k-1} \phi_{i-s-1}\right) \right], \end{aligned} \tag{2.9}$$

where i is modulo N. Note that the phase differences are not independent, but satisfy the constraint

$$\sum_{i=0}^{N-1} \phi_i = 0. \tag{2.10}$$

This can be used to reduce the dimension of the system (2.9) to $N-1$; however it also results in a loss of symmetry in the system. In our analysis below, we choose to work with the full system and the constraint in order to take advantage of this symmetry.

Recall that cluster solutions correspond to periodic solutions of (2.2) where the neurons are phase-locked with some fixed phase difference between different neurons. Such solutions correspond to equilibrium solutions of (2.9). In the next section we will study the existence and stability of such solutions via the phase difference model (2.9). This analysis will be used to make predictions about what kind of cluster solutions can occur in the full model (2.2).

3. Phase Model Analysis.

3.1. Existence of Cluster Solutions. Equilibrium solutions of the phase difference equations (2.9) must satisfy the following N equations

$$\begin{aligned} 0 &= \epsilon \sum_{k=1}^{r} w_k \left[H\left(\sum_{s=0}^{k-1} \phi_{i+s+1} \right) - H\left(\sum_{s=0}^{k-1} \phi_{i+s} \right) \right. \\ &\quad \left. + H\left(-\sum_{s=0}^{k-1} \phi_{i-s} \right) - H\left(-\sum_{s=0}^{k-1} \phi_{i-s-1} \right) \right], \ 0 \le i \le N-1, \end{aligned} \tag{3.1}$$

and the constraint (2.10).

We will focus on equilibrium solutions which are independent of the function H, the weights w_j and the connectivity radius r. Clearly such a solution is given by $\phi_i = \psi, \ i = 0, \dots, N-1$. Applying the constraint equation (2.10) and the 2π-periodicity of the ϕ gives the extra condition

$$N\psi = 0 \bmod 2\pi. \tag{3.2}$$

The choice of ψ determines the type of solution. We can immediately see one simple choice: $\psi = 0$. This means the oscillators are phase-locked with no phase difference between them. In the original model this corresponds to all the neurons firing at the same time. This is called the **synchronous** or **in-phase** solution. A second simple choice is $\psi = \frac{2\pi}{N}$ which corresponds to the oscillators being phase-locked with the same phase difference between any two adjacent neighbors in the network. This is an example of a **splay** solution. In original model, a splay solution is one where the firing of the neurons is equally distributed over the period. Recall that an n-cluster solution is one where the oscillators are phase-locked so that n groups are formed. Oscillators in the same group are synchronized (the phase difference between them is zero) and oscillators in different groups have some fixed phase difference. Note that the synchronized solution can be thought of as a 1-cluster solution and the splay solution as an N-cluster solution.

More generally we have the following.

Theorem 3.1. *The phase difference equations (2.9) admit N solutions of the form $\phi_i = \psi, \ i = 0, \dots, N-1$. These solutions are of three types. The one-cluster or synchronized solution is given by $\psi = 0$. The N-cluster or splay solutions are given by $\psi = 2k\pi/N$ where k and N are* *relatively prime. The other cluster solutions are determined by the nontrivial factors of* N. *For* $1 < n < N$ *where* n *divides* N *evenly there are* n*-cluster solutions given by* $\psi = 2m\pi/n$, *where* $m < n$ *and* m, n *are relatively prime. Solutions come in pairs. If* $\bar{\psi}$ *is a solution then* $2\pi - \bar{\psi}$ *is a solution of the same type.*

Proof. The constraint (3.2) can be written

$$N\psi = 2k\pi, \tag{3.3}$$

where k is an integer. We need only consider $k = 1, \ldots, N$ as larger values of k give solutions which are equivalent to those with $k \leq N$. Thus there are N solutions.

Let $\gcd(N, k) = p$. If $p = 1$, i.e., k, N are relatively prime, then the corresponding solution is

$$\psi = \frac{2k\pi}{N}.$$

This is a splay state where the oscillators are equally distributed over k periods. Note that $k = 1$ corresponds to the simple splay state discussed before. Now $2\pi - \psi = (N - k)2\pi/N$. Since N, k are relatively prime so are N and $N - k$. Clearly $N - k < N$ thus $(N - k)2\pi/N$ is also a splay solution.

If $p > 1$, let $N = np$. Then $\gcd(N, k) = p$ and $k < N$ if $k = mp$ where $m < n$. Clearly one choice is $m = 1$. Others may exist depending on the value of N. In any case, then the corresponding solution is $\psi = m2\pi/n$. Now in terms of the original phases this solution satisfies

$$\theta_{i+1}(t) - \theta_i(t) = 2m\pi/n, \ i \bmod N$$

It follows that

$$\theta_n(t) - \theta_0(t) = \phi_{n-1} + \cdots + \phi_0 = 2m\pi.$$

Thus oscillators 0 and n are synchronized. In a similar way one can show oscillators $0, n, 2n, ..(p - 1)n$ form a synchronized group (cluster) and the rest of the oscillators break into $n - 1$ other clusters. Thus, $\psi = m2\pi/n$ corresponds to a clustered solution with n clusters.

Note that $2\pi - \psi = (n - m)2\pi/n$. Since n, m are relatively prime, so are n and $n - m$. Clearly $N - k < N$ thus $(n - m)2\pi/n$ is an n-cluster solution. □

COROLLARY 3.1. *If* N *is prime then (2.9) only admits the synchronized solution and splay states. If* N *is even then (2.9) always admits the 2-cluster solution (anti-phase state)* $\phi_i = \pi, \ i = 0, \ldots, N - 1$.

In a splay state the phase difference between adjacent cells in the network is given by $\psi = 2\pi k/N$. However, adjacent cells do not necessarily fire in successive order. The firing order of the neurons is given by $\{i_1, i_2, \ldots, i_N\}$ where $i_s = (s - 1)l \bmod N$ with $lk = 1 \bmod N$.

Number of clusters, n	Nearest neighbors phase difference, ψ
2	π
4	$\frac{1}{2}\pi,\ \frac{3}{2}\pi$
5	$\frac{m}{5}2\pi,\ m = 1,2,3,4$
10	$\frac{l}{5}\pi,\ l = 1,3,7,9$
20	$\frac{l}{10}\pi,\ l = 1,3,7,9,11,13,17,19$
25	$\frac{m}{25}2\pi,\ m = 1,2,3,4,6,7,8,9,11,\ldots,24$
50	$\frac{l}{25}\pi,\ l = 1,3,7,9,11,\ldots 49$

TABLE 1
Clustered states for a network with 100 *neurons*

Consider the n-cluster state corresponding to the solution $\psi = m2\pi/n$, where $N = np$. We number the clusters so that neuron j belongs to cluster C_j for $j = 0,\ldots,n-1$:

$$C_0 = \{0, n, \ldots, (p-1)n\},\ C_1 = \{1, n+1, \ldots, (p-1)n+1\}, \ldots$$

Then the phase difference between clusters i and $i+1$ is $\frac{m}{n}2\pi$ and the firing order of the clusters is determined by the firing order of neurons $0,\ldots,n-1$. Let $\{j_1, j_2, \ldots, j_n\}$ be the firing order. Then $j_i = (i-1)l \bmod n$ where $lm = 1 \bmod n$.

For example, for $N = 100$ the clustered states are as shown in Table 1. Aside from the synchronous state all other states are splay states.

3.2. Stability Analysis of Cluster Solutions. Now we consider the stability of the solutions derived above. If we take all N of the phase model equations (using indices mod N), the nature of the coupling and the form of the solution mean that the Jacobian matrix will be circulant. We do not require N equations to define the system, but the circulant form is very convenient for computing eigenvalues, as seen in [21].

In other words, the Jacobian has the form, $J = \epsilon\hat{J}$, where

$$\hat{J} = \begin{bmatrix} c_0 & c_{N-1} & \cdots & c_2 & c_1 \\ c_1 & c_0 & c_{N-1} & & c_2 \\ \vdots & c_1 & c_0 & \ddots & \vdots \\ c_{N-2} & & \ddots & \ddots & c_{N-1} \\ c_{N-1} & c_{N-2} & \cdots & c_1 & c_0 \end{bmatrix}.$$

The eigenvalues of this matrix are given by

$$\lambda_j = \sum_{k=0}^{N-1} c_k [\exp(2\pi i j/N)]^{N-k}$$

where $i = \sqrt{-1}$ and $j = 0, \ldots, N-1$. For stability analysis, we are concerned with the sign of the real parts of these eigenvalues:

$$\begin{aligned}
\mathrm{Re}(\lambda_j) &= c_0 + c_{N-1}\cos(2\pi j/N) + c_{N-2}\cos(4\pi j/N) + \cdots \\
&\quad + c_2\cos(2(N-2)\pi j/N) + c_1\cos(2(N-1)\pi j/N) \\
&= c_0 + (c_1 + c_{N-1})\cos(2\pi j/N) + (c_2 + c_{N-2})\cos(4\pi j/N) + \cdots
\end{aligned}$$

Second nearest neighbors

Consider the case that $w_1, w_2 > 0$. Recall that our solution is given by $\phi_i = \psi,\ i = 0, \ldots, N-1$ where ψ is a constant (and an integer multiple of $2\pi/N$). Define the odd part of the function H as given by $g(x) = \frac{1}{2}[H(x) - H(-x)]$. Then the nonzero entries of $\hat{J}$ are given by

$$\begin{aligned}
c_0 &= -w_1\left[H'(-\psi) + H'(\psi)\right] - w_2\left[H'(2\psi) + H'(-2\psi)\right] \\
&= -2w_1 g'(\psi) - 2w_2 g'(2\psi), \\
c_1 &= w_1 H'(-\psi) + w_2\left[H'(-2\psi) - H'(-2\psi)\right] = w_1 H'(-\psi), \\
c_2 &= w_2 H'(2\psi), \\
c_{N-2} &= w_2 H'(-2\psi), \\
c_{N-1} &= w_1 H'(\psi) + w_2\left[H'(2\psi) - H'(2\psi)\right] = w_1 H'(\psi).
\end{aligned}$$

Note that $\lambda_0 = \sum c_k = 0$, i.e., there is always a zero eigenvalue. Thus to guarantee stability of the solution we need only find a condition that makes $\mathrm{Re}(\lambda_j) < 0$ for $j = 1, \ldots, N-1$. Now the zero eigenvalue is due to the fact that the variables are not independent but satisfy the constraint (2.10). Thus solutions must lie on the $N-1$ dimensional invariant subspace defined by this constraint. The eigenvalue conditions above give asymptotic stability within this subspace. Now

$$\begin{aligned}
\mathrm{Re}(\lambda_j) &= -2w_1 g'(\psi) - 2w_2 g'(2\psi) + 2w_1 g'(\psi)\cos(2\pi j/N) \\
&\quad + 2w_2 g'(2\psi)\cos(4\pi j/N) \\
&= -2w_1 g'(\psi)[1 - \cos(2\pi j/N)] - 2w_2 g'(2\psi)[1 - \cos(4\pi j/N)] \\
&= -2\left[1 - \cos(2\pi j/N)\right]\left[w_1 g'(\psi) + 2w_2 g'(2\psi)\left(1 + \cos(2\pi j/N)\right)\right].
\end{aligned}$$

Noting that $\cos(2\pi j/N) = \cos(2\pi(N-j)/N)$ yields the conditions for (asymptotic) stability:

$$w_1 g'(\psi) + 2w_2 g'(2\psi)\left(1 + \cos(2\pi j/N)\right) > 0, \quad 1 \le j \le \lfloor N/2 \rfloor, \tag{3.4}$$

where $\lfloor N/2 \rfloor$ is the greatest integer less than or equal to $N/2$. This set of inequalities can be reduced to one as follows

$$\begin{aligned}
w_1 g'(\psi) + 2w_2 g'(2\psi)\left(1 + \cos(2\pi\lfloor N/2 \rfloor/N)\right) > 0 &\quad \text{if } g'(2\psi) \ge 0 \\
w_1 g'(\psi) + 2w_2 g'(2\psi)\left(1 + \cos(2\pi/N)\right) > 0 &\quad \text{if } g'(2\psi) < 0.
\end{aligned} \tag{3.5}$$

Recall that if ψ is a solution then so is $2\pi - \psi$. In fact these solutions are strongly related.

THEOREM 3.2. *The solutions ψ and $2\pi - \psi$ have the same stability.*

Proof. Since $g(\psi)$ is an odd, 2π-periodic function, $g'(\psi)$ is an even, 2π-periodic function. It follows that

$$g'(2\pi - \psi) = g'(-\psi) = g'(\psi)$$

and

$$g'(2(2\pi - \psi)) = g'(4\pi - 2\psi) = g'(-2\psi) = g'(2\psi).$$

Thus the stability conditions (3.5) are identical for the solutions ψ and $2\pi - \psi$. □

The stability conditions (3.5) simplify in some special cases as we now discuss. Recall that the synchronous solution corresponds to $\psi = 0$. In this case, the real part of the j^{th} eigenvalue is given by

$$\mathrm{Re}(\lambda_j) = -2g'(0)\left[1 - \cos(2\pi j/N)\right]\left[w_1 + 2w_2(1 + \cos(2\pi j/N))\right].$$

We conclude that in order to have (asymptotic) stability, we need only require $g'(0) > 0$. Thus the stability of the synchronous solutions is *independent of the size of the network and the connection strengths.* We conjecture that this will hold for an arbitrary number of connections. It can be shown for all-to-all coupling using the results of [21].

If N is an even number, the conditions for stability become:

- $g'(\psi) > 0$, and
- $\dfrac{w_1}{w_2} > -\dfrac{2g'(2\psi)\,(1 + \cos(2\pi/N))}{g'(\psi)}$, if $g'(2\psi) < 0$.

The second condition can be replaced by the following size independent condition

$$\frac{w_1}{w_2} > -\frac{4g'(2\psi)}{g'(\psi)}, \text{ if } g'(2\psi) < 0.$$

Nearest neighbors

If the neurons are only connected to their nearest neighbors then $w_2 = 0$ and the eigenvalues for the solution become

$$\begin{aligned}\mathrm{Re}(\lambda_j) &= c_0 + (c_1 + c_{N-1})\cos(2\pi j/N)\\ &= -g'(\psi)\frac{w_1}{2}(1 - \cos(2\pi j/N)).\end{aligned}$$

Thus the solution is asymptotically stable if

$$g'(\psi) > 0. \tag{3.6}$$

This has several consequences. First, the stability of the solution is *independent of the network size.* Second, if two solutions have the same phase difference ψ then the stability will be the same. In particular, the stability of the n cluster solution $\psi = m2\pi/n$ in a network with $N = pn$, is the same as the stability of the corresponding splay solution in a network with n neurons. The simplest example of this is that the stability of the 2-cluster solution in any network with N even is the same as the stability of the anti-phase solution in a network with 2 elements.

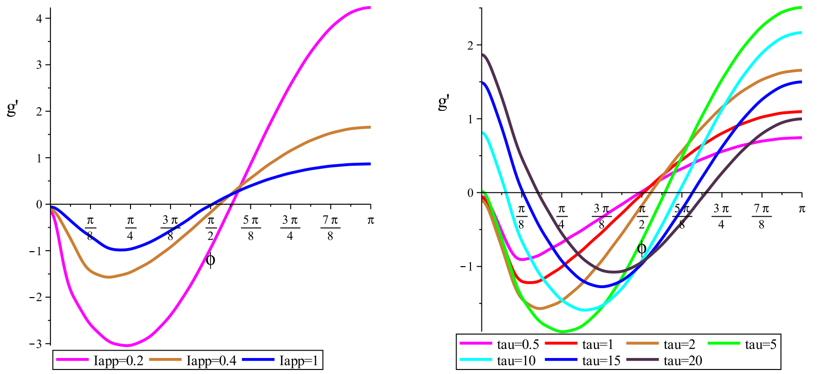
Finally, we compare the stability of solutions in networks with single and two nearest neighbors. Recalling the conditions for stability for a network with N even, it is clear that if a solution is unstable for a network with single nearest neighbor connections then it is unstable for a network with two nearest neighbor connections. However, if N is odd then a solution ψ which is unstable for any network with single nearest neighbor connections ($g'(\psi) < 0$) will be stable for a network with two nearest neighbor connections only if $g'(2\psi) > 0$ and the first condition of (3.5) is satisfied.

3.3. Application to the Inhibitory Network. The results above apply to *any* network of identical oscillators with two nearest neighbor coupling. We now apply those results to predict when clustering can occur in our model of an inhibitory network.

The interaction function H may be calculated from equation (2.7) given a numerical representation of the periodic solution of the single cell model. This computation may be done in the numerical simulation package XPPAUT as described in [8]. The shape of the function depends on the periodic solution and also the coupling in the network. We computed H with the parameters as described in Section 2, but varying I_{app} and τ_{inh}. For each set of parameters, we then used XPPAUT to find a representation of H as a truncated Fourier series containing 30 terms. Note that it is only the derivative of the odd part of H, i.e., g', that is relevant to the stability. We used the Fourier series to calculate g' and then plotted this as a function of ϕ to obtain Figure 2. Varying I_{app} has a small effect on the stability. This is not too surprising. As seen from Figure 1, varying I_{app} in the range $[0, 5]$ has a large effect on the period of the limit cycle, but a small effect on the shape as it has no effect on the coupling. Varying τ_{inh} only affects the coupling. It can have a profound effect as it determines how long the inhibition of the postsynaptic neuron persists after a spike from the presynaptic neuron. Based on these computations we can make the following predictions.

Recall that with single nearest neighbor coupling, a solution with all phase differences equal to ψ will be stable if $g'(\psi) > 0$. This is easy to check just by looking at Figure 2, which was generated by using the Fourier series for g' as described above. We can make the following observations based on the Fourier series for g'.

1. The synchronous or 1-cluster solution (corresponding to $\phi = 0$) is unstable for fast synaptic decay (small τ_{inh}) and stable for slow synaptic decay (large τ_{inh}).
2. The 2-cluster solution (corresponding to $\phi = \pi$) is stable with nearest neighbor coupling for all values of the parameters we have



(a) Varying the applied current. (b) Varying the decay time of the synapse

FIG. 2. *Effect of two parameters on the derivative of the odd part of the interaction function, $g'(\phi)$. Other parameters are as described in section 2. The results are displayed for ϕ between 0 and π because $g'(\phi)$ is symmetric with respect to $\phi = \pi$.*

considered. Note that this solution only exists if the number of neurons in the network is even.

3. If $\frac{11}{16}\pi < \psi < \frac{21}{16}\pi$ then the solution is stable with $I_{app} = 0.4$ for all $\tau_{inh} \leq 20$ that we checked.
4. If $0 < \psi < \frac{\pi}{2}$ then the solution is unstable if $\tau_{inh} \leq 5$.
5. The stability of the splay state depends on the number of neurons in the network. If N is large then $2\pi/N$ is small and the stability is similar to that of the synchronous solution.

We illustrate our results for the n-cluster solutions with $n \leq 10$, with both single nearest neighbor ($w_1 = 1,\ w_2 = 0$) and two nearest neighbor ($w_1 = 1 = w_2$) coupling. The variation of the stability with the synaptic decay constant and the coupling type is shown in Table 2. To begin, we note that for both single and two nearest neighbors there is multistability. The 2-cluster and 3-cluster solutions are stable for large ranges of τ_{inh} with both types of coupling, while others are stable for smaller ranges of τ_{inh} and/or only with single nearest neighbor coupling. As shown in Figure 2(b) increasing τ_{inh} stabilizes the synchronous solution; this can also destabilize a stable solution ($\psi = \frac{4\pi}{7}, \frac{10\pi}{7}$). Further, changing from single nearest neighbor to two nearest neighbor coupling can either cause stability ($\psi = \frac{4}{7}\pi$, $\tau_{inh} = 5$) or cause instability ($\psi = \frac{6\pi}{7}, \frac{8\pi}{7}$, all τ_{inh}). Solutions with phase difference close to 0 have $2\psi \approx \psi$, thus their stability

n	ψ	Nearest Neighbor	Two Nearest Neighbors
1	0	unstable $\tau_{inh} \leq 2$	unstable $\tau_{inh} \leq 2$
2	π	stable all $\tau_{inh} \leq 20$	stable all $\tau_{inh} \leq 20$
3	$\frac{2\pi}{3}, \frac{4\pi}{3}$	stable $\tau_{inh} \leq 15$	stable $\tau_{inh} \leq 15$
4	$\frac{\pi}{2}, \frac{3\pi}{2}$	stable $\tau_{inh} \leq 0.05$	stable $\tau_{inh} \leq 0.05$
5	$\frac{2\pi}{5}, \frac{8\pi}{5}$	unstable all $\tau_{inh} \leq 20$	unstable all $\tau_{inh} \leq 20$
	$\frac{4\pi}{5}, \frac{6\pi}{5}$	stable all $\tau_{inh} \leq 20$	unstable all $\tau_{inh} \leq 20$
6	$\frac{\pi}{3}, \frac{5\pi}{3}$	unstable all $\tau_{inh} \leq 20$	unstable all $\tau_{inh} \leq 20$
7	$\frac{2\pi}{7}, \frac{12\pi}{7}$	unstable all $\tau_{inh} \leq 20$	unstable all $\tau_{inh} \leq 20$
	$\frac{4\pi}{7}, \frac{10\pi}{7}$	stable $\tau_{inh} \leq 2$	stable $\tau_{inh} \leq 5$
	$\frac{6\pi}{7}, \frac{8\pi}{7}$	stable all $\tau_{inh} \leq 20$	unstable all $\tau_{inh} \leq 20$
8	$\frac{\pi}{4}, \frac{7\pi}{4}$	unstable all $\tau_{inh} \leq 20$	unstable all $\tau_{inh} \leq 20$
	$\frac{3\pi}{4}, \frac{5\pi}{4}$	stable all $\tau_{inh} \leq 20$	stable $\tau_{inh} \leq 2$
9	$\frac{2\pi}{9}, \frac{16\pi}{9}$	unstable all $\tau_{inh} \leq 20$	unstable all $\tau_{inh} \leq 20$
	$\frac{4\pi}{9}, \frac{14\pi}{9}$	unstable all $\tau_{inh} \leq 20$	unstable all $\tau_{inh} \leq 20$
	$\frac{8\pi}{9}, \frac{10\pi}{9}$	stable $\tau_{inh} \leq 15$	unstable all $\tau_{inh} \leq 20$
10	$\frac{\pi}{5}, \frac{9\pi}{5}$	unstable all $\tau_{inh} \leq 20$	unstable all $\tau_{inh} \leq 20$
	$\frac{3\pi}{5}, \frac{7\pi}{5}$	stable $\tau_{inh} \leq 5$	stable $\tau_{inh} \leq 5$

TABLE 2

Phase model prediction of stability for n-cluster solution of the inhibitory network model corresponding to solution with ψ as given. Note that solution $2\pi - \psi$ must have same stability. Nearest neighbor coupling corresponds to $w_1 = 1, w_2 = 0$ in (2.9), while two nearest neighbor coupling corresponds to $w_1 = w_2 = 1$. Stability was explicitly checked for the values of τ_{inh} shown in Figure 2(b) and extrapolated to other values based on the variation of g' with respect to τ_{inh} shown in that figure.

is not affected much by the switch from single to two nearest neighbor coupling. As is clear from the expression for the eigenvalues (3.5), if more weighting is put on the second nearest neighbor coupling ($w_2 > w_1$) then the addition of this coupling can have more effect on the stability. For large enough w_2 the 2-cluster solution can be destabilized.

4. Numerical Simulations. Numerical simulations of the full model (2.2) were carried out in MATLAB (The MathWorks Inc., Natick, MA), using a 2nd-order Runge Kutta algorithm (ode23) that implements a variable time step, with the parameter values as described in section 2. In the following we show several numerical simulations that verify the predictions of the phase model. Then we show some behaviour not predicted by the phase model.

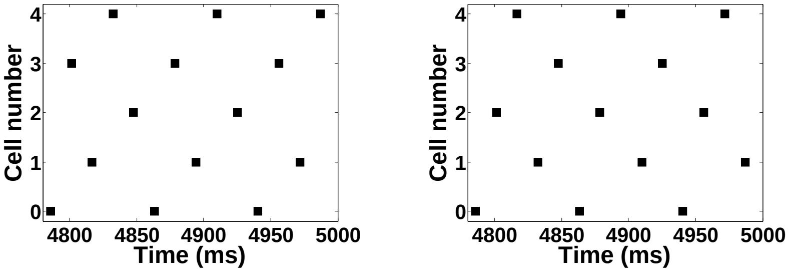
We studied networks with $N = 2 - 10$ neurons, $\tau_{inh} = 2$ ms and one or two nearest neighbor coupling. As an example, consider a network with $N = 5$ neurons. Since N is prime, the network has the synchronous solution and four splay solutions. These latter are described in Table 3 with stability for $\tau_{inh} \in [0.5, 20]$ as predicted by the phase model using Figure 2(b). The numerical simulations agreed with these predictions. The splay states with

Phase difference, ψ	Firing sequence	Phase model	Numerics
$\frac{2\pi}{5}$	$0, 1, 2, 3, 4$	unstable	not found
$\frac{4\pi}{5}$	$0, 3, 1, 4, 2$	stable	found
$\frac{6\pi}{5}$	$0, 2, 4, 1, 3$	stable	found
$\frac{8\pi}{5}$	$0, 4, 3, 2, 1$	unstable	not found

TABLE 3

Stability of splay states for a network of 5 neurons with single nearest neighbor coupling and synaptic decay time $\tau_{inh} = 2$ *ms.*

$\psi = \frac{4\pi}{5}, \frac{6\pi}{5}$ were found but not the other two. See Figure 3.



(a) $\psi = \frac{4\pi}{5}$

(b) $\psi = \frac{6\pi}{5}$

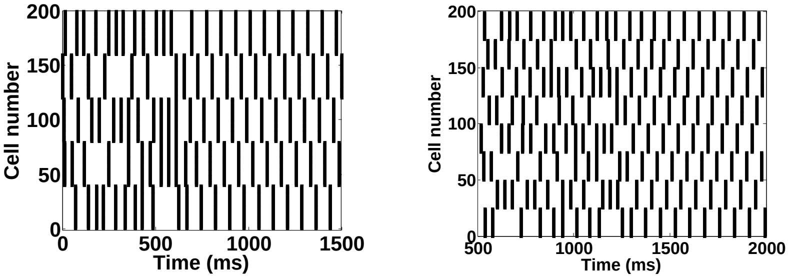
FIG. 3. *Raster plots for two splay (*5*-cluster) solutions in a network with* 5 *neurons and synaptic connections between first nearest neighbors.*

Numerically, we were able to verify the stability of the majority of the n-cluster solutions predicted by the phase model for $N = 2 - 10$ as shown in Table 2. We were not able to find the 4-cluster solutions numerically even with very short synaptic decay rates ($\tau_{inh} \leq 0.05$) that the phase model predicted was necessary for stability. In the $N = 4$ network, the cells tended to the 2-cluster solution with $\psi = \pi$. We were also unable to numerically obtain the $\psi = \frac{4\pi}{7}, \frac{10\pi}{7}$ solutions and the $\frac{3\pi}{5}, \frac{7\pi}{5}$ solutions with single nearest neighbor coupling, and the $\psi = \frac{3\pi}{4}, \frac{5\pi}{4}$ solutions with two nearest neighbor coupling. For the $\psi = \frac{8\pi}{9}, \frac{10\pi}{9}$ solution with single nearest neighbor coupling and the $\psi = \frac{3\pi}{5}, \frac{7\pi}{5}$ solution with two nearest neighbor coupling, instead of a 9-cluster and 10-cluster solution, respectively, in which each cell fired one spike per cluster cycle, we found cluster solutions in which each cell fired two spikes, or a doublet, during each cluster cycle. Below we discuss these doublet solutions in more detail.

In networks with larger numbers of cells, $N = np$, we were able to numerically find all the n-cluster solutions that we found with $N = n$. For example, consider a network with $N = 200$ neurons. Our analysis predicts that there should be stable 5-cluster solutions corresponding to the stable splay states in the 5 neuron network, i.e., $\psi = \frac{m}{5}2\pi$ with $m = 2, 3$. In these solutions, each cluster contains 40 cells with clusters given by $C_0 = \{0, 5, 10, \ldots, 195\}$, $C_1 = \{1, 6, 11, \ldots, 196\}$, $C_2 = \{2, 7, 12, \ldots, 197\}$, $C_3 = \{3, 8, 13, \ldots, 198\}$ and $C_4 = \{4, 9, 14, \ldots, 199\}$. The phase difference between clusters is $\frac{2\pi}{5}$. In the 5-cluster solution corresponding to $m = 2$, the cluster firing order is $\{C_0, C_3, C_1, C_4, C_2\}$ and $\psi = 2\frac{2\pi}{5} = \frac{4}{5}\pi$. For $m = 3$, the cluster firing order is $\{C_0, C_2, C_4, C_1, C_3\}$ and the phase difference between nearest neighbor cells is $\psi = 3\frac{2\pi}{5} = \frac{6}{5}\pi$. See Figure 4(a).

Our analysis of the phase model predicts that in this same network, two stable 8-cluster solutions exist with phase difference between nearest neighbors $\psi = \frac{3\pi}{4}, \frac{5\pi}{4}$ (see Table 2). In these solutions, each cluster contains 25 cells: $C_0 = \{0, 8, 16, \ldots, 192\}$, $C_1 = \{1, 9, 17, \ldots, 193\}$, $C_2 = \{2, 10, 18, \ldots, 194\}$, $C_3 = \{3, 11, 19, \ldots, 195\}$, …, $C_7 = \{7, 15, 23, \ldots, 199\}$. For the 8-cluster solution corresponding to $\psi = \frac{3\pi}{4}$, the cluster firing order is $\{C_0, C_3, C_6, C_1, C_4, C_7, C_2, C_5\}$. For $\psi = \frac{5\pi}{4}$, the clusters fire in the following order $\{C_0, C_5, C_2, C_7, C_4, C_1, C_6, C_3\}$. The phase difference between successively firing clusters is $\frac{\pi}{4}$. See Figure 4(b).

There were some cases where the numerically observed stability of n-cluster solutions did not agree with that predicted by the phase model. While the 3-cluster solution was numerically stable in networks with $N = 3p$ cells and single nearest neighbor coupling, with two nearest neighbor coupling, the maximal synaptic conductance g_{syn} had to be weaker (0.1 instead of 0.2 mS/cm^2) to numerically find these solutions. Additionally, recall that the phase model predicted that the 2-cluster solution is stable for all networks with an even number of neurons and either single or two nearest neighbor coupling. This solution corresponds to the network breaking into two clusters $C_0 = \{0, 2, 4, \ldots, N-2\}$ and $C_1 = \{1, 3, 5, \ldots, N-1\}$, with phase difference $\psi = \pi$ between nearest neighbors. We found this solution numerically in networks with single nearest neighbor coupling and $N = 2, \ldots, 200$. However, with two nearest neighbor coupling we did not find this solution numerically. Closer consideration of the eigenvalues in this case shows that the stability is weaker, in the sense that the magnitude of the real part of the eigenvalues is smaller. Thus it is possible that the solution has a smaller basin of attraction and is harder to find numerically. Alternatively, the phase model may no longer accurately predict the network behaviour as the coupling is too strong. In these networks, a different 2-cluster solution was found when $N = 4p$ in which $C_0 = \{0, 1, 4, 5, \ldots, N-4, N-3\}$ and $C_1 = \{2, 3, 6, 7, \ldots, N-2, N-1\}$.



(a) 5 clusters

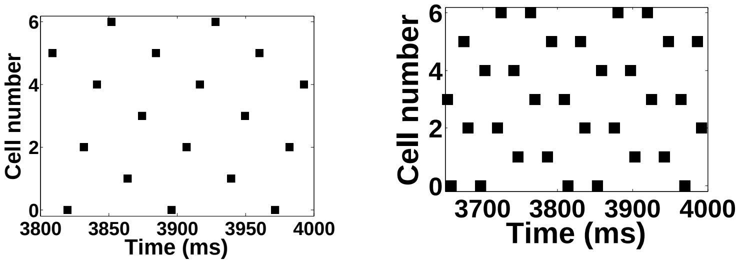
(b) 8 clusters

FIG. 4. *Raster plots showing evolution to stable* 5*-cluster solution (a) and* 8*-cluster solution (b) in a network with* $N = 200$ *and synaptic connections between first nearest neighbors. The cell order was re-permuted such that the cluster solutions are clearly visualized.*

In this solution, the phase difference between every nearest neighbor is not the same. We discuss these 2-cluster solutions in more detail below.

4.1. Further investigation. In some networks we observe a different type of N-cluster/splay solution in which there is 1 cell in each cluster but the cells fire 2 consecutive spikes (doublets), rather than single spikes in each cluster cycle (see Figure 5(b)). These solutions can be characterized by the fixed phase difference, ψ, between the first spikes fired by nearest neighbor cells. The doublet N-cluster solution has the same character as the single spike N-cluster solution with the same ψ. The cells fire in the same order but they are able to fire off 2 spikes before inhibition from other cells arrives to suppress their firing. The phase difference between the first spikes of cells that fire consecutively is $\frac{2\pi}{N}$. The doublet splay solutions were only observed when the corresponding regular (single spike) splay solutions were predicted to be stable by the phase model. In some networks we observed the doublet and regular splay solutions corresponding to the same ψ coexisting (Figure 5). In other networks only the doublet splay solution was observed, as noted above for the $\psi = \frac{8\pi}{9}, \frac{10\pi}{9}$ solution with single nearest neighbor coupling and the $\psi = \frac{3\pi}{5}, \frac{7\pi}{5}$ solution with two nearest neighbor coupling.

Numerically, we observe different 2-cluster solutions in networks with



(a)

(b)

FIG. 5. *Single spike firing and doublet spike firing splay solutions in a network with $N = 7$ and synaptic connections between first nearest neighbors. Raster plots for 7-cluster solutions associated with $\psi = \frac{8\pi}{7}$ for single spike firing (a) and doublet spike firing (b).*

$N = 4k$ where k is an integer, as shown in Figure 6. These are not in the form of the solutions discussed above as the phase difference between left and right nearest neighbors is not the same. They are described by the following.

THEOREM 4.1. *If $N = 4k$ for some integer k, then the system (2.9) admits solutions of the form*

$$\phi_1 = \phi_3 = \cdots = \phi_{N-1} = \psi, \qquad \phi_2 = \phi_4 = \cdots = \phi_N = \pi - \psi. \tag{4.1}$$

Proof. Substitution shows that the form (4.1) satisfies the equilibrium equations (3.1). Applying the constraint shows

$$\frac{N}{2}(\psi + \pi - \psi) = 2k\pi$$

which is only satisfied if $N = 4k$. □

The solutions in Figure 6 are described by $\psi = 0$. Thus these solutions have the two clusters

$$\hat{C}_0 = \{0, 1, 4, 5, \ldots\}, \quad \hat{C}_1 = \{2, 3, 6, 7 \ldots\}.$$

Another 2-cluster solution is given by $\psi = \pi$ with clusters

$$\bar{C}_0 = \{0, 3, 4, 7, \ldots\}, \quad \bar{C}_1 = \{1, 2, 5, 6, \ldots\}.$$

It is easy to see that four 4-cluster solutions also exist and are given by

$$\psi = \frac{\pi}{4},\ \frac{3\pi}{4},\ \frac{5\pi}{4},\ \frac{7\pi}{4}.$$

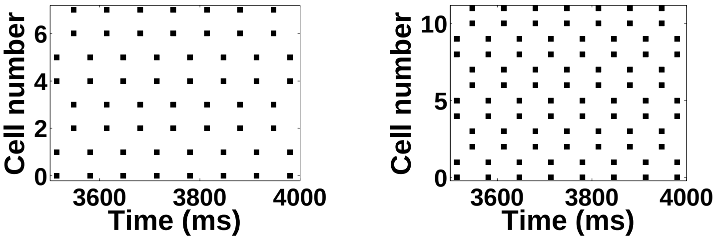


FIG. 6. *Two cluster solutions of the form (4.1) with* $\psi = 0$ *for* $N = 8$ *and* $N = 12$*.*

The stability of these cluster solutions cannot be determined by the analysis of section 3 as the Jacobian matrix is not circulant. However, the 2-cluster solutions seem quite robustly stable in networks with both single and two nearest neighbor coupling.

To supplement our analysis, we investigated the addition of further connections to the network. Our simulations showed that adding more connections could stabilize unstable N-cluster or splay solutions. For example, in a network with $N = 9$ neurons, the 9-cluster solutions defined by $\psi = \frac{4\pi}{9}, \frac{14\pi}{9}$ which the theory predicted and numerics confirm are unstable with single nearest and two nearest neighbor coupling, were numerically found with three nearest neighbor coupling. Similar results for N-cluster solutions in other networks with $N > 5$ led to the following.

CONJECTURE 4.1. *Consider an* N *cell network with* N *odd. Let* $p_1 = \frac{N-1}{2}$ *and* $p_2 = \frac{N+1}{2}$*. If* $gcd\{p_1, N\} = 1$ *and* $gcd\{p_2, N\} = 1$*, then two* N*-cluster solutions exist and are stable when the connectivity radius* $r = \frac{N-3}{2}$*. The* N*-cluster solutions have the following properties:*

- *Associated with* p_1*: firing order* $\{i_1, i_2, \dots, i_N\}$ *where* $i_s = (s-1)p_1 \pmod{N}$*,* $\psi = (N-2)\frac{2\pi}{N}$
- *Associated with* p_2*: firing order* $\{i_1, i_2, \dots, i_N\}$ *where* $i_s = (s-1)p_2 \pmod{N}$*,* $\psi = 2\frac{2\pi}{N}$

In these cluster solutions, these specific values p_1 and p_2 dictate a firing order and the connectivity radius r is sufficiently large so that during the majority of the cluster solution cycle, a cell in the network is inhibited by successively firing cells. For example, consider the cluster solution associated with p_1. The firing order starting at cell 0 is the following:

1: 0
2: $p_1 = \frac{N-1}{2}$
3: $2p_1 = 2\frac{N-1}{2} = N - 1$
4: $3p_1 = 3\frac{N-1}{2} = \frac{3N-3}{2} \pmod{N} = \frac{N-3}{2}$
5: $4p_1 = 4\frac{N-1}{2} = \frac{4N-4}{2} \pmod{N} = N - 2$
$\vdots$

N-1: $(N-2)p_1 = (N-2)\frac{N-1}{2} = N\frac{N-1}{2} - N + 1 = N(\frac{N-3}{2}) + 1 = 1 \pmod{N}$

N: $(N-1)p_1 = (N-1)\frac{N-1}{2} = \frac{(N-1)N}{2} - \frac{N-1}{2} = -\frac{N-1}{2} \pmod{N} = \frac{N+1}{2} \pmod{N}$

With connectivity radius $r = \frac{N-3}{2}$, each cell in the network sends synaptic inhibition to every other cell in the network except for itself and the cells $\frac{N-1}{2}$ and $\frac{N+1}{2}$ steps away from it. Cell 0, for example, receives inhibition from all cells except for cell $\frac{N-1}{2}$ and cell $\frac{N+1}{2}$. Thus, in this solution, cell 0 is inhibited as every cell in the network fires except the cells that fire immediately after and immediately before it. The symmetry in the network and the firing order guarantees that this is true for every cell in the network. The firing order dictated by p_1 ensures that every cell receives continuous inhibition except in a short time window around the time when the cell is supposed to fire.

The N-cluster solution associated with p_2 has the opposite firing order as the solution associated with p_1. Specifically, in the firing order starting at cell 0, cell $\frac{N+1}{2}$ fires immediately after cell 0 and cell $\frac{N-1}{2}$ fires immediately before it. Since the network connectivity is the same, the firing order ensures successive, uninterrupted synaptic inhibition except in the time window around the time when a cell is supposed to fire.

This N-cluster solution does not seem to be stable numerically for N even. In this case, with connectivity radius $r < \frac{N}{2}$, each cell will not receive inhibition from the cell $\frac{N}{2}$ places away from it. That cell is also in position $\frac{N}{2}$ in the cluster solution firing order. So, in the middle of the cluster cycle, there will be a break in the inhibition that a cell receives, allowing a window for it to fire out of turn. We note that if additional connections were added between cells i and $i + \frac{N}{2}$ for $i = 0, \dots, N-1$, then the break in inhibition would not occur and an N-cluster solution could be stable. We do not further discuss this case as the coupling is not nearest neighbor, thus the Jacobian matrix would not be circulant and our analysis would not apply.

5. Discussion.

In this paper we considered a network of inhibitory interneurons with nearest neighbor coupling and periodic boundary conditions. Thus, the cells compose a 1-dimensional ring. We used a phase model approach to derive conditions for the existence and stability of solutions in which all cells in the network fire repetitively, so none are completely suppressed, and all cells have equal phase differences with their nearest neighbor in ascending order around the network. In particular, we focused on *cluster solutions* where the neurons break into subgroups. Elements within a group are synchronized, while elements in different groups are phase-locked with some nonzero phase difference.

We first derived conditions that can be applied to *any* network with up to two nearest neighbor coupling. Our existence results can be summarized as follows. An network with N elements has N solutions of the form described above. The minimum number of clusters is 1 and the maximum number is N. The network always admits one synchronous or 1-cluster solution. The network always admits at least two N-cluster or splay solutions. If N is prime then it has the 1-cluster solution and $N-1$ splay solutions. If N is even then it has one 2-cluster solution. For every nontrivial factor $n \neq 2$ of N the network has at least two n-cluster solutions. Our stability analysis showed that for a network with single nearest neighbor coupling the stability depends only on the value, ψ, of the phase difference between nearest neighbors. For a network with two nearest neighbor coupling the stability depends on the value of the phase difference between nearest neighbors and next nearest neighbors, the relative sizes of the coupling strengths and the size of the network.

We then applied these conditions to our particular interneuron network and compared the results to numerical simulations of the full network. For single nearest neighbor coupling solutions, we found (both analytically and numerically) that solutions with nearest neighbor phase difference close to half a period were robustly stable. Solutions where this phase difference was close to zero were largely unstable. The stability results can be understood from a biological standpoint as follows. In the splay solution, each cell fires once in a fixed sequence that then repeats, defining the cluster period 2π. In general, one does not expect nearest neighbor cells in the network to fire in successive order since they inhibit each another. For this reason we may expect the synchronous solution and splay solutions which have a firing order where nearest neighbors fire close together to be unstable for our inhibitory network. Similarly, one may expect that stable cluster solutions will not have nearest neighbors in the same cluster. However, it is well documented that slow synapses may lead to counter-intuitive synchronization properties [24] and our model is no different. If the decay time of the synapse is long enough then the synchronous solution and other solutions one may "expect" to be unstable are stable.

Our analysis shows that changing to two nearest neighbor coupling could destabilize or stabilize solutions. In the examples we considered destabilization was more common, but this could be changed if the relative strengths of nearest and second nearest neighbor synaptic connections were changed.

This variation of stability with coupling is the key result that supports the hypothesis that cluster solutions may play a role in cell assemblies. Let us consider an example to illustrate this. Consider a network with 15 neurons. Our analysis shows that for single nearest neighbor coupling there are two stable 3-cluster states and two stable 5-cluster states. The 5-cluster states are more stable in the sense that the real part of the eigenvalue is larger. With second nearest neighbor coupling the 5-cluster states lose stability leaving only the 3-cluster state. Thus switching from nearest neighbor to second nearest neighbor coupling gives a mechanism where the system can switch from a 5-cluster state to a 3-cluster state, thus reorganizing which neurons spike together.

Since our stability results depend on the number of clusters and not the size of the network, our results for the synchronous (1-cluster) solution and the 2-cluster solution can be compared to results for synchronous and anti-phase solutions in pairs of coupled neurons. As mentioned above for the parameter values we have considered numerically, the model is close to a SNIC bifurcation and hence can be considered as a Type I oscillator. Our results are consistent with those for pairs of Type I oscillators found by Ermentrout [7]. Based on results for pairs of Type II oscillators [24] we conjecture that in networks of Type II oscillators the stability results would be different than what we observe for Type I. In particular, we expect that, for fast synapses, the synchronous solution would be stable and the antiphase solution unstable, but that this could be reversed for slower synapses.

Acknowledgments

The work described in this article is a result of a collaboration made possible by the IMA's workshop, *WhAM! A Research Collaboration Workshop for Women in Applied Mathematics: Dynamical Systems with Applications to Biology and Medicine*.

REFERENCES

[1] M. Bartos, I. Vida, M. Frotscher, J. R. P. Geiger, and P. Jonas, *Rapid signaling at inhibitory synapses in a dentate gyrus interneuron network*, J. Neurosci., 21 (2001), pp. 2687–2698.

[2] M. Bartos, I. Vida, M. Frotscher, A. Meyer, H. Monyer, J. R. P. Geiger, and P. Jonas, *Fast synaptic inhibition promotes synchronized gamma oscillations in hippocampal interneuron networks*, Proc. Natl. Acad. Sci., 99(20) (2002), pp. 13222–13227.

[3] C. Choe, T. Dahms, P. Hövel, and E. Schöll, *Controlling synchrony by delay coupling in networks: From in-phase to splay and cluster states*, Physical Review E, 81 (2010), p. 025205.

[4] A. Destexhe, Z. Mainen, and T. Sejnowski, *Kinetic models of synaptic transmission*, in Methods in Neuronal Modeling: From Synapses to Networks, C. Koch and I. Segev, eds., MIT Press, Cambridge, MA, 1998, ch. 1.

[5] G. Dragoi and G. Buzsáki, *Temporal encoding of place sequences by hippocampal cell assemblies*, Neuron, 50 (2006), pp. 145–157.

[6] A. Engel, P. Fries, and W. Singer, *Dynamic predictions: oscillations and synchrony in top–down processing*, Nature Reviews Neuroscience, 2 (2001), pp. 704–716.

[7] G. Ermentrout, *Type I membranes, phase resetting curves, and synchrony*, Neural Computation, 8 (1996), pp. 979–1001.

[8] ———, *Simulating, analyzing, and animating dynamical systems: a guide to XPPAUT for researchers and students*, vol. 14, SIAM, 2002.

[9] G. Ermentrout and N. Kopell, *Frequency plateaus in a chain of weakly coupled oscillators I*, SIAM J. Applied Math., 15 (1984), pp. 215–237.

[10] ———, *Multiple pulse interactions and averaging in couple neural oscillators*, J. Math. Biol., 29 (1991), pp. 195–217.

[11] G. Ermentrout and D. Terman, *Mathematical Foundations of Neuroscience*, Springer, New York, NY, 2010.

[12] R. Galán, G. Ermentrout, and N. Urban, *Predicting synchronized neural assemblies from experimentally estimated phase-resetting curves*, Neurocomputing, 69 (2006), pp. 1112–1115.

[13] D. Golomb and J. Rinzel, *Clustering in globally coupled inhibitory neurons*, Physica D, 72 (1994), pp. 259–282.

[14] K. Harris, J. Csicsvari, H. Hirase, G. Dragoi, and G. Buzsáki, *Organization of cell assemblies in the hippocampus*, Nature, 424 (2003), pp. 552–556.

[15] A. Hodgkin and A. Huxley, *A quantitative description of membrane current and its application to conduction and excitation in nerve*, Journal of Physiology, 117 (1952), pp. 500–544.

[16] F. Hoppensteadt and E. Izhikevich, *Weakly connected neural networks*, Springer-Verlag, New York, 1997.

[17] J.-C. Lacaille and S. Williams, *Membrane properties of interneurons in stratum oriens-alveus of the CA1 region of rat hippocampus in vitro*, Neuroscience, 36 (1990), pp. 349–359.

[18] G. Laurent and H. Davidowitz, *Encoding of olfactory information with oscillating neural assemblies*, Science, 265 (1994), pp. 1872–1875.

[19] Y.-X. Li, *Clustering in neural networks with heterogeneous and asymmetrical coupling strengths*, Physica D, 180 (2003), pp. 210–234.

[20] Y.-X. Li, Y.-Q. Wang, and R. Miura, *Clustering in small networks of excitatory neurons with heterogeneous coupling strengths*, J. Computational Neuroscience, 14 (2003), pp. 139–159.

[21] K. Okuda, *Variety and generality of clustering in globally coupled oscillators*, Physica D, 63 (1993), pp. 424–436.

[22] E. Pastalkova, V. Itskov, A. Amarasingham, and G. Buzsáki, *Internally generated cell assembly sequences in the rat hippocampus*, Science, 321 (2008), pp. 1322–1327.

[23] Y. Sakurai, *Hippocampal and neocortical cell assemblies encode memory processes for different types of stimuli in the rat*, The Journal of neuroscience, 16 (1996), pp. 2809–2819.

[24] C. Van Vreeswijk, L. Abbott, and G. Ermentrout, *When inhibition not excitation synchronizes neural firing*, Journal of computational neuroscience, 1 (1994), pp. 313–321.

[25] X.-J. Wang and G. Buzsáki, *Gamma oscillation by synaptic inhibition in a hippocampal interneuronal network model*, J. Neurosci., 16 (1996), pp. 6402–6413.