An Analytical Approach to Neuronal Connectivity

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This paper describes how realistic neuromorphic networks can have their connectivity properties fully characterized in analytical fashion. By assuming that all neurons have the same shape and are regularly distributed along the two-dimensional orthogonal lattice with parameter \( \Delta \), it is possible to obtain the accurate number of connections and cycles of any length from the autoconvolution function as well as from the respective spectral density derived from the adjacency matrix. It is shown that neuronal shape plays an important role in defining the spatial spread of network connections. In addition, most such networks are characterized by the interesting phenomenon where the connections are progressively shifted along the spatial domain where the network is embedded. It is also shown that the number of cycles follows a power law with their respective length. Morphological measurements for characterization of the spatial distribution of connections, including the adjacency matrix spectral density and the lacunarity of the connections, are suggested. The potential of the proposed approach is illustrated with respect to digital images of real neuronal cells.

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A particularly meaningful way to understand neurons is as cells optimized for selective connections, i.e. connecting between themselves in a specific manner so as to achieve proper circuity and behavior. Indeed, the intricate shape of dendritic trees provide the means for connecting with specific targets while minimizing both the cell volume and the implied metabolism (e.g. [1,2]). While great attention has been placed on the importance of synaptic strength over the emerging neuronal behavior, geometrical features such as the shape and spatial distribution of the involved neurons play a particularly important role in defining the network connectivity. In addition, the topographical organization and connections pervading the mammals’ cortex provide further indication that adjacencies and spatial relationships are fundamental for information processing by biological neuronal networks. The importance of neuronal geometry has been reflected by the growing number of related works (see, for instance, [3]). However, most of such approaches target the characterization of neuronal morphology in terms of indirect and incomplete measures such as area, perimeter and fractal dimension of the dendritic and axonal arborizations, to name but a few. Interesting experimental results regarding the connectivity of neuronal cells growth in vitro have been reported in [4,5] and what is possibly the first direct computational approach to neuronal connectivity was only recently reported in [6], involving the experimental estimation of the critical percolation density as neuronal cells are progressively superposed onto a two-dimensional domain. At the same time, the recent advances in complex network formalism (e.g. [7,8,9,10,11]) provide a wealthy of concepts and tools for addressing connectivity. Initial applications of such a theory to bridge the gap between neuronal shape and function were reported in [12,13,14].

As such developments are characterized by computational approaches involving numerical methods and simulation, a need arises to develop an analytical framework for neuromorphic characterization that could lead to additional insights and theoretical results regarding the relationship between neuronal shape and function. The current paper describes how regular neuromorphic complex networks can be obtained and their connectivity fully characterized in analytical terms. By regular it is meant that all cells have the same shape and are regularly distributed along the two-dimensional orthogonal lattice with parameter \( \Delta \). Such a kind of networks can be considered as models of biological neuronal networks characterized by planarity and morphologic regularity, as is the case with ganglion cell retinal mosaics [14] and the basal dendritic arborization of cortical pyramidal cells.

Let the neuronal cell be represented in terms of the triple \( \eta = [A,S,D] \) where \( A \) is the set of points belonging to its axonal arborization, \( S \) is the set of points corresponding to the respective soma (neuronal body) and \( D \) are the dendritic arborization points. For simplicity’s sake, a finite and discrete neuronal model is considered prior to its continuous general formulation. We therefore assume that the points used to represent the neuron belong to the square orthogonal lattice \( \Omega = \{1,2,\ldots,N\} \times \{1,2,\ldots,N\} \), with parameter \( \Delta = 1 \). The axon and soma are represented by a single point each, i.e. \( A = \{a\} \) and \( S = \{s\} \). Such points could be understood as corresponding to the tip of the axon and the soma center of mass, respectively. The dendritic arborization is represented in terms of the finite set of dendrite points \( D = \{D_1,D_2,\ldots,D_M\} \), and it is henceforth assumed that a dendrite point never coincides with the axon. Figure 1 illustrates such a geometrical representation for a neuron with 3 dendrite points. Observe that the coordinate origin coincides with the axon, which is taken as reference for the soma and dendrite coordinates.
Neuromorphic networks (actually digraphs [8]) can now be obtained by placing one such a neuron at all possible nodes of the orthogonal lattice $\Omega$. By fully characterizing such neuronal architectures, the connections established whenever an axon is overlaid onto a dendrite point (no connections with soma are allowed) stand out as particularly important features of the obtained network. Consequently, it is important to obtain analytical expressions fully characterizing neuronal connectivity, in the sense of the spatial distribution of paths and cycles of any specific length. We start by considering the connections initiated from a single specific neuron $i$ placed at position $\vec{p}$. As illustrated in Figure 2, the three neurons identified by the vectors $\vec{c}_1 = \vec{p} - \vec{d}_1 - \vec{s}$, $\vec{c}_2 = \vec{p} - \vec{d}_2 - \vec{s}$, $\vec{c}_3 = \vec{p} - \vec{d}_3 - \vec{s}$ are directly connected to $i$ through paths of unit length. As is clear from such a construction, the set of neurons connected to $i$ through unit-length paths can be obtained by convolving the initial point $\delta \{\vec{p}\}$ with the function $g(x, y) = \delta \{-\vec{d}_1 - \vec{s}\} + \delta \{-\vec{d}_2 - \vec{s}\} + \delta \{-\vec{d}_3 - \vec{s}\}$. In other words, given a set of initial neurons with axons located at $\xi(x, y)$, the number $\chi(x, y)$ of connections received from that set by a neuron at position $(x, y)$ is obtained as in Equation 1. The binary-valued (1-true, 0-false) function $\nu(x, y)$ given in Equation 2 indicates whether there is a unit-length path between the neuron at $(x, y)$ and the initial set of points $\xi(x, y)$, where $\phi()$ is the hard-limiting function. The functions expressing the number of connections of length $k$ between $\xi(x, y)$ and the neuron at position $(x, y)$ and the presence of at least one such a connection at that position are given by Equations 3 and 4 respectively. The total number of connections from length 1 to $k$ received by the neuron located at position $(x, y)$ from $\xi(x, y)$ is given as in Equation 5. Observe that the use of the Dirac delta function in such a formulation allows the immediate extension of such results to continuous spatial domains. It should be also observed that the above framework can be immediately extended to generalized axons by having the dendritic arborization to undergo Minkowski dilation [15] with the axonal shape and considering as axon only the single point corresponding axon a reference along its shape. While the analytical characterization of the connectivity of the considered network models has been allowed by the fact that identical neuronal shapes are distributed along all points of the orthogonal lattice, it is interesting to consider extensions of such an approach to other situations. An immediate possibility is to consider sparser configurations, characterized by larger lattice parameters $\Delta$. Such an extension involves sampling the neuronal cell image at larger steps.
FIG. 3: Two real neuronal cells (a-b) and their respective total number of connections of length \( k = 1 \) (c-d) and 2 (e-f). The axon has been placed at the cell centroid (considering soma plus dendrites). The neuronal cell figures in (a) and (b) are adapted with permission from [14].

FIG. 4: The total number of connections of length \( k = 1 \) (a), 2 (b), 3 (c) and 4(d) for the neuronal cell in Figure 3(a) with the axon placed over the cell centroid, which is itself displaced from the cell centroid by \( \vec{s} = (0, 7) \) pixels.

related measurements. Let \( P(x, y) \) be a density function obtained by normalizing \( \chi_k(x, y) \). Thus, the spatial scattering of the connections can be quantified in terms of the respective covariance matrix \( K_k \), and the spatial displacement of the centroid of \( P(x, y) \) can be quantified in terms of the ‘speed’ \( v = ||\vec{s}|| \). Additional geometrical measurements of the evolution of the neuronal connectivity that can be derived from the covariance matrix \( K \) include the angle \( \alpha_k \) that the distribution main axis makes with the x-axis and the ratio \( \rho_k \) between the largest and smallest respective eigenvalues.

Another interesting network feature related to connectivity is its number \( C_{\ell,k} \) of cycles of length \( \ell \) established by the synaptic connections. This feature can be calculated from the enlarged matrix \( A \) obtained by stacking the columns of the matrix where the neuronal cell image is represented in order to obtain the rows of \( A \), while the reference point of the cell is shifted along the main diagonal of \( A \). Observe that the image size \( N \times N \) has to be large enough in case dynamics near the toroidal boundary conditions are to be avoided. The \( N^2 \) eigenvalues of the thus obtained adjacency matrix \( A \) of the whole two-dimensional network are henceforth represented as \( \lambda_i, i = 1, 2, \ldots, N^2 \). As \( A \) is circulant, these eigenvalues can be immediately obtained from the Fourier transform of its first row. Observe that the simplicity and speed of such an approach allow for systematic investigation of a variety of different neuronal shapes. As the cell reference point is assumed never to coincide with a dendrite point, we also have that \( \sum_{\lambda=r}^{N} \lambda = 0 \). As \( A \) is a non-negative matrix, there will always be a non-negative eigenvalue \( \lambda_M \), called the dominant eigenvalue of \( A \), such that \( \lambda_r \leq \lambda_M \) for any \( r = 1, 2, \ldots, N \). The (unnormalized) cycle density of \( \Gamma \), defined in Equation 6, provides a clear characterization of the network cycles in terms of their respective populations. The total number of cycles up to length \( P \) is defined as \( T = \sum_{p=1}^{P} \Lambda(p) \). The spectral density (e.g. 7) of the adjacency matrix, defined in Equation 7, where \( \lambda_p \) is the \( p \)-th eigenvalue of \( A \), provides an additional way to characterize the topology of the obtained networks.

\[
\Phi(t) = \sum_{p=1}^{P} \Lambda(p) \delta(t - p) \tag{6}
\]

\[
\rho(\lambda) = \frac{1}{N} \sum_{r=1}^{N} \delta(\lambda - \lambda_r) \tag{7}
\]

It is interesting to note that as the maximum length \( p \) in Equation 6 increases, the number of cycles with that length can be approximated as \( \Lambda(p) \approx \lambda_M^p \), i.e. the dynamics of \( p \) is defined by the dominant eigenvalue of \( A \), and the distribution of \( \Lambda(p) \) tends to follow a power law. The eigenvalue \( \lambda_M \), which depends on the specific dynamics through which new edges are incorporated into the network, therefore represents an interesting parameter for characterizing the cyclic composition of complex.
FIG. 5: Spectral density of the adjacency matrices obtained for the neuronal cells in Figure 3 considering $\Delta = 1$ (a) and $\Delta = 5$ (b). The crossed lines refers to the sparser neuronal cell.

FIG. 6: Lacunarities for the spatial distributions of connections for the cells in Figure 3.

networks. Figures 5(a) and (b) show the real part (recall that the adjacency matrix for a digraph is not necessarily symmetric) of the spectral density of the adjacency matrices obtained for the neuronal cells in Figure 5(a) and (b) considering $\Delta = 1$ and 5. The wider dispersion of the spectrum of the denser cell in Figure 5(a) reflects a higher potential for connections of that neuron in both cases. It is also clear that the separation of cells by $\Delta = 5$ leads to a substantially smaller spectrum, with immediate implications for the respective neuronal connectivity.

An additional morphological property of the spatial distribution of the connections is their respective lacunarity (e.g. [16]), which expresses the degree of translational invariance of the obtained densities. Figure 6 shows the lacunarities of the connection densities obtained for the two considered cells with respect to $k = 1$ to 4. It is interesting to observe that most of the lacunarity differences are observed for $k = 1$, with similar curves being obtained for larger values of $k$. At the same time, the denser cell led to lower lacunarity values. Given their immediate implications for neuronal connectivity, the above proposed set of neuronal shape measurements present specially good potential for neuron characterization and classification.

In addition to paving the way for the complete analytical characterization of the connections in regular neuro-morphic networks in terms of paths and cycles, the framework proposed in this article can be immediately adapted to express the spread of neuronal activity starting from the stimulus $\xi(x, y)$. The neurons are understood to accept input and produce output in synchronous manner at each clock cycle $T$. For instance, the situation where the neuronal cell output corresponds to the inner product between its shape and the respective area of the input space can be immediately characterized in terms of the eigenvalues and eigenvectors of precisely the same adjacency matrix $A$ constructed as described above. Although the proposed methodology assumes identical, uniformly distributed neuronal cells, it is expected that they provide a reference model for investigating and characterizing real networks characterized by a certain degree of regularity, such as some subsystems found in the retina and cortex. Mean-field extensions of the reported approach are currently being investigated.

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