

Connection strategies in neocortical networks

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Abstract.

This study considers the impact of different connection strategies in developing neocortical networks. An adequate connectivity is a requisite for synaptogenesis and the development of synchronous oscillatory network activity during maturation of cortical networks. In a defined time window early in development neurites have to grow out and connect to other neurons. Based on morphological observations we postulate that the underlying mechanism differs from common strategies of unspecific global or small world strategies. We show here that a displaced local connection mode is a very effective approach to connect neurons with minimal costs.

1 Introduction

Spontaneous large-scale wave-like activity during early development of the neocortex can be observed in cell cultures [1], where networks show similar development as in the brain, using imaging techniques and electrophysiological patch-clamp-measurements. The synchronous activity appear in culture at the beginning of the second week and eventually includes the entire neuronal population about 1 wk later [2]. In standard culture conditions neurons become electrically active spontaneously and independently. Next neurons connect to each other, form synapses, and begin to burst simultaneously, discharging collectively about once per minute. Time histograms show that the portion of synchronously firing neurons increases with time. Because non-active neurons die before the end of the second week in vitro [3], the participation in synchronous oscillatory activity seems to play an important role in the early development of the mammalian cortex.

In [4] we have investigated conditions and parameters for the emergence of oscillatory network activity by accumulated activity of distinct single cells in intrinsic driven networks. Tabak et al. [5] described a global model to transform spontaneous activity in random connected networks in episodic events of synchronized activity. Like Tabak's model, many population models consist only of unspecific random connections (overview in [6]). Maeda et al. [7] showed in physiological experiments that the source of synchronized bursts change on every stimulation episode and there is a time delay from source of burst to distance

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neurons. This behaviour is coherent with a locally connected network. On the other hand, 'small world' networks [8] contain a majority of local connections between cells, but a few of the connections are long distance connections. This content of long-distance connections can impact the synchronization and waves in epilepsy [9].

The correlation between neuritic growth dynamics and the development of effective network connectivity was recently highlighted [10]. To build a functionally interconnected network, single neurons have to become interconnected in a defined time window, that is limited by the emergence of synchronous network activity. The biologically most plausible mechanism is not a global random or a small world one, and simple local connections do not have the capacity to connect a network in a way that it can easily perform synchronized events. Latham [11] introduced a local connection type which build a cluster of connections at a distance of the source neuron. This connection mode resembles the connection mode of neurons in vivo [1]. The mechanism to build these connections are very similar to local connections by a probability map with falling probability from center, but here the probability map is displaced. The center is not the source cell itself but a branching point in a specified distance from neuron. Here we analyse the displaced connection strategy and compare it with small world topologies.

2 Methods

A *network section* of $n = 400$ neurons was assembled, arranged on the planar area of $1 \times 1 \text{ mm}^2$, a simple representation reproducing culture dish plating. Assuming the network structure to be homogenous (and prevent overlying of neuronal positions), these cells positions were de-clustered, scattered uniformly over the section's area using the neural-gas-algorithm according to [12], which minimizes the spatial entropy of the position's distribution.

We compare two connection methods. The *small world connections* starts by pure *local connections* (Fig. 1). Cells connect only in the immediate neighbourhood. The probability to connect a cell a on position \mathbf{x}_a with a cell b on position \mathbf{x}_b directly depends on the Euclidean distance $d_{ab} = |\mathbf{x}_a - \mathbf{x}_b|$ and is modulated by Gaussian function $p_{ab}^l = p_m e^{-d_{ab}/\sigma^2}$. In small world mode a defined part (ρ) of connections breaks and reconnects as *global unspecific connections*. The probability of these connections is independent from relative position of source and destination cell and constant to all pairs of cells $p_{a,b}^g = p_m = \text{const.}$

Based on work of Latham [11] and morphological observations [[2], [1], [10]] we defined an advanced type of local connections with a displaced local probability map (*displaced local connections*). In the early development of network the neurites (axons) first grow and then at a certain distance from the cell body build connections in a local area (see Fig. 1 D). In that way neurons may protect themselves against formation of small feedback loops and self-excitation. Each axon grows in a random direction \mathbf{y} . In a distance of l_{disp} it builds a local probability map in same way as on pure local connections: $p_{a,b}^l = p_m e^{-d_{a,b}^c/\sigma^2}$ but distances

are defined from the displaced cluster center: $d_{a,b}^c = |(\mathbf{x}_a + l_{disp} * \mathbf{y}) - \mathbf{x}_b|$. The cluster center approximates the branching of axons. The small world network by Watts [8] allows a floating transition from local to unspecific global connections by defining the fraction of global connections. The displacement of probability map allows a floating transition from pure local connections to a more natural connections mode by defining the branching distance of axon.

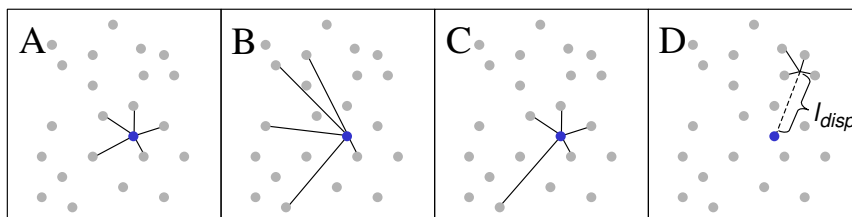


Fig. 1: Connection methods: (A) Local ($\rho = 0$), (B) Global ($\rho = 1.0$) (C) Small world ($\rho = 0.2$) (D) Displaced local (l_{disp})

Network generation and analysis are done by c++ programs on a linux pc-cluster (42 nodes). Additional simulations are done by *neuron* [13] program.

3 Experiments and Results

3.1 Network properties

Networks were generated using two connection modes. The parameters (see Fig. 2) of probability maps for different connection types are set in a way that the *degree* of neurons, i.e. the number of incoming and outgoing connections per neuron, is nearly constant. The total connection length per neuron is estimated by the summed length of its outgoing connections. In pure local ($\rho = 0$) and in global ($\rho = 1.0$) connections the total connection length is simply the sum of Euclidian distances to destination cells. On displaced local connection a branching point of axon is defined. The total connection length result here as the sum of the Euclidian distance to the branching point and the Euclidian distances from branching point to destination cells. To check the overall connectivity we measured the minimal network distance among neurons. We define the minimal network distance as the minimal number of synaptic connections between two neurons. The minimal network distance between neurons is important for the capacity of the network to synchronize activity. We show in [14] that the shortcuts in small world networks can stabilize synchrony.

The connection length per neuron is small on local connection method compared to the random unspecific method (see Fig. 2 A-B). A moderate proportion of global (long range) connections ($\rho = 0.034$) minimally raises the connection length of local networks (Fig. 2 C). If we compare minimal network distance, the opposite effect is shown. In locally connected networks neurons are separated by a relatively large number of nodes (Fig. 3). Information transmission through

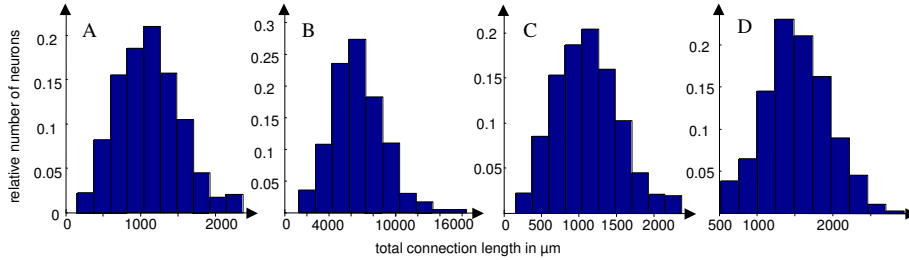


Fig. 2: Histograms of total connection length per neuron. Degree $mean = 12.5$, $standarddeviation = 4$. Connection methods: (A) Local ($\rho = 0$, $\sigma = 100\mu m$, $p_m = 1.0$), (B) Global ($\rho = 1.0$, $p_m = 0.06$) (C) Moderate small world ($\rho = 0.034$) (D) Displaced local ($l_{disp} = 300\mu m$, $\sigma = 100\mu m$, $p_m = 1.0$)

the network is slow and it is hard to synchronize neuronal activity. On other side neurons in networks with unspecific random connections are separated by few nodes ($max.= 4$), what allows a very fast synchronization of activity with small phase lags. Even a moderate number of long range connections decreases the minimal network distance dramatically (Fig. 3 A-C). Similarly, in a network with displaced local connections the total connection length increases minimally with the additional length from source cell to the axonal branching point (Fig. 2 D). Again, the minimal network distance is considerably smaller than in locally connected networks (Fig. 3 D). The additional cost is relative small and disappear by a larger number of postsynaptic neurons.

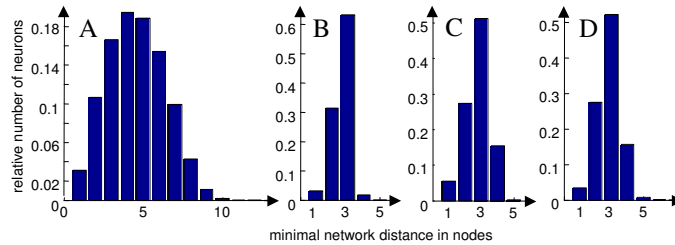


Fig. 3: Histograms of minimal network distance. Parameters as in Fig. 2. Connection methods: (A) Local (B) Global (C) Small world (D) Displaced local

3.2 Optimal displacement

In summary this experiment shows that local connection with displaced probability map is an effective way to reach a good connectivity with minimal costs. Fig 4 (left) shows the minimal network distance and the connection length in relation to the distance between source neuron and axonal branching point in displaced local connections. In biology connection length is limited by energy

costs. If we assumed the consumption of network as average of network distance times average of connection length per neuron, we found a minimum which may be considered as the optimal displacement for this placement area and neuron degree (Fig. 4 (right)).

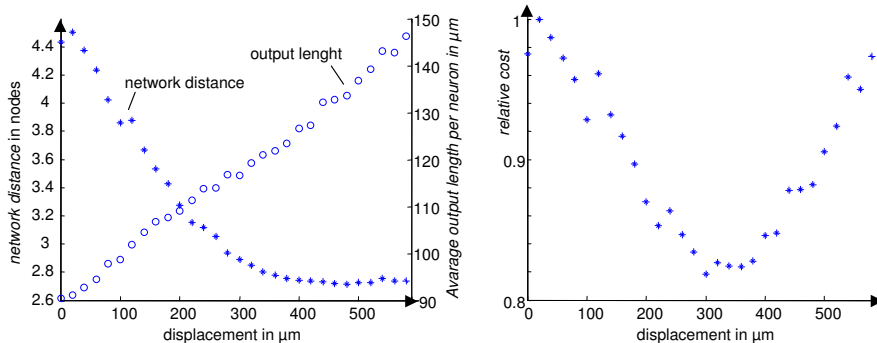


Fig. 4: Variation of Displacement ($l_{disp} = 0.600\mu\text{m}$, other parameters as in Fig. 2). left: network properties; right: minimum cost at $330\mu\text{m}$.

4 Discussion and Conclusion

This paper shows that local network connection mode with displaced center of probability map is an effective way to build recurrent networks. The obtained network properties are similar to the very effective small world networks. We proved the rhythmic activity capacity in all network by simulations with the same parameter as in [14]. The dynamics of networks with displaced local connections are not different from those networks with small world connections. But it is a local mechanism with limited connection length. During development the networks must be connected as fast as possible to start rhythmic bursting. Neuritic growth in young networks is thus limited to a permissive time window, what may bias the network to a local connection mode.

Comparing local with global and small world methods we also have to consider the different effects of scaling the network. On *local methods* the total connection length per neuron is constant, but the minimal network distance grows with the placement area. On *global* and *small world* methods the minimal network distance between neurons do not depend on placement area but only on number of neurons. But on other hand the average and the maximal connection length is dependent on placement area. So local connections with displaced probability map is very interesting to interconnect neurons in small areas. Larger areas can be overlaid by a global network. To combine it, some local connections can be reconnected in the same way as in small world networks. In young network there are hints that a special type of neurons (large GABA, note that GABA is excitatory at this period of maturation) builds an

overlay network and synchronizes large arrays of neurons [1]. This result may also be of interest for hardware realizations of artificial neural networks. Here local connections can be wired directly on chips, but global connection must be designed addressable by a router [15]. Displaced maps can be established by first delivering one output signal by a router to a cluster center anywhere on the chip and spread it from there by wiring. This may reduce the number of routed global connections enormously.

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