Neurotechnologies For The Analysis of Neural Dynamics, 2016 Report

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1 Introduction

This report concerns the work that I performed during the Neurotechnologies for the Analysis of Neural Dynamics, 2016 summer school and the progress that I made while continuing to work with professor Berry in the subsequent six months after the school. I would like to begin by thanking the course organizers for a very inspiring summer school and the full scholarship that I was provided with. Without the financial support offered by the course, I wouldn't have had the resources to come and learn. The work that I performed during the course and while continuing to work on the project expanded my horizons and gave me one of the first experiences of modeling an actual experimental phenomenon in computer simulations. The general methodology of taking a complex circuit function and iteratively developing models that reproduce its behavior is one that I would like to work with over the course of my career. Mathematical description and computer simulations are a test of how well we understand an observed phenomenon. Developing models that describe experimental data can provide mechanistic insight into the forces that shape circuit function.

After six months of work, I can proudly say, that the model that I arrived at, qualitatively approximates some the experimental results. While there is more work to be done, I can now communicate the positive and negative results, e.g. what worked and what didn't. This report is accordingly divided into two sections. I first outline the the experimental findings subject to modeling efforts. I then give three explored modeling pathways and their respective results. I conclude with a discussion on what I learned through the experience of developing a model of a neural phenomenon.

2 Description of Experimental Findings

The modeling begins with experimental results from Calcium imaging experiments in layer 2/3 of the area V1 in mice. V1 has traditionally been studied for the orientation selectivities that its cells exhibit. The novelty of the experiments, conceived by professor Berry, lie in studying predictive computation on temporal sequences in V1. V1 is at the early stage of visual processing and thus results that indicate that it has non-trivial computations on visual sequences are groundbreaking. Professor Berry's group discovered two parallel streams

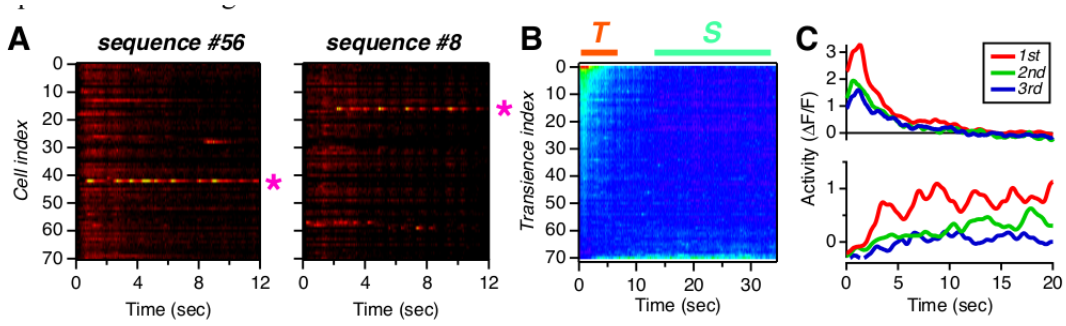

Figure 1: Experimental results, from (Berry, 2016)

of information processing in V1, one corresponding to coding for predictable aspects of the stimulus and the other for unpredictable deviations.
Specifically head-fixed mice were presented with sequences of Gabor patches in a virtual reality environment. First a predictable sequence was displayed for several times, consisting of the same sequence of frames, ABCD. Then after several presentations, the sequence was violated, e.g. ABCX was shown. The experiments showed that there is small number of cells that fire in a sustained way in response to the sequence ABCD, different cells locking onto particular cells (see panel A, B and C in Figure 1). The rest of the cells exhibit a transient response, activating at the start of the experiment and then keeping mostly silent (see panel A, B and C in Figure 1). When the sequence is violated, many of the previously silent cells activate, composing a population novelty response. Our modeling aim was to capture the transient response of cells, locking unto different frames in the stimulus and to capture the novelty response, where a large proportion of the population fires in response to a novelty frame.

3 Feed-forward Model

The first model that we consider is a model where the layer 2/3 synapses receive feed-forward input from layer 4 cells. These synapses are plastic. In particular the follow a short-term depression and facilitation developed by (Varela et al, 1997) to fit experimental measurements in layer 2/3. The model thus consists of two layers, layer 4 activations and layer 2/3 responses. We connect these two layers randomly. Notice that in this model there are no recurrent connections between the cells in the same layer. For an illustration of the model see Figure 2.

We randomly sample the layer 4 activations from a zero-mean Gaussian distribution. This is due to the observation that layer 4 cells encode a mixture of orientation selectivities. The Gabor stimulus can be imagined as consisting of a random mixture of edges and that excite the cells in layer 4 through thalamic input. The Gaussian distribution is convenient way to summarize these random activations. If we assume that the thalamic stimulation represents a sum of independent random activations to the layer 4 cells, then due to the Central Limit Theorem, the activations of layer 4 cells would be approximately Gaussian. Notice that the inputs to the layer 2/3 can be both inhibitory and

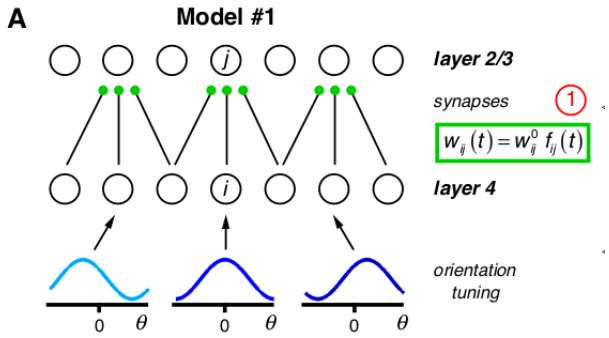

Figure 2: Illustration of feed-forward model, from (Berry, 2016)

excitatory, e.g. positive and negative.

The short-term synaptic plasticity acting on the layer 4 input obey the following equation for facilitation and depression:

$$\tau_D \frac{df_{ij}}{dt} = 1 - f_{ij} - \alpha r_i f_{ij}$$

$$\tau_F \frac{df_{ij}}{dt} = 1 - f_{ij} - \beta r_i [f_{max} - f_{ij}]$$

The rates of the layer 2/3 cells obey a simple dynamic from (Vogels et al, 2005):

$$\tau \frac{dr_i}{dt} = -r_i + F(\sum W_0 f_{ij} I_j(t))$$

where $I_i(t)$ are the activations from layer 4, W_0 are baseline weights drawn from a zero-mean normal distribution, with some weights randomly set to 0 and F is a rectifier function that ensures that the rates never go below 0.

The model has parameters α, β, τ, τ_F, τ_F. We set the parameters according to (Varela, 1997). We also tried a range of parameters and the qualitative behavior of the model didn't change, in particular we couldn't obtain the novelty response.

We use a rate-based model to understand the qualitative behavior of layer 2/3 cells to the layer 4 activation. The layer 4 activations form a sequence, where each sequence element (sampled from a zero-mean normal distribution, see above) lasts for 250 milliseconds. We repeat a sequence ABCD for 5 times, before inserting one violation frame, ABCX. The results of the simulations are given below.

3.1 Results

Figure 2 shows the responses in layer 2/3 for 5 random cells, for 6 trials. The plots for the other cells are qualitatively similar. Different cells lock onto different frames of the stimulus and decay rapidly after their preferred stimulus.

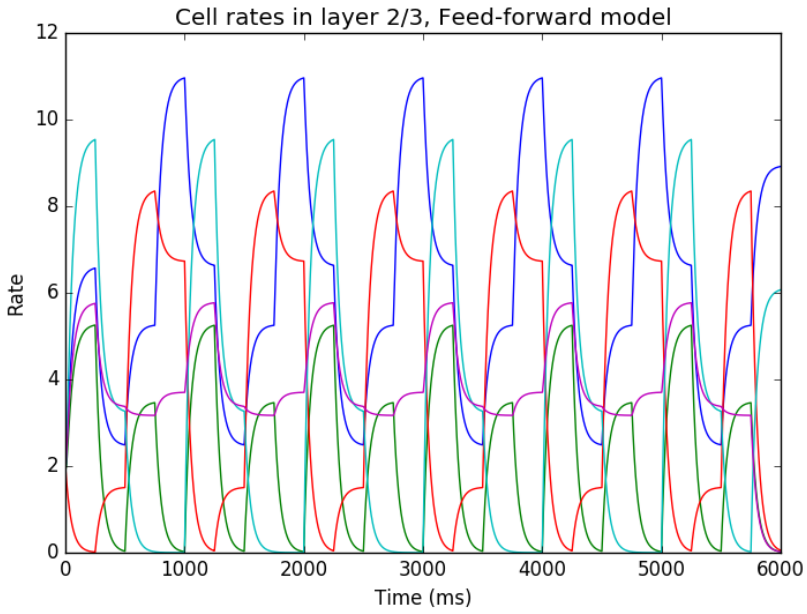

Figure 3: Rates in the feedforward network

One of the cells has a sustained response, where its activation doesn't decay to 0, but remains in some range.
This model does not exhibit a novelty response in the 6th trial.

4 Recurrent Network

In the the recurrent network model, we implement recurrent connectivity between layer 2/3 cells. In this model, the synaptic weights are fixed and there is no plasticity. Accordingly, we inject layer 4 activations to the layer 2/3 cells without intermediate synaptic weights. Layer 2/3 recurrent connectivity is drawn from a zero-mean normal distribution and does not obey Dale's law (e.g. neurons can emit both excitatory and inhibitory synapses). The rationale of implementing this model is that the recurrent connectivity can generate echoes of the stimulus that propagate the encoding of the sequence forward in time and thus construe sequence specific responses. The model structure is illustrated in Figure 4.

The rates of the layer 2/3 cells obey a similar dynamic as the feedforward network, except that now there is additional recurrent input and the layer 4 activations are injected directly into the layer 2/3 cells:

$$\tau \frac{dr_i}{dt} = -r_i + F(I_i(t) + \sum W_{ij} r_j)$$

where $I_i(t)$ are the activations from layer 4 and F is a rectifier function that

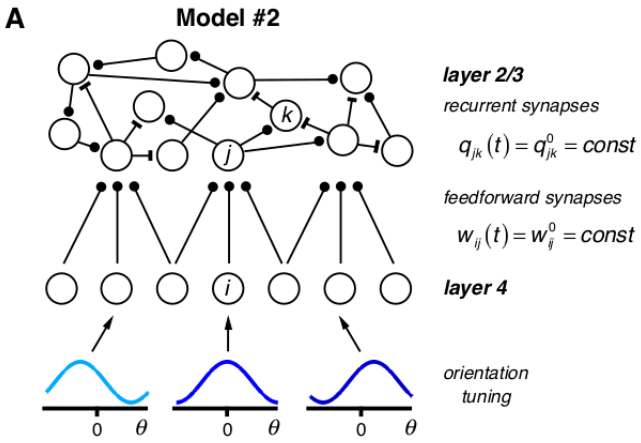

Figure 4: Illustration of the structure of the recurrent network, from (Berry, 2016)

ensures that the rates are not negative.

4.1 Results

Even though the weight matrix has on average the same amount of inhibitory and excitatory synapses, the model is unstable and the rates go rapidly to infinity. This means that the circuit very rapidly amplifies the input signal.

5 Networks with Bienenstock-Munro-Cooper Plasticity

We next implement a model that obeys Dale's law, meaning that the cells in layer 2/3 can emit only excitatory or only inhibitory connections. The first model has random connectivity, without excitation and inhibition balance. In the second model, we employ a method from (Hennequin, 2013) to match the weights of the inhibitory and excitatory cells, so that excitation and inhibition balance is achieved.

The currents from layer 4 cell are injected directly into the layer 2/3 cells, without any plasticity at those synapses.

To obtain the novelty response, we endow the recurrent connections with Bienenstock-Munro-Cooper plasticity (Toyoizumi et al, 2014). This is form of plasticity that incorporates both Hebbian learning and homeostatic plasticity. It obeys the following equations:

$$\tau_w \frac{dw}{dt} = xy(y - \theta)$$

$$\tau_\theta \frac{d\theta}{dt} = -\theta + y\frac{y}{y_0}$$

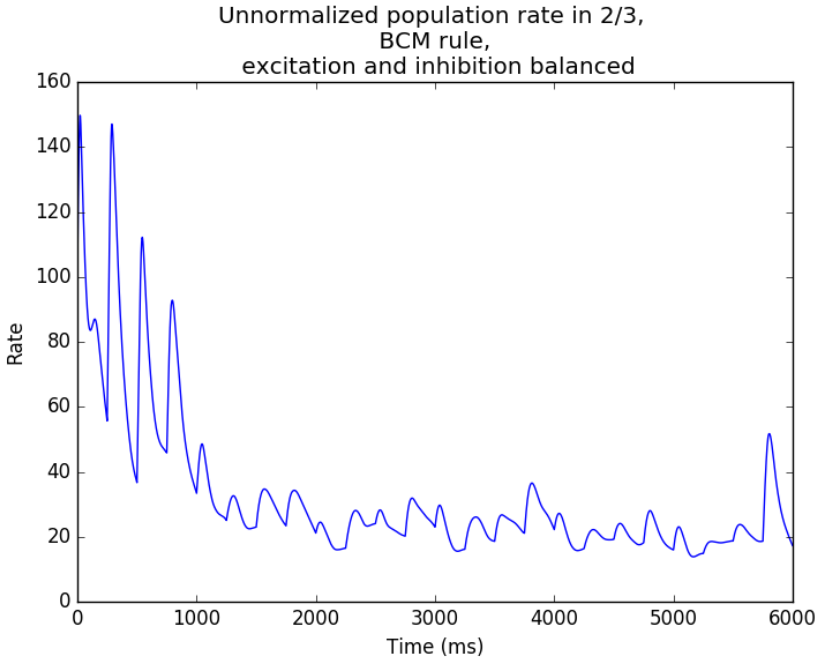

Figure 5: Unnormalized population rate in layer 2/3, excitation-inhibition balance, excitatory cells

where x and y are pre-synaptic and post-synaptic rates, respectively and θ is a sliding threshold that maintains homeostatic balance, e.g. ensures that the post-synaptic activity is close to y_0. The model undergoes LTP if $y > \theta$ and conversely LTD if $y < \theta$. We clip the weights in the simulations so that excitatory synapses would never go below 0 and inhibitory synapses never above 0.

We set the parameters of the plasticity model according to another model implementing this form of plasticity ($\tau_w = 100$ ms, $\tau_\theta = 0.1$ ms).

The evolution of the rates in the network again obeys the equation from (Vogels et al, 2005):

$$\tau \frac{dr_i}{dt} = -r_i + F(I_i(t) + \sum W_{ij} r_j)$$

where $I_i(t)$ are the activations from layer 4 and F is a rectifier function that ensures that the rates are not negative.
The layer 4 activations are again sampled from a zero-mean Gaussian and form a periodic pattern, with each activation level lasting for 250 ms.

These simulations contain 100 excitatory and 100 inhibitory cells.

5.1 Results

Both the models with random inhibitory and excitatory connections and the model with balanced excitation and inhibition exhibit a novelty response due

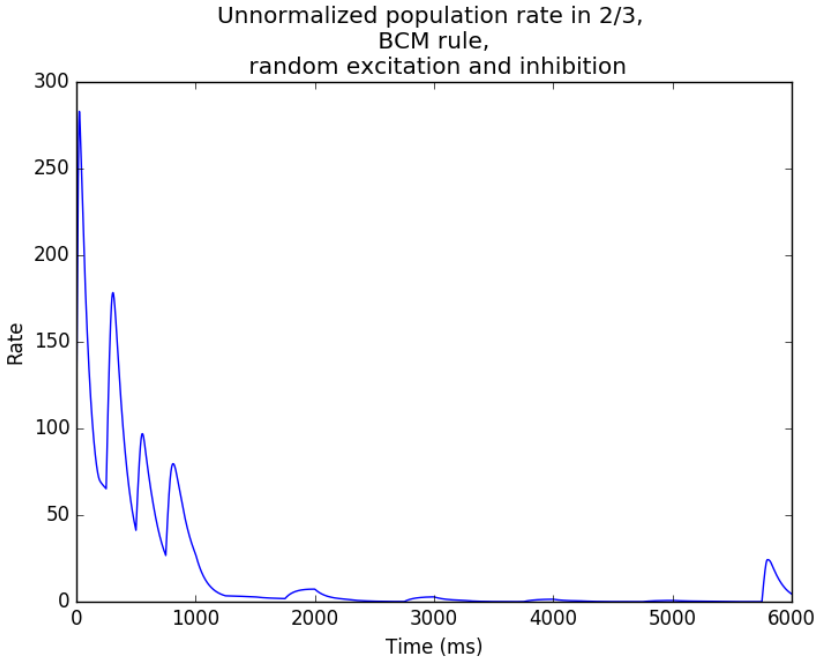

Figure 6: Unnormalized population rate in layer 2/3, random excitation and inhibition, excitatory cells

to the BCM plasticity rule. However, the model with random inhibition and excitation does not exhibit the sustained responses that lock to different frames. Excitation-inhibition balance, an important feature of cortical information processing (Deneve and Machens, 2016), thus appears to contribute to encoding of sequence frame identities in the sustained responses of cells.
In Figure 5 and 6 we plot the unnormalized population activity in the layer 2/3 cells (we sum the activities from all cells at each time point).
Figure 7 makes it apparent that the majority of the cells do not respond to the stimulus and their rates are close to 0 after the first trial (reminder: there are 100 excitatory cells in the simulation).
This reproduces a feature of the experimental data (see Figure 1). This effect is likely due to the common inhibitory pool, that suppresses the firing of most of the cells, due to the Winner-Take-All dynamic (Ermentrout, 1992).
We also investigate if the population activity during the novelty response increases as compared to the average of the previous trials (excluding the earliest trials when there is a heightened transient response). The strength of the population response to the novel frame X does not increase with the number of previous trials. This is a feature of the experimental data does not capture and this is left for future work.

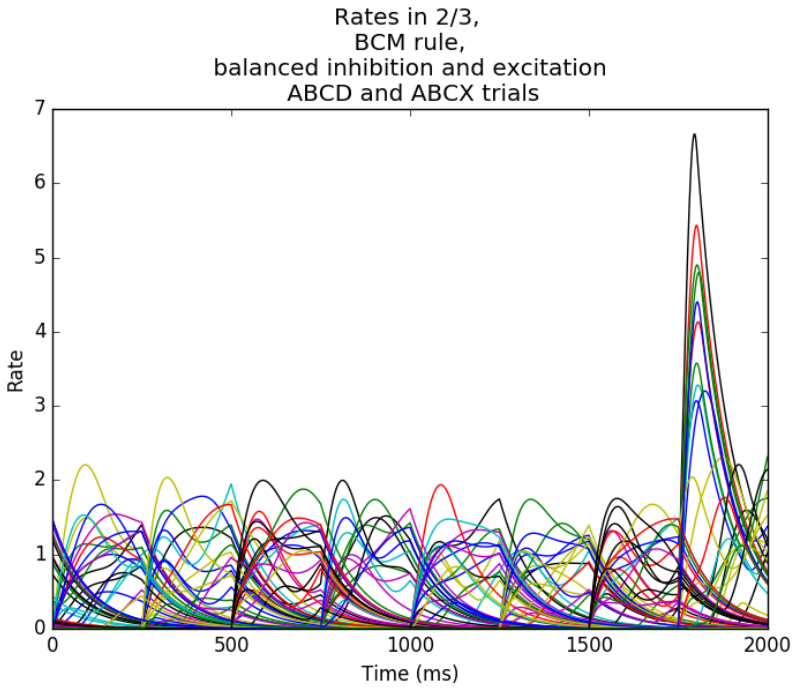

Figure 7: Rate in layer 2/3, excitation-inhibition balance, ABCD and ABCX trials (after 4 presentations of ABCD), excitatory cells

6 Conclusion

This section summarizes the broader lessons that I've learned through this project.

Firstly, I deepened my interest in computationally modeling experimental phenomena. Finding an approximate solution to the current problem gives me more confidence to further train as a Computational Neuroscientist. In truth, when I started the project, I didn't know how long it would take me and how much work it would require. It was like diving into the unknown. I didn't know if my ideas would have any relevance. When I obtained results, I was deeply happy. It was intellectually exciting to make the journey from a problem to a solution and it was highly rewarding when my ideas worked. In addition, I now have material for my Master's thesis, meaning that I can graduate this summer.

Constructing the final model required me to perform a thorough literature search. I had the intution that excitation and inhibition balance had something to do with the results and I independently found a method for optimizing the recurrent connectivity matrix for balance. I wrote to a Cambridge scientist 4 times, before he finally provided me with code:-). I find it a perk of the job that you can come into contact with the work of very interesting scientists.

I also learned how to implement rate-based models in the simulator DANA, which is similar to the simulator Brian for spiking neural networks that I've worked with before. I made implementation errors when I was just starting to work with the simulator in Princeton and later corrected them. There is no

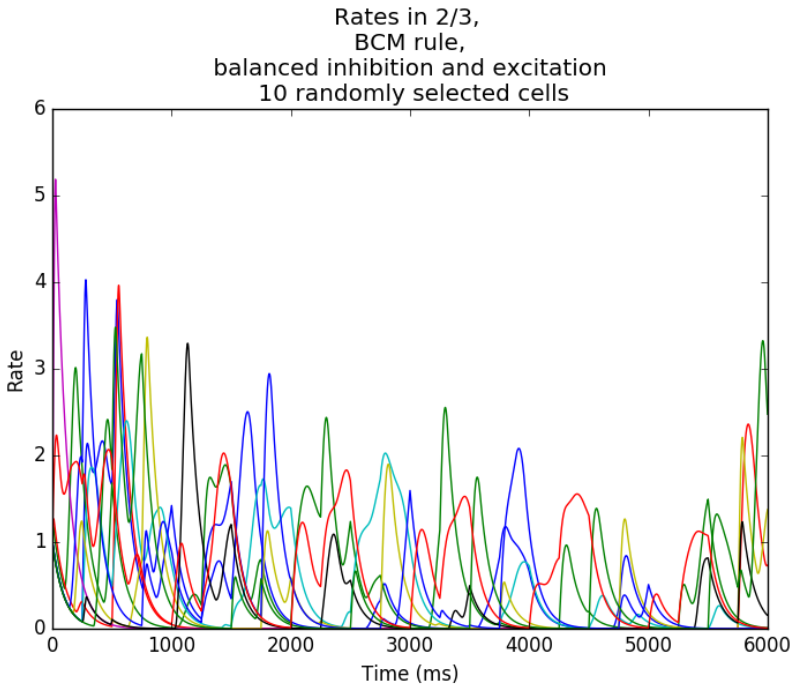

Figure 8: Rate in layer 2/3, excitation-inhibition balance, ten randomly chosen excitatory cells

better teacher than practice.
In summary, I would again like to thank the Princeton Neuroscience Institute for their wonderful summer school and the scholarship and professor Berry for his supervision. After this experience, I am more than certain that I want to develop a career in Computational Neuroscience.

7 Citations

Berry, M., 2016, "Cortical Mechanisms of Selectivity to Long Temporal Sequences", US-French Collaboration Research Proposal

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