Development of Neural Network Structure with Biological Mechanisms

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Abstract. We present an evolving neural network model in which synapses appear and disappear stochastically according to bio-inspired probabilities. These are in general nonlinear functions of the local fields felt by neurons—akin to electrical stimulation—and of the global average field—representing total energy consumption. We find that initial degree distributions then evolve towards stationary states which can either be fairly homogeneous or highly heterogeneous, depending on parameters. The critical cases—which can result in scale-free distributions—are shown to correspond, under a mean-field approximation, to nonlinear drift-diffusion equations. We show how appropriate choices of parameters yield good quantitative agreement with published experimental data concerning synaptic densities during brain development (synaptic pruning).

Keywords: Neural networks, Brain development, synaptic pruning.

1   Introduction

Neural systems, whether natural or artificial, are paradigmatic cases of complex systems consisting of many interacting dynamical elements [1,2]. The phenomenology that ensues depends not only on the nature of the neurons and synapses [3], but also on the topology of the underlying network, with the result that structure influences function [4]. In the case of biological neural networks, the inverse also appears to be true: topology is dynamic and related to neural activity. This relation is probably very complex; however, we will try to account for the some of main mechanisms described in the biological literature that lead to the forming or elimination of synapses.

One of the most striking features of brain development is the systematic and relatively rapid net reduction in the density of synapses undergone as of a very early age—resulting, in humans, in adult brains with about half the synaptic density of newborns [5]. Another interesting feature is synaptogenesis, which has been related to various interacting local influences such as the concentration

of different neurotransmitters and electrical stimulation [6,7]. On the other hand, synapses can suffer atrophy and die, probably if not potentiated enough by use.

Chechik *et al.* have proposed a model for synaptic pruning based on Hebbian learning in which the weakest synapses are systematically removed [8,9], and show how this scheme allows for a reduction in synaptic density while preserving near-optimal properties. However, this research is not concerned with topological aspects of network evolution. Meanwhile, in the field of complex networks, many authors have studied a variety of evolving network models (for a review, see for example Boccaletti *et al.* [10]), in which nodes and/or edges appear or disappear according to local rules such as preferential attachment. In line with this, we here endeavour to show how a rather general evolving network model which mimics biological mechanisms can result in topological features which are in good accord with experimental data.

2   The Model

We consider a neural network with N neurons. The adjacency matrix $\epsilon_{ij} = \{1, 0\}$ defines whether there is some form of synaptic interaction between neurons i and j (if $\epsilon_{ij} = 1$, we say i and j are *neighbours*). Each neuron can then be characterised by its *degree*, $k_i = \sum_j \epsilon_{ij}$. The strength of the interaction is determined by the weights ω_{ij} which typically will store information via the application of some learning rule [11,12]. The state of neuron i is described at each time t by its *activity* s_i, which for concreteness we will consider to be a binary variable as in a Hopfield model [1]. The dynamics for the activity of neuron i responds to the total incoming *field* $h_i \equiv \sum_j \epsilon_{ij}\omega_{ij}s_j$ it receives at each time from its neighbours. One can then assume particular transition rates for the activities, s_i, as functions of the fields, h_i. However, for the purposes of this study we need not assume any particular form for this dependence, since the conclusions are valid independently of the rates used.

The adjacency matrix also has a dynamics, based on a combination of local and global rules for the emergence and disappearance of edges—representing, for example, growth and death of synapses. Initially, we will have a random network where the degrees k_i follow some distribution $p(k, t = 0)$—i.e., edges are placed randomly among the nodes until this distribution is achieved, implying a total of $\langle k \rangle N/2$ edges, where $\langle \cdot \rangle \equiv N^{-1}\sum_i(\cdot)$ stands for an average over neurons. Every time step, each neuron has a probability, to be defined, of gaining a new synapse, P_i^{gain}, to a random neuron. It also has a probability of loosing a (randomly chosen) synapse, P_i^{lose}. To define these probabilities, we will take into account the two mechanisms which are widely thought to define synaptic growth and death in biological neural networks. Firstly, Chechik *et al.* [8,9] have proposed that the phenomenon known as *synaptic pruning*, whereby the mean synaptic density in the brain during development drops considerably, could be related to energy conservation requirements. In our model, the total energy E (or total current) can be identified with the mean value of the field, $E = \sum_i h_i$. The second mechanism is that by which synaptic growth is stimulated by local

electrical activity [6,7]. This would correspond here, for a given neuron i, to the field it feels, h_i. Taking both these consiedrations into account, we will assume that the probabilities factorise as follows:

$$P_i^{\text{gain}} = u(E)\pi(h_i)$$

and

$$P_i^{\text{lose}} = d(E)\sigma(h_i),$$

where both E and h_i are time-dependent, although for clarity this is not explicitated. The functions $\pi(h_i)$ and $\sigma(h_i)$ can be any (in general, nonlinear) functions of the field of neuron i. The terms $u(E)$ and $d(E)$ can also be arbitrary functions.

In a mean-field approximation, we can treat the dynamics for the synapses independently of the activity, and therefore render our results very general, simply by assuming that the field of a node is proportional to its degree. This can be derived formally as follows. The expected value of the adjacency matrix for a network in the configuration ensemble[1] is $[\epsilon_{ij}] = k_i k_j / (\langle k \rangle N)$, where the expected value operator $[\cdot]$ can be interpreted as an average over all configurations in the ensemble. Inserting this value in the definition of h_i yields $h_i = k_i \mu_i$, where for large networks the term $\mu_i \equiv (\langle k \rangle N)^{-1} \sum_j \omega_{ij} k_j s_j$ can be considered independent of i as long as the weights ω_{ij} are statistically independent of k_i and k_j [4]. By the same reasoning, the total energy is proportional to the mean degree of the network, $E \propto \langle k \rangle$ (though see note[2]).

Under this approximation, we can now write the probabilities for growth and death as

$$P_i^{\text{gain}} = u(\langle k \rangle)\pi(k_i)$$

and

$$P_i^{\text{lose}} = d(\langle k \rangle)\sigma(k_i),$$

The local probabilities $\pi(k)$ and $\sigma(k)$ correspond to preferential attachment and detachment, similar to those used by Barabási and Albert for their evolving network model [13] and later implemented in many models. For example, we have already studied the case of nonlinear preferential rewiring of one edge at a time [14] while maintaining the number of nodes and edges in the network fixed (equivalent, over large enough times, to keeping $P_i^{\text{gain}} = P_i^{\text{lose}} = 1$). Here we report on the main results concerning this more general scenario. A more detailed and extensive analysis is underway [15].

3   General Results

The probabilities P_i^{gain} and P_i^{lose} a given neuron i has, at each time step, of increasing or decreasing its degree can be interpreted as transition probabilities between states. Furthermore, for each synapse that is withdrawn form the

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[1] This is the collection of all possible network configurations which respect a given degree sequence $\{k_1, ... k_N\}$ but are otherwise randomly wired.

[2] Note that this is possible because we are considering N to remain constant. It is known that in reality neurons can die and also be replenished. However, in this simplified model we are neglecting this effect.

network, two neurons decrease in degree. One is neuron i chosen according to $\sigma(k_i)$, the other, say neuron j, is a random neighbour of i's; therefore, there is an added effective probability of loss $k_j/(\langle k \rangle N)$. Similarly, for each synapse placed in the network, not only neuron l chosen according to $\pi(k_l)$ increases its degree; a random neuron m will also gain, with the consequent effective probability of (approximately) N^{-1}. Thus, by summing over all these probabilities, we can obtain an equation for the expected value of the increment in a given $p(k,t)$ at each time step, $\Delta p(k,t)$, which we will equate with a temporal partial derivative:

$$\frac{\partial p(k,t)}{\partial t} =$$

$$u(\langle k \rangle)\left[\pi(k-1)+\frac{1}{N}\right]p(k-1,t) + d(\langle k \rangle)\left[\sigma(k+1)+\frac{k+1}{\langle k \rangle N}\right]p(k+1,t) -$$

$$-\left\{u(\langle k \rangle)\left[\pi(k)+\frac{1}{N}\right]+d(\langle k \rangle)\left[\sigma(k)+\frac{k}{\langle k \rangle N}\right]\right\}p(k,t)\,(1)$$

Assuming that $p(k,t)$ evolves towards a stationary distribution, $p_{st}(k)$, we can set Eq. (1) equal to zero and, after again substituting a difference for a partial derivative, obtain a condition for stationarity:

$$\frac{\partial p_{st}(k)}{\partial k} = \frac{u(\langle k \rangle)}{d(\langle k \rangle)}\left[\frac{\pi(k)+\frac{1}{N}}{\sigma(k+1)+\frac{k+1}{\langle k \rangle N}}-1\right]p_{st}(k). \tag{2}$$

In fact, $p_{st}(k)$ must also be such that $u(\langle k \rangle) = d(\langle k \rangle)$ (since the total number of synapses must then be conserved) with $\langle k \rangle = \sum_k k p_{st}(k)$. From Eq. (2) we can see that $p_{st}(k)$ will have an extremum at some value k_e if it satisfies $\pi(k_e)+\frac{1}{N} = \sigma(k_e+1)+\frac{k_e+1}{\langle k \rangle N}$. Assuming, for example, that there is one and only one such k_e, then, depending on the concavity of $p_{st}(k)$ at this point, it will correspond to a maximum (implying a relatively homogeneous distribution) or a minimum (with the result that $p_{st}(k)$ will be split in two, and therefore highly heterogeneous). The critical case separating these two regimes occurs when $\pi(k)$ and $\sigma(k)$ are such that $\pi(k) + N^{-1} = \sigma(k) + k/(\langle k \rangle N)$, $\forall k$. For this critical choice, Eq. (1) can be shown [15] to reduce to a nonlinear drift-diffusion equation, with a non-uniform velocity $c = u(\langle k \rangle) - d(\langle k \rangle)$ in the increasing k direction.

To the best of our knowledge, this is the first dynamic network model to be proposed and studied in which the rewiring actions respond to completely general nonlinear functions of local degrees and the global mean degree.

4   The Effects of Drift: Application to Synaptic Pruning

Let us define $\langle k \rangle \equiv \kappa(t)$ and assume the following linear forms for $u(\langle k \rangle)$ and $d(\langle k \rangle)$:

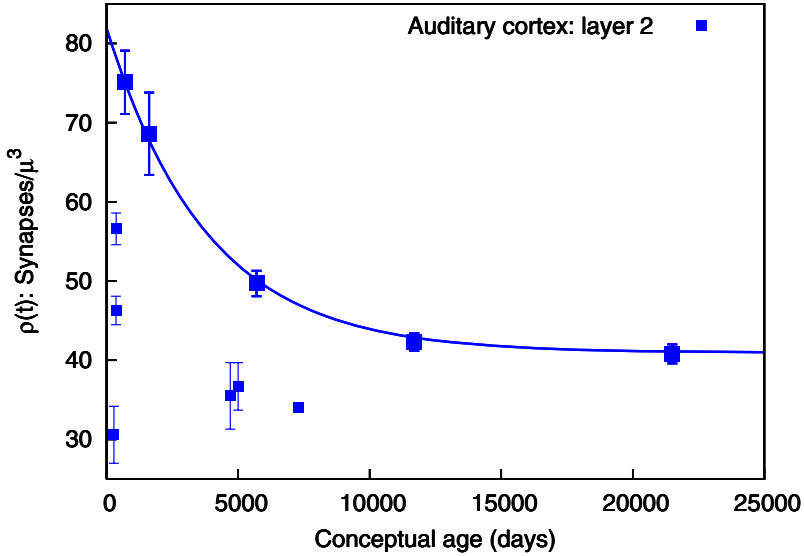$$u(t) = \frac{n}{N}\left(1 - \frac{\kappa(t)}{\kappa_m}\right), \tag{3}$$

Fig. 1. Synaptic pruning in cortical layer 2 of the human auditory cortex. Experimental data from Huttenlocher and Dabholkar [5]. The line follows the best fit to Eq. (6), where parameters are $\rho(0) = 81.93$ and $\nu = 0.0107$, measured in synapses/μm^3 and synapses/μm^3/day, respectively. Correlation was $r^2 = 0.906$. Data pertaining to the rapid overgrowth of the first year after conception were omitted from the fit, as were those measured at days 4700, 5000 7300—which, for unknown reasons, fall abnormally far below the line marking the general tendency. These data points are plotted with smaller squares than the rest.

$$d(t) = \frac{n}{N} \frac{\kappa(t)}{\kappa_m}, \tag{4}$$

where the parameter n can be interpreted as the expected value of the number of additions and deletions of synapses per MCS and κ_m is the maximum value the mean degree can have. This choice describes a situation in which the higher the density of synapses, the less likely new synapses are to "sprout" and the more likely existing synapses are to "atrophy". The increment in $\kappa(t)$ is

$$\frac{d\kappa(t)}{dt} = 2[u(t) - d(t)] = \frac{2n}{N} \left[1 - \frac{2\kappa(t)}{\kappa_m} \right], \tag{5}$$

where the factor 2 after the first equality appears because for each addition or deletion of a synapse, the degrees of two neurons are modified. We have, therefore, that temporal evolution of the mean degree will increase or decrease exponentially from $\kappa(0)$ to $\kappa_m/2$. Defining the mean synaptic density in some volume V, $\rho(t) \equiv \kappa(t)N/(2V)$ (which is the magnitude usually measured experimentally), and assuming for simplicity that $\kappa(0) = \kappa_m$ (or $\rho(0) = \rho_m$), the solution of Eq. (5) is

$$\rho(t) = \frac{1}{2}\rho(0)\left[1 + \exp\left(-\frac{2\nu}{\rho(0)}t\right)\right]. \tag{6}$$

where $\nu \equiv n/V$ (the only parameter) is the number of synapses modified (added plus deleted) per unit volume per unit time.

This equation is fitted to experimental data on layer 2 of the human auditory cortex, obtained by Huttenlocher and Dabholkar [5], and shown in Fig. 1. Time is measured in days since conception and synaptic density is in synapses per cubic micron. We assume that the initial overgrowth is governed by other factors and use Eq. (6) only as of the onset of synaptic pruning. In this way we can estimate a value of $\nu \simeq 0.01$ synapses per μ^3 per day. The data for three particular days does not seem to fit the general tendency very well. We do not know what the source of these deviations is, but it is unlikely that densities actually fluctuate to that extent within one individual. Rather, it seems more probable that they correspond to data from subjects with inherently lower synaptic density (it is important to note that data points corresponding to different times were taken from different subjects).

5   The Effects of Diffusion: Heterogeneous Topologies

Figure 2 shows typical stationary degree distributions obtained in the three regimes that emerge: in the subcritical regime, the distribution remains relatively homogeneous; in the supercritical regime, a phenomenon akin to gelation in polymers occurs, in which a small number of neurons is connected to most of the network. In the critical case, $p(k)$ is seen to evolve towards a scale-free stationary state, $p_{st}(k) \sim k^{-2}$, as is characteristic of second order phase transitions. Interestingly, the functional topology, as defined by correlated activity between clusters of neurons, in the human cortex during cognitive tasks has also been found to acquire a scale-free distribution with exponent $\gamma \simeq -2$ [16]. The same authors have argued that the reason for this is that the brain maximises its performance in a complex world by becoming critical. Recent theoretical work [4] also suggests that random topologies with distribution $p_{st}(k) \sim k^{-2}$ can result in optimal performance for neural networks executing dynamical tasks.

It is still not clear what kind of degree distribution the structural topology of the brain follows. However, it seems that function reflects structure at least to some extent [17]. Furthermore, it has been suggested, based on indirect methods, that the structural connectivity of cat and macaque brains, at the level of brain areas, may indeed be scale free [18] — and in any case displays significantly higher heterogeneity than that of, say, Erdős-Rényi random graphs.

6   Discussion

We have presented a very general evolving neural network model in which local and global rules for synaptic growth and death are coupled to the local fields and
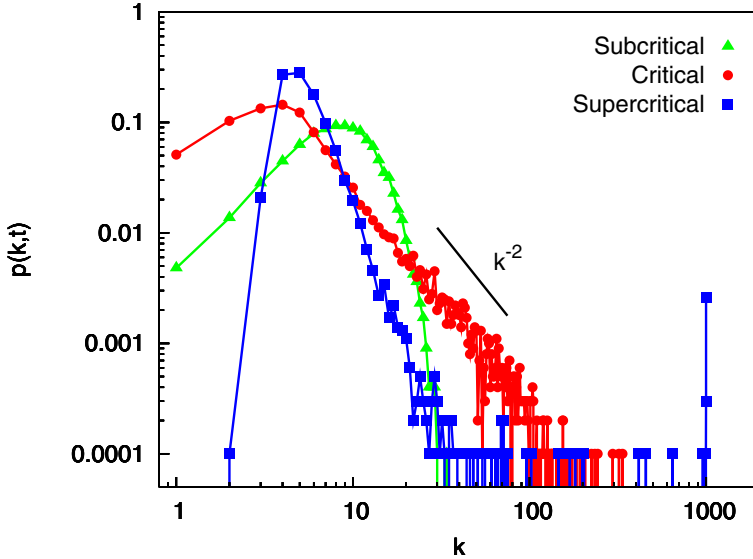
Fig. 2. Stationary distributions $p_{st}(k)$ obtained from MC simulations of the model after 10^5 MCS. The networks all started as regular random graphs with $\kappa(0) = 20$. Local probabilities were $\sigma(k) = k/(\langle k \rangle N)$ in all cases and $\pi(k) = \sigma(k)$, $\pi(k) = 2\sigma(k) - N^{-1}$ and $\pi(k) = k^{1.5}/(\langle k^{1.5} \rangle N)$ for the subcritical (triangles), critical (circles) and supercritical (squares) cases, respectively. Global probabilities $u(\langle k \rangle)$ and $d(\langle k \rangle)$ were as in the example in the main text, with $n = 10$ and $\kappa_m = 20$. $N = 1000$.

total energy consumption, respectively. Under a mean-field approximation, the situation can be reduced to a nonlinear preferential rewiring model, similar to the one studied in Ref. [14] but more general. We derive analytical expressions which can be compared to experimental data. In particular, our results are in good quantitative agreement with results for synaptic pruning. Furthermore, they show how scale-free stationary degree distributions can be obtained with biologically inspired mechanisms. To the best of our knowledge, this is the first attempt to model emergent topological properties of the brain from this kind of microscopic considerations.

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