Note 3

Yuhang Cai, Tianyi Wu   October 16, 2020

In this note, we will review some results concerning continuous-time Markov chain and introduce two reduced models. In fact, we find that time t is independent of the transition probabilities, which indicates that considering embedded Markov chains is enough to observe gamma oscillations. Therefore, we propose two reduced models, in terms of the full model introduced in Note 1.

1 Continuous-Time Markov Chain

According to the introduction in Note 1, we know that our full model is a continuous-time Markov Chain. Thus, we have a Q-matrix, where each element is a parameter for its corresponding Poisson process. Since the time intervals of a Poisson process follow an exponential distribution, we list some properties of exponential distribution here.

Proposition 1. *Given two independent random variables $X_1 \sim Exp(\lambda_1), X_2 \sim Exp(\lambda_2)$, we have $\min\{X_1, X_2\} \sim Exp(\lambda_1 + \lambda_2)$.*

Corollary 1. *Given n independent random variables $X_1 \sim Exp(\lambda_1), X_2 \sim Exp(\lambda_2), ..., X_n \sim Exp(\lambda_n)$, we have $\min\{X_1, X_2, ..., X_n\} \sim Exp(\lambda_1 + \lambda_2 + \cdots + \lambda_n)$.*

Proposition 2. *Given two independent random variables $X_1 \sim Exp(\lambda_1), X_2 \sim Exp(\lambda_2)$, we have for all $t \geq 0$,*

$$\mathbb{P}(\min\{X_1, X_2\} = X_1 | \min\{X_1, X_2\} = t) = \frac{\lambda_1}{\lambda_1 + \lambda_2}.$$

Corollary 2. *Given n independent random variables $X_1 \sim Exp(\lambda_1), X_2 \sim Exp(\lambda_2), ..., X_n \sim Exp(\lambda_n)$, we have for all $t \geq 0$,*

$$\mathbb{P}(\min\{X_1, X_2, ..., X_n\} = X_i | \min\{X_1, X_2, ..., X_n\} = t) = \frac{\lambda_i}{\lambda_1 + \lambda_2 + \cdots + \lambda_n}.$$

In fact, given a continuous-time Markov chain, we can imagine there are k independent exponential distributed clocks for each states and once a clock rings, the chain will move to its corresponding state. Thus, according to **Corollary 2**, the waiting time will not influence which clock rings first, since the conditional probabilities are fixed.

In other words, it's fine for us to consider embedded Markov chain, since for the time interval between two states, we can generate it later according to the states.

2 Reduced Models

In this section, we will introduce two reduced models. This first model is 2-state reduced model, which is similar to the full model but only has 2 states. We hope the 2-state model can help us find a good partition of neurons into *gate* and *base* neurons. The second model is statistical reduced model. In this model, we focus on the population of the E-neurons and I-neurons instead of caring each single neuron. Hence, we can use four quantities $(N_{GE}, N_{BE}, H^E, H^I)$ to characterize each state.

2.1 2-State Reduced Network Model

As for the elements in the 2-state Reduced model, they are similar to those in the full model, except the **Membrane Potential**.

- We assume that N_E excitatory neurons are labeled $1, 2, ..., N_E$ and N_I inhibitory neurons are labeled $N_E + 1, N_E + 2, ..., N_E + N_I$.

- The **membrane potential** of a neuron i, denoted V_i, only has two states, *gate* and *base*.

- Each neuron receives synaptic input from an **external source** in the form of Poisson kicks; these kicks are independent from neuron to neuron.

Since membrane potential only takes value in two states, the interactions in the reduced model is completely different from those in the full model.

- **External drive to neurons**: The action from external drive to neurons are inputs delivered in the form of impulsive kicks, arriving at random (Poissonian) times and the Poisson processes are independent from neuron to neuron. We assume there are two parameters $\lambda^E, \lambda^I > 0$, representing the rate of the Poisson kicks. When a kick arrives, if $V_i = base$, with probability P_{Ex}^B, V_i will change to *gate*. Otherwise, if $V_i = gate$, with probability P_{Ex}^G, the neuron will spike and V_i change to *base*.

- **Spikes of neurons**: When the membrane potential of a neuron i change from *gate* to *base*, the neuron spikes immediately.

- **Connections of neurons**: We assume the connectivity in our model is random and time-dependent, so that every time a neuron spikes, a random set of postsynaptic neurons is chosen anew. More precisely, for $Q, Q' \in \{E, I\}$, we let $P_{Q,Q'} \in [0, 1]$ be the probability that a neuron of type Q is postsynaptic when a neuron of type Q' spikes, and the set of postsynaptic neurons is determined by a coin flip with these probabilities following each spike.

- **Effects of kicks**: Firstly, we assume an kick received by an neuron takes effect at a random time after its arrival. This delay is given by an exponential random variable with mean τ^E for the excitatory kick and τ^I for the inhibitory kick. We let the H_i^E, H_i^I to denote the number of E-kicks and I-Kicks received by neuron i. Thus the state of neuron i at any moment in time can be described by the triplet (V_i, H_i^E, H_i^I).

  As for the effect of E-kicks, it depends on the membrane potential and the class of neuron i. With different membrane potentials and classes, the effect will cause the neuron to change its membrane potential with different probabilities. Thus, we have parameters $P_E^{GE}, P_E^{GI}, P_E^{BI}, P_E^{BE}$.

  As for the effect of I-kicks, it's a little different from the effect of E-kicks. Firstly, the I-kicks won't have any effect on a *base* neuron. As for a *gate* neuron, I-kicks will change its membrane potential with probabilities P_I^{GE}, P_I^{GI}.

This completes the description of the 2-state reduced model. We can observe the parameters are

$$\{N_I, N_E, \lambda^E, \lambda^I, \tau_{\mathcal{R}}, P_{Q,Q'}, \tau^E, \tau^I, P_E^{GE}, P_E^{GI}, P_E^{BI}, P_E^{BE}, P_I^{GE}, P_I^{GI}, P_{Ex}^G, P_{Ex}^I\}.$$

2.2 Coarse Grained Model

In coarse grained model, we only care the populations of E-neurons and I-neurons. Therefore, we don't have to record each neurons and can characterize the populations with fewer variables, which greatly decrease the total states. About the elements in the model:

- We assume there are N_E excitatory neurons and N_I inhibitory neurons.

- The **membrane potential** of a neuron only has two states, *gate* and *base*. We use $N_{GE}, N_{GI}, N_{BE}, N_{BI}$ to denote the numbers of *gate* E-neurons, *gate* I-neurons, *base* E-neurons and *base*-I neurons. In fact, we can observe that $N_{GE} + N_{BE} = N_E, N_{BI} + N_{GI} = N_I$.

- Each neuron receives synaptic input from an **external source** in the form of Poisson kicks; these kicks are independent from neuron to neuron.

Then, we are going to introduce the interactions between different elements in the model:

- **External drive to neurons**: The action from external drive to neurons are inputs delivered in the form of impulsive kicks, arriving at random (Poissonian) times and the Poisson processes are independent from neuron to neuron. We assume there are one parameter λ^E, λ^I, representing the rate of the Poisson kicks. When a kick arrives, if the state is $(N_{GE}, N_{GI}, H_E, H_I)$, we have four different cases:

  - With probability $\frac{N_{GE}}{N_E+N_I}$, this kick works on a *gate* E-neuron. Then, with probability $\frac{N_{GE}}{N_E+N_I} \cdot P_{Ex}^G$, $N_{GE} = N_{GE}-1, N_{BE} = N_{BE}+1, H_E = H_E+S_E$, where S_E is a constant we give. With probability $\frac{N_{GE}}{N_E+N_I} \cdot (1 - P_{Ex}^G)$, the state will keep the same.

  - Similarly, with probability $\frac{N_{BE}}{N_E+N_I} \cdot P_{Ex}^B$, this kick works on a *base* E-neuron and this E-neuron's membrane potential switches to *gate*. $N_{GE} = N_{GE} + 1, N_{BE} = N_{BE} - 1$.

  - With probability $\frac{N_{BI}}{N_E+N_I} \cdot P_{Ex}^B$, this kick works on a *base* I-neuron and this I-neuron's membrane potential switches to *gate*. $N_{GI} = N_{GI} + 1, N_{BI} = N_{BI} - 1$.

  - With probability $\frac{N_{GI}}{N_E+N_I} \cdot P_{Ex}^B$, this kick works on a *gate* I-neuron and this I-neuron's membrane potential switches to *base*. $N_{GI} = N_{GI}-1, N_{BI} = N_{BI}+1, H_I = H_I+S_I$, where S_I is a constant we give.

- **Effect of kicks**: Firstly, we use H_E, H_I to denote the total pending E-kicks and I-kicks, and these pending spikes delay after an exponential distributed time with parameters $\tau^{EE}, \tau^{IE}, \tau^I$. Then we are going to introduce the effects of two different kicks:

  - **Effect of E-kicks**: As for the E-kicks, we assume with probability a_{EE}, it takes effect on an E-neuron and with probability a_{IE} on an I-neuron. Therefore,

    * With probability $a_{EE} \cdot \frac{N_{GE}}{N_E} \cdot P_E^{GE}$, the E-kick takes effect on a *gate* E-neuron and changes it's membrane potential. $N_{GE} = N_{GE} - 1, N_{BE} = N_{BE} + 1, H_E = H_E + S_E - 1$, where S_E is decided by the connectivity.

    * With probability $a_{IE} \cdot \frac{N_{GI}}{N_I} \cdot P_E^{GI}$, the E-kick takes effect on a *gate* I-neuron and changes it's membrane potential. $N_{GI} = N_{GI} - 1, N_{BI} = N_{BI} + 1, H_I = H_I + S_I, H_E = H_E - 1$, where S_I is decided by the connectivity.

    * With probability $a_{EE} \cdot \frac{N_{BE}}{N_E} \cdot P_E^{BE}$, the E-kick takes effect on a *base* E-neuron and changes it's membrane potential. $N_{BE} = N_{BE}-1, N_{GE} = N_{GE}+1, H_E = H_E-1$.

    * With probability $a_{IE} \cdot \frac{N_{BI}}{N_I} \cdot P_E^{BI}$, the E-kick takes effect on a *base* I-neuron and changes it's membrane potential. $N_{BI} = N_{BI}-1, N_{GI} = N_{GI}+1, H_E = H_E-1$.

    * As for the other probability, $H_E = H_E - 1$.

  - **Effect of I-kicks**: The effect of I-kicks is relatively simpler, since it has no effect on *base* neurons. Assume an I-kicks takes effect on an E-neuron with probability a_{EI} and a_{II} on an I-neuron.

    * With probability $a_{EI} \cdot \frac{N_{GE}}{N_E} \cdot P_I^{GE}$, the I-kick takes effect on a *gate* E-neuron and changes it's membrane potential. $N_{GE} = N_{GE}-1, N_{BE} = N_{BE}+1, H_I = H_I-1$.

* With probability $a_{II} \cdot \frac{N_{GI}}{N_I} \cdot P_I^{GI}$, the I-kick takes effect on a *gate* I-neuron and changes it's membrane potential. $N_{GI} = N_{GI} - 1, N_{BI} = N_{BI} + 1, H_I = H_I - 1$.
    * As for the other probability, $H_I = H_I - 1$.

This finishes our statistical reduced model. We can observe that the parameters are:

$$\{N_E, N_I, \lambda^E, \lambda^I, S_E, S_I, P_{Ex}^G, P_{Ex}^B, a_{Q,Q'}, P_E^{GQ}, P_E^{BQ}, P_I^{GQ}, \tau^{EE}, \tau^{IE}, \tau^I\},$$

where $Q \in \{E, I\}$.

In conclusion, if we are going to consider the embedded Markov chain, for a given state, there are 12 possible transitions listed in Table 1 while the corresponding transition rate (of $\mathcal{Q}$-matrix) listed in Table 2. Note that quantities not mentioned will not change.

external input operates	pending E spikes operates	pending I spikes operates
$N_{GE} + 1$	$N_{GE} + 1 \quad H_E - 1$	$N_{GE} - 1 \quad H_I - 1$
$N_{GI} + 1$	$N_{GI} + 1 \quad H_E - 1$	$N_{GI} - 1 \quad H_I - 1$
$N_{GE} - 1 \quad H_E + S_E$	$N_{GE} - 1 \quad H_E - 1 + S_E$	$H_I - 1$
$N_{GI} - 1 \quad H_I + S_I$	$N_{GI} - 1 \quad H_E - 1 \quad H_I + S_I$	
	$H_E - 1$	

Table 1: possible transitions

external input operates	pending E spikes operates	pending I spikes operates
$P_{Ex}^{BE} N_{BE}/\lambda_E$	$P_E^{BE} a_{EE} \frac{N_{BE}}{N_E} H_E/\tau_{EE}$	$p_I^{GE} a_{EI} \frac{N_{GE}}{N_E} H_I/\tau_I$
$P_{Ex}^{BI} N_{BI}/\lambda_I$	$p_E^{BI} a_{IE} \frac{N_{BI}}{N_I} H_E/\tau_{IE}$	$p_I^{GI} a_{II} \frac{N_{GI}}{N_I} H_I/\tau_I$
$P_{Ex}^{GE} N_{GE}/\lambda_E$	$p_E^{GE} a_{EE} \frac{N_{GE}}{N_E} H_E/\tau_{EE}$	$(1 - p_I^{GE} a_{EI} \frac{N_{GE}}{N_E} - p_I^{GI} a_{II} \frac{N_{GI}}{N_I}) \cdot H_I/\tau_I$
$P_{Ex}^{GI} N_{GI}/\lambda_I$	$p_E^{GI} a_{IE} \frac{N_{GI}}{N_I} H_E/\tau_{IE}$	
	$(1 - P_E^{BE}) a_{EE} \frac{N_{BE}}{N_E} H_E/\tau_{EE}$ $+ (1 - p_E^{BI}) a_{IE} \frac{N_{BI}}{N_I} H_E/\tau_{IE}$ $+ (1 - p_E^{GE}) a_{EE} \frac{N_{GE}}{N_E} H_E/\tau_{EE}$ $+ (1 - p_E^{GI}) a_{IE} \frac{N_{GI}}{N_I} H_E/\tau_{IE}$	

Table 2: transition rate

3 Implementation

In this section we will introduce how to set our parameters. Now we have 3 models and their parameters:

* **Full Model**:

$$\{N_I, N_E, M_r, M, \lambda^E, \lambda^I, \tau_{\mathcal{R}}, P_{Q,Q'}, S_{Q,Q'}, \tau^{EE}, \tau^{IE}, \tau^I\}.$$

* **Reduced Network Model**:

$$\{N_I, N_E, \lambda^E, \lambda^I, \tau_{\mathcal{R}}, P_{Q,Q'}, P_E^{GQ}, P_E^{BQ}, P_I^{GQ}, P_{Ex}^{BQ}, P_{Ex}^{GQ}, \tau^{EE}, \tau^{IE}, \tau^I\}.$$

* **Coarse Grained Model**:

$$\{N_E, N_I, \lambda^E, \lambda^I, S_E, S_I, a_{Q,Q'}, P_E^{GQ}, P_E^{BQ}, P_I^{GQ}, P_{Ex}^{GQ}, P_{Ex}^{BQ}, \tau^{EE}, \tau^{IE}, \tau^I\}.$$

We fix some universal parameters for all models:

$$N_I = 25, N_E = 75, \tau_{\mathcal{R}} = 0, \lambda_e = \lambda_i = 1/7, P_{EE} = 0.15, P_{IE} = 0.5, P_{EI} = 0.5, P_{II} = 0.4.$$

As for the full model, we have 3 settings for 3 types of gamma:

- Homogeneous:

$$M_r = 66, M = 100, S_{EE} = S_{EI} = S_{II} = 25, S_{IE} = 10, \tau_{EE} = 4, \tau_{IE} = 1.2, \tau_I = 4.5.$$

- Regular:

$$M_r = 66, M = 100, S_{EE} = S_{EI} = S_{II} = 25, S_{IE} = 10, \tau_{EE} = 2, \tau_{IE} = 1.2, \tau_I = 4.5.$$

- Synchronized:

$$M_r = 66, M = 100, S_{EE} = S_{EI} = S_{II} = 25, S_{IE} = 10, \tau_{EE} = 1.3, \tau_{IE} = 0.95, \tau_I = 4.5.$$

Here we show some rasterplots of our full model.
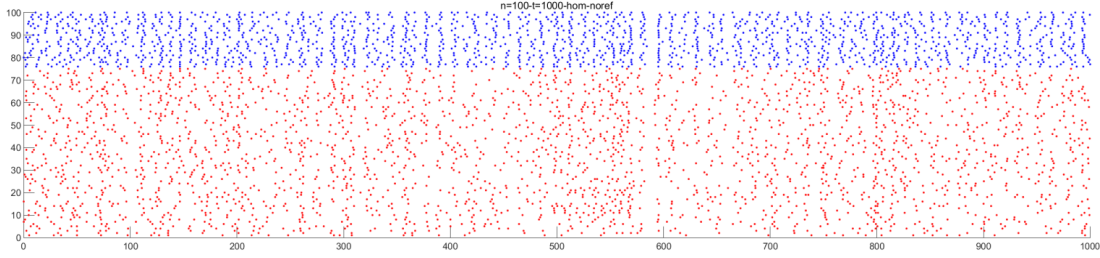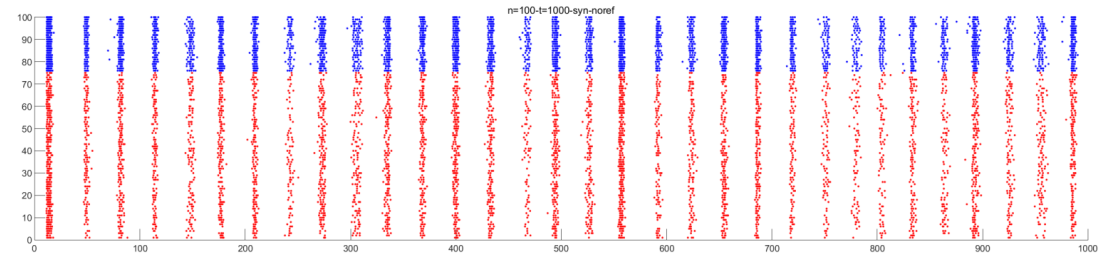

Figure 1: Homogeneous
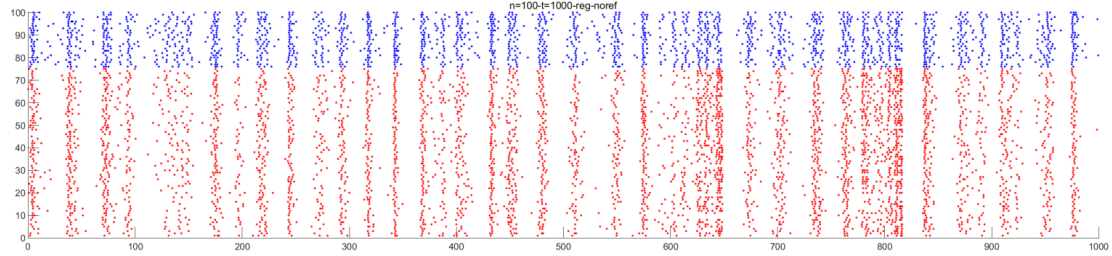
Figure 2: Regular

Figure 3: Synchronized

As for our two reduced models, we set the parameters the same as those in full model if they are in the intersection of their parameter sets. Therefore, in reduced network models and coarse grained models:

$$N_I = 25, N_E = 75, \lambda_E = \lambda_I = 1/7.$$

5

In reduced network models:

$$P_{EE} = 0.15, P_{IE} = 0.5, P_{EI} = 0.5, P_{II} = 0.4.$$

In Coarse Grained Model, we can calculate $S_E, S_I, a_{Q,Q'}$ in terms of the parameters in full model. Thus, the most challenging thing for us is to find suitable

$$\{P_E^{GQ}, P_E^{BQ}, P_I^{GQ}, P_{Ex}^{BQ}, P_{Ex}^{GQ}\}$$

for those reduced models. Recall that

- P_E^{GQ} is the probability that a *gate* Q-Neuron spikes and switches to *base*-Q Neuron under the effect of an E-spike;

- P_E^{BQ} is the probability that a *base* Q-Neuron switches to *gate*-Q Neuron under the effect of an E-spike;

- P_I^{GQ} is the probability that a *gate* Q-Neuron switches to *base*-Q Neuron under the effect of an I-spike;

- P_{Ex}^{BQ} is the probability that a *base* Q-Neuron switches to *gate*-Q Neuron under the effect of an external kick;

- P_{Ex}^{GQ} is the probability that a *gate* Q-Neuron spikes and switches to *base*-Q Neuron under the effect of an external kick;

In fact, our effects are quantified in Full model. The effect of external kicks is that $V_i = V_i + 1$ and the effects of spikes are quantified by $S_{Q,Q'}$. For convenience, we set the *gate* neurons are neurons with membrane potential larger than 75. The reason that we select 75 as a bar is because just 1 E-spike can make these E-neurons spike and 1 I-spike can depress these *gate* neurons to *base* state.

Therefore, if we know the distributions of E,I-neuron's membrane potentials at time t, we could calculate those probabilities at time t directly. Hence, the easiest method to do model reduction is assuming that the distributions of membrane potentials is stable in our model, and we could use an empirical distributions of membrane potentials to estimate P according to our full model simulation results.

However, a bad news is that according to our simulation results distributions of membrane potentials is not stable. In fact, there is a periodic change in the distributions. But after some meticulous observations, we found that the shape of distributions at different times are similar. More specifically, the distributions of membrane potentials looks like an "iceberg" and this "iceberg" moves along the axis of mean. In other words, as spikes accumulate and take effects, the distributions of membrane potential are stable except that their means increase. After the mean reaches about 60-70, the "iceberg" passes across a "door" and a small part of it appears again with 0 membrane potential.

Therefore, this phenomenon inspires us to estimate the changing P with the shape of "iceberg". Firstly, we could collect an empirical shape of the distribution class with our full model simulation results. Then, for each time t, we could use the number of gate E,I-neurons to estimate the means of the distributions. Thus, with the means we could uniquely identify the distributions and then estimate P.

Here we give the detailed steps of two methods of estimations for P.

- **Fixed P method:**

    - Step 1: Run full model and collect the membrane potential samples V_e , V_i;
    - Step 2: Use the empirical distribution to estimate P.

- **Non-fixed P methods:**

  – Step 1: Run full model and collect the centralized samples (subtract the mean at each time) V'_e, V'_i;

  – Step 2: Use V'_e, V'_i to construct two centralized empirical distributions F_e, F_i;

  – Step 3: For different N_{GE}, N_{GI}, find two means μ_e, μ_i such that

$$F_e(75 - \mu_e) \approx 1 - \frac{N_{GE}}{N_E},$$
$$F_i(75 - \mu_i) \approx 1 - \frac{N_{Gi}}{N_i}.$$

  – Step 4: Use $F_e(\cdot - \mu_e), F_i(\cdot - \mu_i)$ to estimate P.

Remark. For Non-fixed P methods, P are regarded as functions of N_{GE}, N_{GI}. Besides using histograms, we can also use Gaussian distributions to fit distributions of membrane potentials.

Then we are going to show some simulation results.

3.1 Simulations with fixed P

Here are some rasterplots of our reduced models:

3.2 Simulations with non-fixed P

When we are dealing non-fixed P, we would slightly modify the P since we cannot really regard our P as functions of N_{GE}, N_{GI}. Thus, we have another parameter vector q to multiply P.
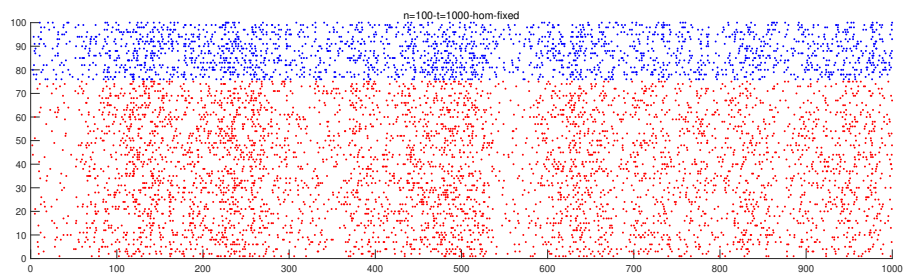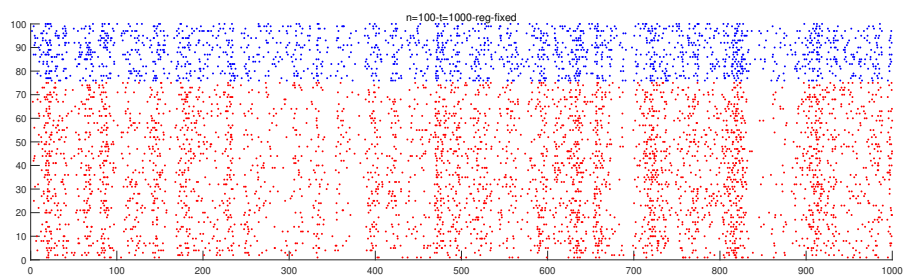 Here are some rasterplots of our reduced models:

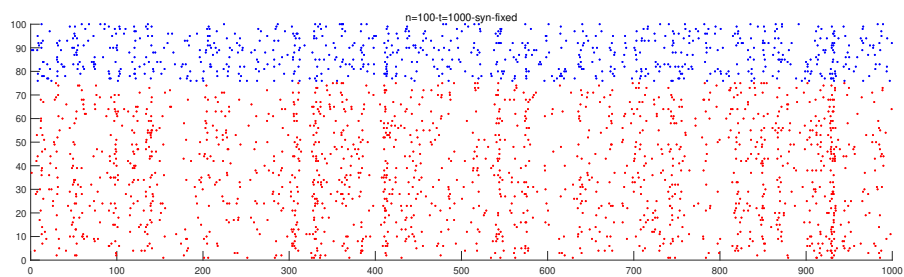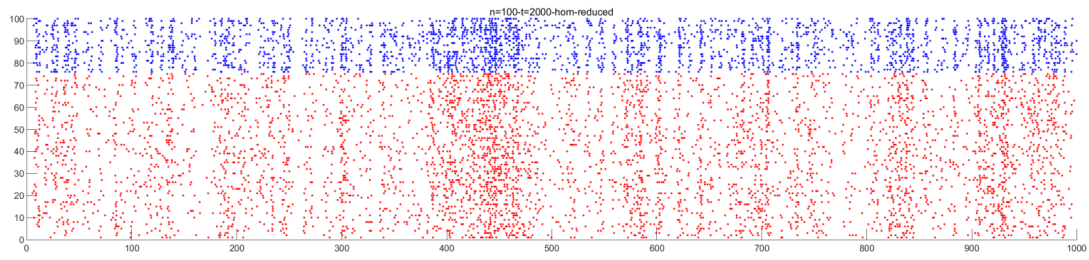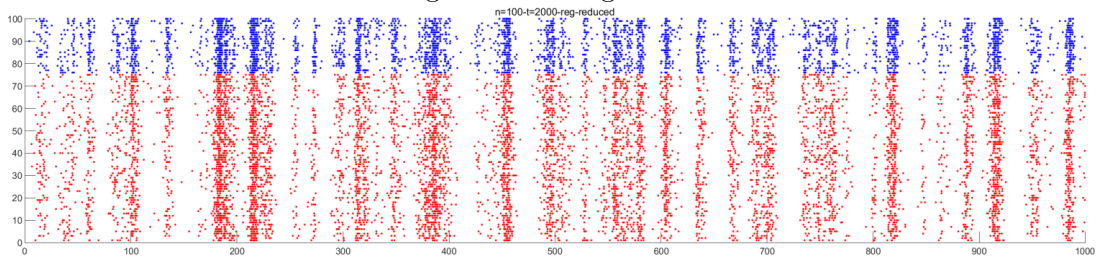Figure 4: Homogeneous

Figure 5: Regular

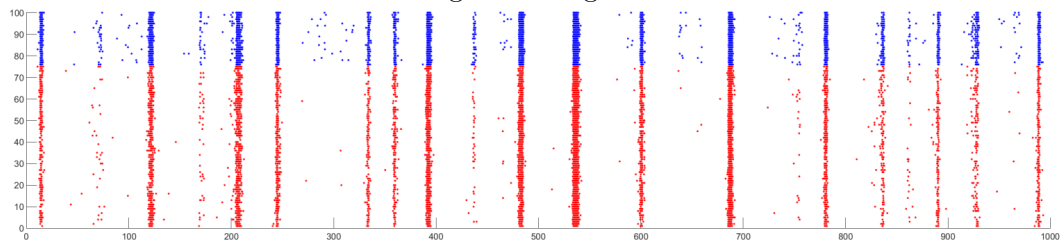Figure 6: Synchronized

Figure 7: Homogeneous

Figure 8: Regular

Figure 9: Synchronized