Activity-dependent growth and self-organization in a neural network model

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The development of neural circuits is determined to a large extent by experience during critical periods of early postnatal life. Several interacting processes have been identified to be involved in the formation of new synaptic connections and the elimination of already existing connections: functional competition between inputs, neuronal activity, structural consolidation at the end of the critical period and regulation of synaptic connections by experience. In this study we introduce a neuron model for activity-dependent growth and self-organization of a neural network based on a neurobiologically plausible mechanism of competition for neurotrophic growth factors among synaptic connections inside every neuron. We extend previous models by including a detailed topological model of neuronal outgrowth in combination with recurrent lateral excitation among neurons. In a series of simulation studies we investigate the influence of neurotrophic factors and firing rate dynamics on the connectivity of generated neural networks. We find that providing a network of initially fully connected neurons with two different baseline input patterns leads to differentiation into two corresponding clusters. Furthermore, we show that the total amount of neurotrophic factors available for each neuron plays an important role in the development of the connectivity of the neural network and we hypothesize that this might be involved in the initialization and dynamics of critical periods.

I. INTRODUCTION

Cortical plasticity occurs extensively throughout the life cycle [1], yet most computational models of neural function treat neural networks as static with regard to rewiring. Models that explore the space of rules governing neural development could potentially produce insights into the way that normal and pathological network structures arise. Patterned neural activity from the retina plays an important role in the formation of structured maps in higher processing centers of the cerebral cortex [2]. Competition between neural inputs plays an important role in this process - sensory deprivation in one eye causes the cortical representation of that eye to shrink while the representation of the opposite eye grows [3]. A class of neural growth factors (neurotrophins) has been suggested as the central mediator of this activity-dependent competition [4], because (1) overexpression of neurotrophins abolishes the effects of monocular deprivation and (2) neurotrophins are necessary for both the growth of axonal fibers and the of neural connections [5].

Harris et al [6] proposed a simple, biologically plausible model of the role of competition for neurotrophins in the self-organization of cortical neurons into two columns representing inputs from the left and right eyes, respectively. Van Ooyen and Van Pelt [7, 8] created a simple model for generating connections between neurons in the developing brain - the growth zone of each neuron is represented by a circle whose radius changes in an activity-dependent manner, and when the circles overlap, the neurons are said to have established a connection.

Here, we propose a model that combines these two models by allowing neurotrophin levels to control both the strength of existing connections and the search for new connections. This is biologically plausible, since neurotrophins regulate both neural growth and the plasticity of neural connections. We use this model to develop a network of directed, weighted connections and then analyze the resulting network topologies. Despite the existence of detailed descriptive models [9] dealing with the development of the visual system, the topological consequences of neurons competing for scarce resources have not been considered. By studying the network topologies that result from this simple model, we hope to gain insight into the mechanisms by which neurons self-organize into functional groups in the visual cortex.

II. THE MODEL

The model describes the formation of a connected network between a fixed number of neurons, distributed randomly across the unit square. Neurons in the network fire with a certain rate $r_i(t)$ and transmit this information to all connected neurons according to the strength of the connection, denoted by $w_{ij}(t)$ for a connection from neuron j to neuron i. Initially all neurons are unconnected.

In order to study the outgrowth and development of neuronal connections we modeled these as depending on changes in the use and distribution of neurotrophic growth factors, referred to as neurotrophin (N). The total amount of neurotrophin available to each neuron

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was held constant. In the development of the network, the neuron's neurotrophin could be distributed to enlarge the growth region of the neuron in order to establish new connections or to increase the strength of existing incoming synaptic connections. We denote the amount of neurothrophin allocated by neuron i to all incoming synaptic connection from neuron j by $n_{ij}(t)$.

The outgrowth of neuritic axons and dendrites is described in a way similar to [7, 8]. There's no distinction between axonal and dendritic outgrowth regions and both are modeled as a circle with variable radius $a_i(t)$ around the position of each neuron. Whereas in [7, 8] the radius depends only on the firing rate of each neuron, we introduced a dependence on neurotrophin.

The behavior of neuron i is therefore governed by a set of four dynamic variables: the rate $r_i(t)$, the vector of connection strengths $w_{ij}(t)$, the vector of allocated neurotrophin $n_{ij}(t)$ and the radius of the growth region $a_i(t)$. For ease of notation we will further on drop the explicit notation of time dependency and denote the variables by r_i,w_{ij},n_{ij} and a_i respectively. In the following we will introduce and discuss the differential equations governing these variables.

A. Firing rate

Each neuron is modeled as a firing rate neuron. The rate of neuron i, r_i, depends on the rates of all the other neurons to which it is connected according to

$$r_i = \frac{exp\left(\sum_j w_{ij} r_j + r_0\right) - 1}{exp\left(\sum_j w_{ij} r_j + r_0\right) + 1} \tag{1}$$

where w_{ij} denotes the strength of the synaptic connections going from neuron j to neuron i, $w_{ij} = 0$ for unconnected neurons, and $r_0 = 1$ is a baseline input. The model in [6] used a linear mapping from input to output. Since we restricted the model to excitatory connections this would have meant a positive feedback loop and the infinite growth of firing rates. Therefore, the non-linear function in Eq. 1 is used to constrain the firing rate between 0 and 1. Figure 1 gives the graph of Eq. 1 as a function of the input sum. Note that it is an almost linear mapping for small weighted input sums.

B. Synaptic connection strengths

The synaptic connection strengths w_{ij} change according to

$$\tau_w \dot{w}_{ij} = n_{ij} r_i r_j (1 - w_{ij}) - r_i^2 w_{ij} \tag{2}$$

which can be seen as a modification of Ojas rule [10], i.e. a linearized version of the normalized Hebbian Learning rule. The first modification is the introduction of the $(1 - w_{ij})$ term, which keeps the weights below 1. The second is that the growth rate is made proportional to n_{ij}, the total amount of neurotrophin allocated by neuron i to incoming connections from neuron j. Note that Eq. 2 is different from the equation used in [6], since here the decay term is proportional to the square of the firing rate r_i. The time constant τ_w was set to $\tau_w = .005$.

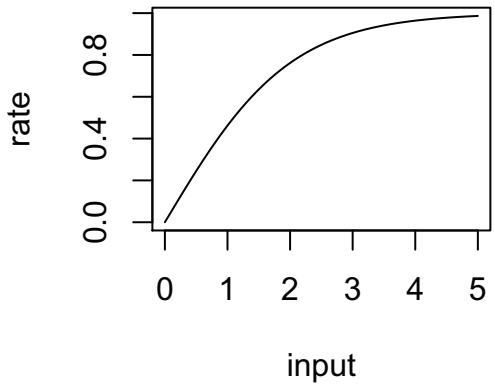

FIG. 1: The firing rate of a single neuron as a function of the sum of the inputs.

C. Allocation of neurotrophin

As in [6] the allocation of neurotrophin is governed by:

$$\tau_n \dot{n}_{ij} = \left(N - \sum_j n_{ij}\right) w_{ij} - \eta n_{ij} \tag{3}$$

where $\eta = .01$ is a decay constant and $\tau_n = .005$. Similar to Eq. 2 the growth rate is proportional to the synaptic strength, which amounts to a positive coupling between n_{ij} and w_{ij}.

D. Outgrowth regions

The change in radius a_i of the growth region is governed by the fraction of neurotrophin not allocated to any of the incoming connections $(N - \sum_j n_{ij})$ according to

$$\tau_a \dot{a}_i = \frac{\alpha}{N}\left(N - \sum_j n_{ij}\right) - a_i \tag{4}$$

where the choice of $\alpha = .5$ determines the maximum radius. If the growth regions of two unconnected neurons - say of neuron i and j - overlap, the corresponding neurons i and j will establish an initially bidirectional connection and their connection strengths w_{ij} and w_{ji} are set to a constant small initial value $w_0 = .01$. We have set $\tau_a = .5$.

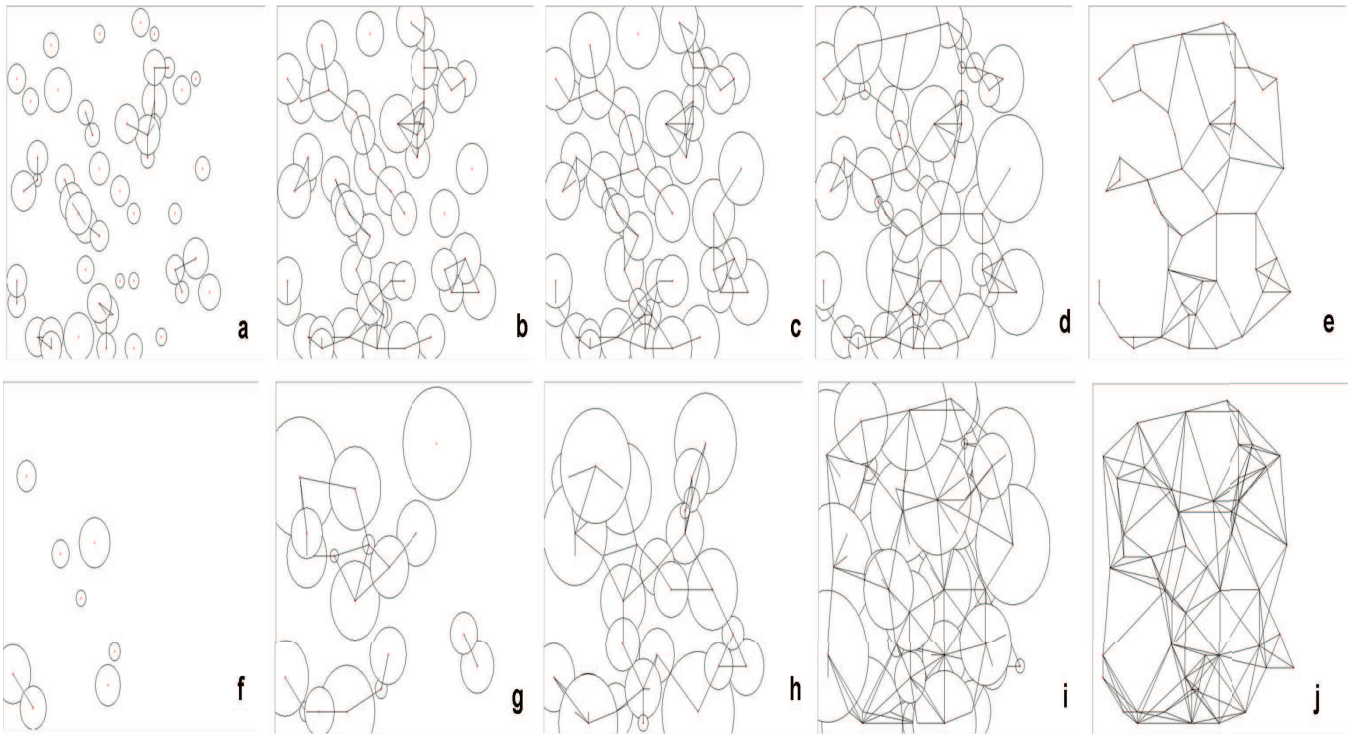

FIG. 2: The evolution of the network over time for simultaneous seeding of neurons (a-e) and random pop-up (f-j). Small red circles show the position of the neurons, the growth region of each neuron - if larger than 0 - is given by the black circle. Lines between neurons denote connections. (e) and (j) only show the final network connectivity.

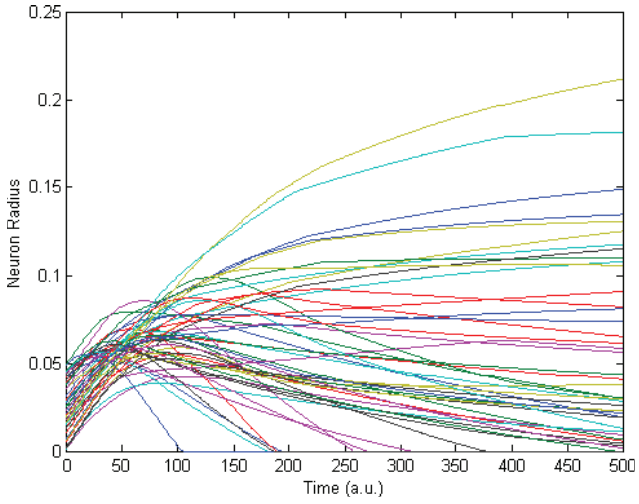

FIG. 3: Evolution of each neurons radius as a function of time. The radius grows and shrinks as the weights of the connections are strengthened and weakened. Many neurons are seen to exhibit overshoot - their radius grows initially and then shrinks.

III. RESULTS

Here we discuss two different models used to study neuronal growth under the previously described dynamics. First, we examine a many neuron model in which neurons are placed on a grid and allowed to grow over time, establishing weighted connections with other neurons. We then examine the degree distribution of the resulting network. Next, we examine a four neuron model in which all neurons are fully connected and show that distinct groups of neurons emerge when given different baseline inputs.

A. Many neuron model

In this simulation, neurons are randomly placed on a lattice and allowed to evolve under the dynamics given by Eqns. 1-4. We studied two cases of neuron placement. In the first case, 50 neurons are simultaneously placed on the grid and allowed to evolve over time as shown in Fig. 2 (a-e). As seen in Fig. 3, the radii of the neurons grow over time, and then in many neurons, the radius actually begins to shrink after some amount of time. This reflects a biological phenomenon known as overshoot in which the growth cone of a neuron will expand over some region but then shrink after the establishment of synapses. In this case, the resulting network structure is largely dependent on the initial placement of neurons, ie, regions of dense neurons will be densely connected, while regions with few neurons will develop a sparse number of connections. In order to remove some of the effects of neuronal distribution, we then ran a simulation where neurons were

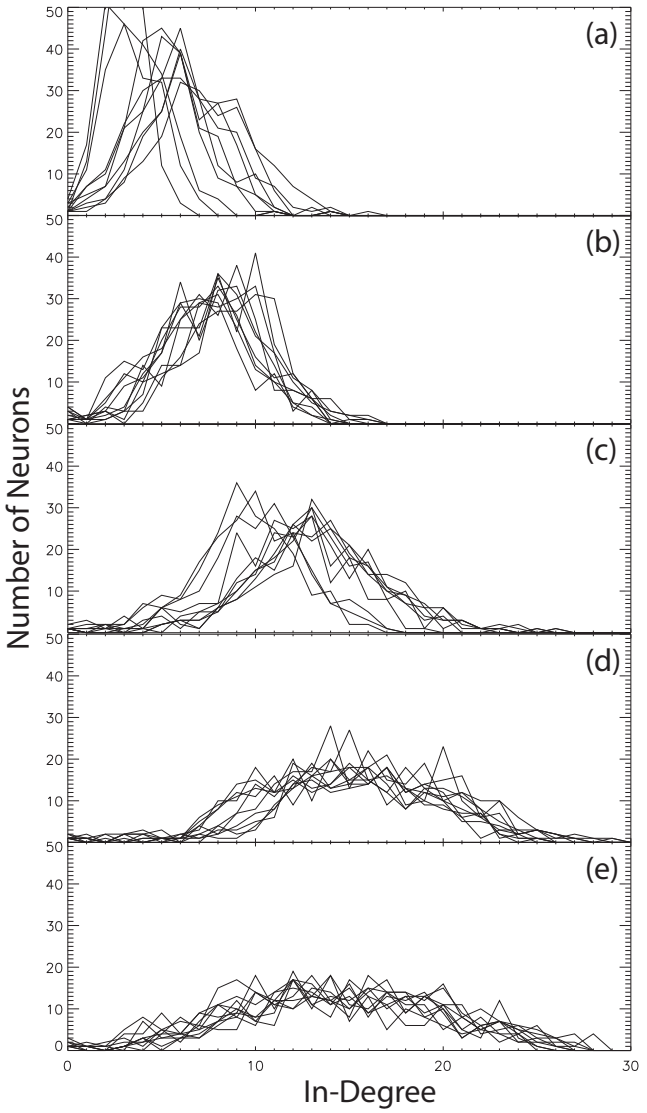

FIG. 4: The final in-degree distribution shown for 10 simulations with all 200 neurons seeded simultaneously. (a) $N = .1$ (b) $N = .5$ (c) $N = 1$ (d) $N = 2$ (e) $N = 5$ As the amount of neurotrophins is increased, the peak of the distribution shifts to a larger number. However, for large N ($N = 5$), the peak no longer continues to shift to the right. In this case, the depletion of the supply of neurotrophins does not occur and is no longer a factor in neuron growth.

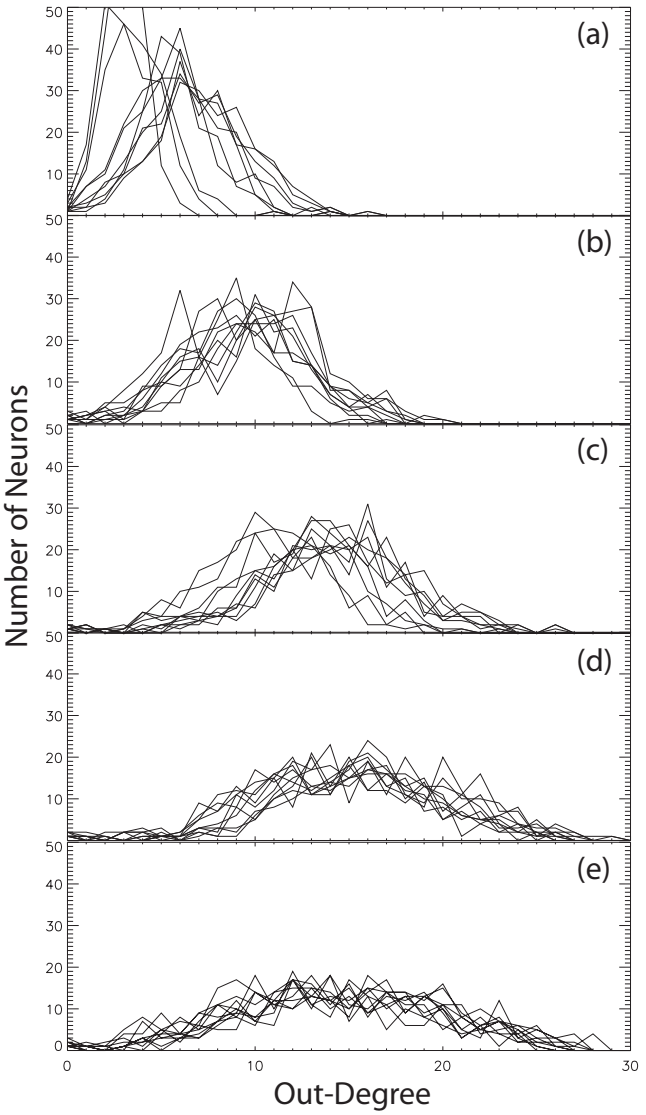

FIG. 5: The final out-degree distribution shown for 10 simulations with all 200 neurons seeded simultaneously. (a) $N = .1$ (b) $N = .5$ (c) $N = 1$ (d) $N = 2$ (e) $N = 5$ Here we see a behavior similar to the case of the in-degree distribution.

allowed to randomly pop-up in time (still with a random placement) throughout the simulation as shown in Fig. 2 (f-j). This was done so that the neurons would not necessarily only establish connections with their neighbors, but could establish longer range connections as well. The final network structure for the two cases was quite different implying that the spatial initial placement of the neurons plays a large role in the resulting network structure.

In attempt to remove the effects of neuron placement, we increased the number of neurons used to 200, which increased the density of neurons on the grid and led to a more uniform spatial distribution of neurons. We then allowed the neurons to evolve and evaluated their final network structure by examining the degree distribution. Figure 4 shows the final in-degree distribution for 10 simulations for 5 different levels of total neurotrophin. As the amount of available neurotrophin is increased, we see a shift in the peak of the distribution toward a higher degree. This reflects the neurons ability to maintain more connections with the higher level of available neurotrophin. However, beyond a certain point ($N = 2$), this increase stops. At this point, the neurons are not able to exhaust the supply of neurotrophin so having additional neurotrophin available does not create a shift in the distribution. In Fig. 5 we see that the out-degree distribution follows a similar pattern.

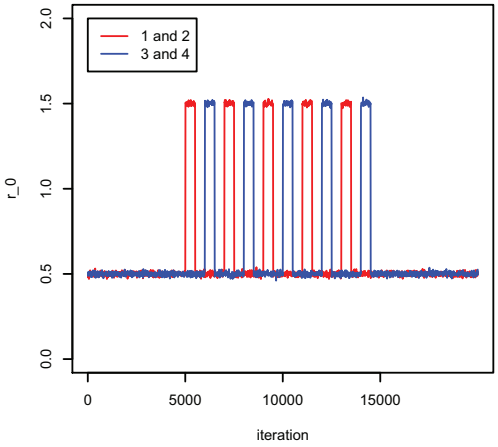

FIG. 6: Dynamical changes in the baseline input for simulations of the fully connected 4 neuron model.

B. Four neuron model

In this simulation we study the influence of the total amount of neurotrophin available to neurons on the ability of the network to reflect correlations in the input firing rates. That is, how the classical Hebb paradigm of increased connection strength between neurons with correlated firing dynamics [11] is modulated by the influence of neurotrophin competition.

To decrease the computational demand we investigate a toy network of 4 fully connected neurons with equal initial connection weights $w_{ij}(0) = 0.1$ and their dynamics given by Eqs. 1-3. Initially all neurons receive the same noisy baseline input $r_0(t) = 0.5 + \epsilon(t)$, where $\epsilon(t)$ are normally distributed random variables with mean 0 and standard deviation 0.01 computed for each iteration. After 5000 iterations the baseline input shifts into a switching dynamic as shown in Fig. 6. For 500 iterations neurons 1 and 2, group A, receive elevated baseline input $r_0(t) = 1.5 + \epsilon(t)$, then for another 500 iterations all neurons receive again the same lower baseline input. Now, for 500 iterations neurons 3 and 4, group B, receive elevated baseline input, then again 500 iterations of equal baseline input. This switching dynamic between groups is kept for a total of 10000 iterations, followed by 5000 iterations of equal baseline input for all neurons.

Results for different runs of the simulation with different amounts of neurotrophin (N = 0.5, 0.7, and 1.2) are shown in Fig. 7. Plotted as straight lines are the firing rates for all four neurons. The dotted lines show the strengths of incoming connections to neuron 1. For the ease of clarity we do not show incoming connection strengths to neurons 2, 3, and 4, which show the same grouping dynamics.

The total amount of neurotrophin affects the dynamics of the network. For low levels of neurotrophin ($N = 0.5$) the connection strengths decrease asymptotically to zero, independent of the input group. For intermediated levels ($N = 0.7$) one can see the differentiation of the network

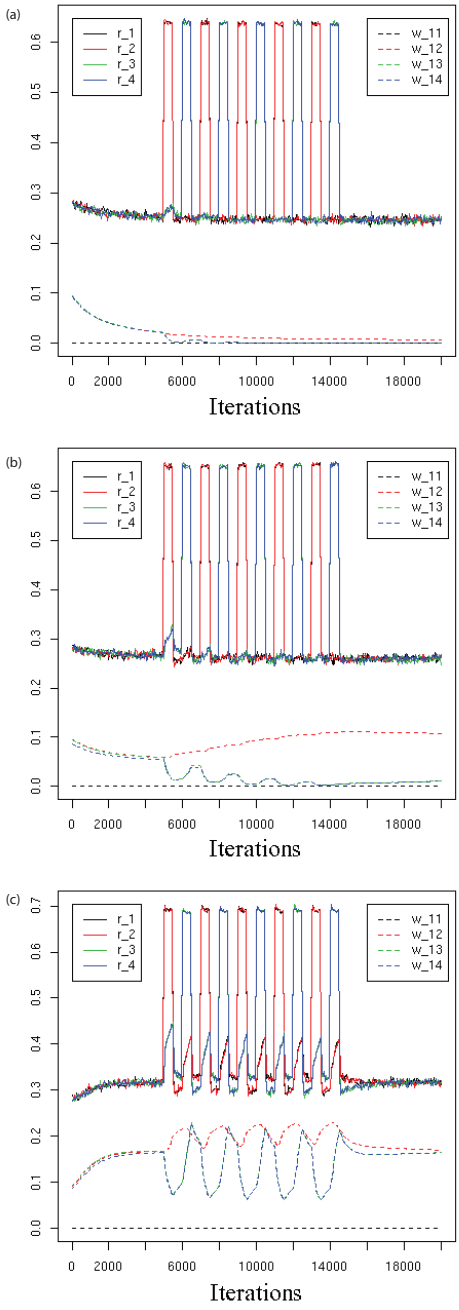

FIG. 7: Firing rate and connection strength dynamics for three different levels of total neurotrophin available to each neuron. (a) $N = 0.5$ (b) $N = 0.7$ (c) $N = 1.2$

connectivity according to input group. Whereas the connection strength to neurons in the same group increase, here w_{12}, those to other groups decrease to zero. If the amount of neurotrophin is set to a large value ($N = 1.2$), no competition takes place and the connection strengths vary periodically reflecting the input switching dynamic.

IV. DISCUSSION AND CONCLUSIONS

The model combines the formation and dynamics of synaptic connections in a neural network, subject to a biologically plausible constraint mechanism. It displays overshoot of the growth area followed by contraction to a steady state. This phenomenon has been widely observed in a number of aspects of neural development, including the number of synaptic connections. The steady state connectivity depends crucially on the amount of neurotrophin available, as reflected in changes in the in- and out-degree distributions of the connectivity matrix. Future work should examine the resulting degree distributions in a manner which also takes into account the weight of each connection.

We were also able to show using a small four neuron model that existing connections are still plastic to changes according to different input patterns. The mechanism of competition for neurotrophin between the synaptic input strengths of every neuron can lead to the separation of the network into functionally defined modules. We hypothesize that the introduction of different baseline firing rates into the larger model would also lead to the separation of the network into separate communities.

Further research is needed to study the firing rate dynamics, the plasticity and formation of functional modules during the outgrowth and establishment of neuronal connections. Studying the recovery of artificially damaged networks, e.g. by cutting randomly or spatially restricted neuronal connections could lead to insights into the ability of networks to recover and again form connections. The introduction of a time dynamic of the total amount of neurotrophin available to each neuron could lead to the on- and offset of critical periods during which competition and outgrowth take place.

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