Intrinsic bursting properties and pattern of activity in spatially distributed networks

Abstract

In previous work we demonstrated that spatially distributed networks with local connectivity patterns can reproduce the spread of synchronous bursting activity in response to brief current stimulation. In contrast periodic stimulation of the same network does not produce any repetitive spatiotemporal pattern in such networks (e.g. sequence of propagating bursting activity). Instead we observed self-sustaining complex patterns of propagating activity, which resemble behaviors seen in a number of different distributed oscillating non-linear chemical systems. In this paper we show that the intrinsic bursting properties of neurons can account for the degree of organization of the repetitive pattern of activity in networks in the presence of periodic stimulation.

Introduction

Traveling waves of activity observed in spatially distributed networks with local connectivity patterns represents abnormal periods of increased excitation and synchronized bursting of large group of neurons. These waves reassemble epileptiform activity (EA) observed in a numerous of experimental models of synchronous neural activity including hippocampal slice (Miles et. al 1988), neocortical slice (Wadman and Gutnick 1993), cultures of dissociated spinal cord neurons (Bergey et. al 1987) and cortical neurons (Chervin et. al 1988). Similar to EA, traveling waves can originate in a one site of the network as a result of stimulation and then rapidly spread through adjacent regions to the other remote sites. Previously we have demonstrated this effect in a network array of neurons with local connectivity pattern (Kudela et. al 1999). In the response to the periodic stimulus we observed in these networks complex interactions of propagating activities which produce irregular spatiotemporal pattern of activity in this network (Kudela et. al 2001). This is in contrast to observed organized recurrent periodic bursting of neurons during EA. The close examination of the observed effects shows that the slow calcium dynamic component in neurons can be responsible for the transition from regular to irregular spatiotemporal activity pattern in network. We investigate how changes in slow calcium dynamic in neurons result in changes of recurrent bursts in neurons and spatiotemporal pattern of activity in network.

Methods

An array of 240 by 240 excitatory and 80 by 80 inhibitory neurons is simulated. Each neuron receives excitatory and inhibitory inputs from nearest neighboring neurons. Repetitive bursting activity in the network is triggered by periodic stimulation of 293 excitatory neurons (0.5% of all) in the center of the array.

Neurons are modeled as single-compartment units using the conductance-based model with a reduced number of variables. During simulation we vary baseline levelsof the intercellular calcium concentration by changing the calcium removal rate parameter or calcium influx parameter. We also alter the recovery time from the AHP process in neurons

Results

The parameters of neuron and synaptic models were selected to allow for propagation of bursts of action potentials along the network. Periodic stimulation with a frequency in the range 2 - 10 Hz produces repetitive bursts in individual neurons and complex spatiotemporal pattern in the network lasting for a long period after the stimulation (up to 10 min). Figure 1 shows the pattern of activity in a 250 x 250 neuronal network emerging in t = 10 sec of simulation. This resembles the behavior seen in a number of different distributed oscillating non-linear chemical systems. The simulation of the network performed with a slow constant decrease of the base line level of the intercellular calcium concentration (by increasing of calcium removal rate parameter R or decreasing calcium influx parameter K_p) results in the emergence of periodic waves of activity that propagate through the network. Figure 2 illustrates the periodic regular pattern of activity in an array of 240x240 excitatory neurons contrasting with complex irregular pattern seen of Figure 1

Discussion

Periodic stimulation of the selected region initiates the activity in the network. The mechanism of spreading of waves is simple: each active region is the source of activity in its adjacent regions. The velocity of spread of the activity between regions may differ because the connections between neurons in network were assigned randomly. Differences in the velocity of propagation result in differences in activation time of the neighboring regions. In situation when bursting activities in two neighboring (but separate) regions are not correlated in time, one can become the source of the secondary activity for the other and vice versa. These secondary activities interlace with activities induced by periodic stimuli. This effect produces gradual disappearance of the recurrent organized spatiotemporal pattern induced by periodic stimuli, initially observed at the onset of stimulation. Burst activities in neurons are regulated by slow calcium regulated potassium dynamics. This means that the ability of neurons to generate bursts is regulated by the afterhyperpolarization (AHP) process in these neurons. The probability of simultaneous activation of two neighboring regions is decreased because the AHP periods in neurons in these two regions may overlap. Weak dependence on AHP increases the chance to synchronize activities in neighboring regions and results in stable periodic spatiotemporal patterns of activity in the network. This effect in observed in simulation of networks when the baseline level of intracellular calcium in neurons gradually decreases (Figure 2).

References

Bergey G.K., Bigalke H. and Nelson P.G. , Differential effects of tetanus toxin on inhibitory and excitatory synaptic transmission in mammalian spinal cord neurons in culture: a presynaptic locus of action for tetanus toxin. J. Neurophysiol. 57:121-131, (1987)

Chervin R.D., Pierce P.A. and Connors B.W., Periodicity and directionality in the propagation of epileptiform discharges across neocortex. J. Neurophysiol. 60:1695-1713, (1988)

Kudela P., Franaszczuk P.J., and Bergey G.K. Model of the propagation of synchronous firing in a reduced neuron network. Neurocomputing, 26-27:411-418, (1999)

Kudela P., Franaszczuk P.J., and Bergey G.K. Periodic stimuli can induce oscillating activity in simulated neural networks. Epilepsia 42:121, (Suppl. 7), 2001

Miles R., Traub R.D. and Wong R.K.S. Spread of synchronous firing in longitudinal slice from the CA3 region of the hippocampus. J. Neurophysiol. 60:1481-1496, (1988)

Wadman W.J. and Gutnick M.J. Non-uniform propagation of epileptiform discharge in brain slice of rat neocortex, Neurosci. 52:255-262 (1993)

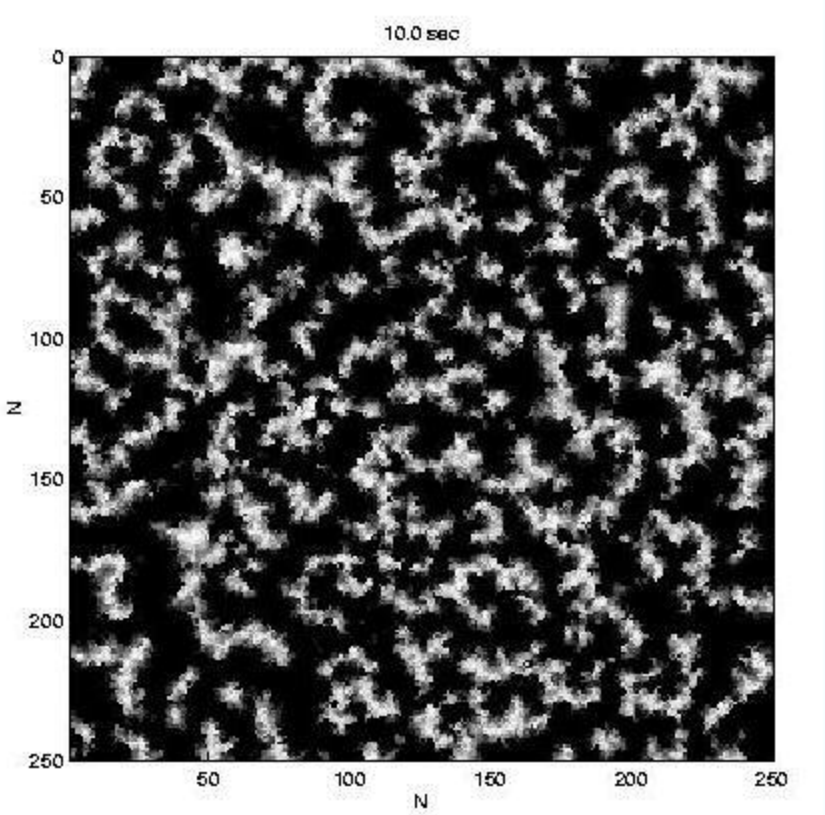

Figure 1 Pattern of activity in an array of 250 by 250 excitatory neurons in t = 10 sec of simulation.

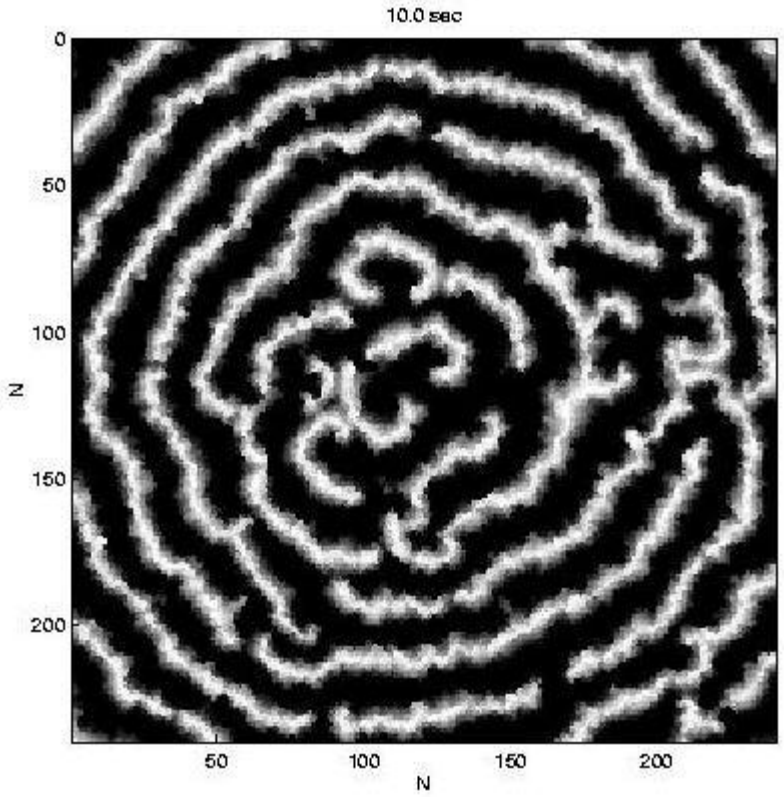

Figure 1 Pattern of activity in an array of 240 by 240 excitatory neurons in t = 10 sec of simulation when the base line level of intracellular calcium concentration was decreased. The parameter R of intracellular calcium removal rate was increasing gradually from 0.006 to 0.01.