



NEURAL NETWORKS LETTER

A New Approach to the Analysis of Multidimensional Neuronal Activity: Markov Random Fields

VLADIMIR I. MAKARENKO,¹ JOHN P. WELSH, ERIC J. LANG AND RODOLFO LLINÁS

Department of Physiology and Neuroscience, NYU School of Medicine

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Abstract—How can information hidden in a spatial configuration of neuronal activity be addressed? The Markov Random Field method for the analysis of the spatial component of a multidimensional neuronal process is introduced and after simulations is applied to experimental data on rat at olivocerebellar activity. Using this method it was determined, for the first time, that the activity demonstrates dynamic coupling and may have different fine spatial substructures. The results obtained support the view that the inferior olive serves as a movement organizing centre that controls motor activity by means of spatially as well as temporally organized patterns of coherent activity. © 1997 Elsevier Science Ltd.

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1. INTRODUCTION

The multiple and simultaneous electrical recording technique utilizing single cell electrodes is presently becoming one of the most important experimental tools in neuroscience. However the data glut resulting from such methodology poses enormous difficulties in the extracting of the meaningful information for reasons of sheer volume. Because traditionally only the temporal component of the electrical activity of neurons was studied, the spatial structure of such activity remained hidden in the experimental data. A new approach introduced here based on the Markov Random Fields (MRF), bridges this gap effectively. It offers for the first time, the possibility of quantifying multidimensional neuronal activity in a manner that informs about group coupling, character of clustering, stability with respect to fluctuations and some other features readily available for quantification.

Historically the development of this type of analysis began with work by Little (1974) who noticed a close

connection between neuronal network properties and phase transitions in statistical physics. He compared a transition matrix of the Ising model with that of a stochastic neuronal network and related phase transitions to a degeneracy of the maximum eigenvalue of the transition matrix and presented examples of neuronal networks having this property. The spatial dynamics, in a context of phase transitions of a two-dimensional deterministic neural network, with only nearest neighbors connected, was studied by Kürten (1988) and the stochastic case by Borisjuk, Borisjuk, Kirillov, Kovalenko & Kryukov (1990). A successful example of the application of MRF based on the analysis of EEG data was offered in 1986 (Borisjuk, Borisjuk, Kirillov, Kovalenko & Kryukov, 1986). In an earlier paper (Kirillov & Makarenko, 1991) we demonstrated formally the existence of phase transition in a model neural network which consists of nonformal neurons and a new method of estimation of parameters of MRF was developed. This enabled us to find an Ising model with identical parameters, i.e. one which has the same MRF parameters as the state of the studied neural network, and thus provided information about the dynamic position of the network on a phase diagram. Applying this approach in the recent study, we characterized quantitatively the non-random nature of the spatial pattern of activity recorded by the multiple electrode technique and attained a new set of significant insights from such measurement.

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Requests for reprints should be sent to Dr. Rodolfo Llinás, Department of Physiology and Neuroscience, New York University Medical Center, 550 First Avenue, New York, NY 10016, USA; Tel.: +1 212 263 5415; Fax: +1 212 689 9060.

¹ Permanent address: Institute for Mathematical Problems of Biology, Russian Academy of Sciences, Pushchino, Moscow Region 142292, Russia.

2. MARKOV RANDOM FIELDS

Consider the activity for every instant t of a group of neurons arranged on a rectangular lattice described by gaussian variables x_{ij} placed in nodes of $N \times N$ of the rectangular lattice. A random field is called Markov if for every lattice site (i,j) conditional probability.

$$P(x_{ij}/\text{all other } x_{k,l}) \quad (1)$$

depends only on some neighborhood of x_{ij} . We will consider the simplest case when conditional probabilities eqn (1) depend on the sum of the four nearest neighbors:

$$\begin{aligned} P(x_{ij}/\text{all other } x_{k,l}) \\ = P(x_{ij}/\text{neighbors}) = \exp(x_{ij}y_{ij}) / (\exp(y_{ij}) + \exp(-y_{ij})) \end{aligned} \quad (2)$$

where $y_{ij} = \alpha + \beta \sum_{(k,l) \in \Psi_{i,j}} x_{k,l}$, and $\Psi_{i,j} = \{x_{i-1,j}, x_{i+1,j}, x_{i,j-1}, x_{i,j+1}\}$.

The sum here presents the four nearest neighbors of x_{ij} , where α and β are the function parameters. A joint probability distribution on a set of configurations $X = \{x_{ij}\}$ can be constructed using these conditional probabilities (Besag, 1974):

$$\begin{aligned} P(X; \alpha, \beta) &= (Z(\alpha, \beta))^{-1} \exp \\ &\times \left(\alpha \sum_{(i,j)} x_{i,j} + \beta \sum_{(i,j)} \sum_{(k,l) \in \Psi_{i,j}} x_{i,j} x_{k,l} \right) \end{aligned} \quad (3)$$

where Z is a normalizing constant. For the case of the binary variables the distribution eqn (3) defines a two-dimensional Ising model in statistical physics for which a phase diagram is known exactly. In such a diagram there is a region demonstrating very special behavior (where phase transitions occur) located along the straight line $\alpha + 2\beta = 0$. Phase transition for this Ising model implies metastability property for the dynamic model.

In the neuronal network models, the theoretical calculation of phase diagrams, while very valuable is almost impossible, save in some special cases. As we are not dealing with the case, we estimated the MRF network parameters for a neural network using the statistical method as described below.

MRF parameters can be estimated using one MRF sample configuration X_0 . Applying a standard approach of maximum likelihood we could estimate parameters α and β by solving the following problem.

2.1. Find α and β maximizing $P(X_0; \alpha, \beta)$

However, the calculation of the normalizing constant $Z(\alpha, \beta)$ is possible only when N is very small and so we applied a method developed for MRF parameter estimation—a method known as coding technique or maximum pseudolikelihood (sometimes called conditional likelihood) (Besag, 1974). We can divide the initial lattice into two sublattices so that their nodes will be located

with respect to each other as black and white chess fields. Then a variable in each node is to be independent (for the first order MRF) of any other variable of its own sublattice.

Now consider conditional probabilities eqn (2). The maximum pseudolikelihood method uses instead of likelihood the following function:

$$L_{ps} = \prod_{(i,j)} P(x_{i,j}/\text{neighbors})$$

This function is easy to calculate as are its first and second order partial derivatives. It is concave (Geman & Graffine, 1987) and so we can find its maximum with respect to α and β . Pseudolikelihood estimates are consistent in the sense that if X_0 is a sample from MRF with parameters α_0 and β_0 , then corresponding estimates converge to α_0 and β_0 as the size of the configuration N increases (Geman & Graffine, 1987).

For our case the pseudolikelihood function is presented as:

$$(2\pi\sigma^2)^{-m/2} \exp \left\{ -\frac{1}{2\sigma^2} \sum_{(i,j) \in \Omega} (x_{i,j} - \alpha - \beta y_{i,j})^2 \right\},$$

where $y_{ij} = x_{i-1,j} + x_{i+1,j} + x_{i,j-1} + x_{i,j+1}$, σ^2 -dispersion, m -is the number of the coded points of Ω , where Ω is one of two sublattices.

Again, we get estimates finding the maximum of the function with respect to α and β :

$$\begin{aligned} \beta &= \frac{\sum_{(i,j) \in \Omega} x_{ij} y_{ij} - \frac{1}{m} \left(\sum_{(i,j) \in \Omega} x_{ij} \right) \left(\sum_{(i,j) \in \Omega} y_{ij} \right)}{\sum_{(i,j) \in \Omega} y_{ij}^2 - \frac{1}{m} \left(\sum_{(i,j) \in \Omega} y_{ij} \right)^2} \\ \alpha &= \frac{1}{m} \left(\sum_{(i,j) \in \Omega} x_{i,j} - \beta \sum_{(i,j) \in \Omega} y_{ij} \right), \\ \sigma^2 &= \frac{1}{m} \sum_{(i,j) \in \Omega} (x_{i,j} - \alpha - \beta y_{i,j})^2, \end{aligned}$$

α and β is taken as an arithmetic mean over the two subsets (Besag, 1974; Borisyuk et al., 1986; Kirillov & Makarenko, 1991).

3. RESULTS

3.1. Simulations

Our simulation model consisted of 50×50 “integrate and fire” neurons placed in the nodes of a square lattice. The initial configuration chosen was as a square cluster of ~ 200 neurons which were allowed to run until reaching the steady state with respect to α and β . Our goal was to see how the coupling strength w (which was a constant over the network) between nearest neighbors could

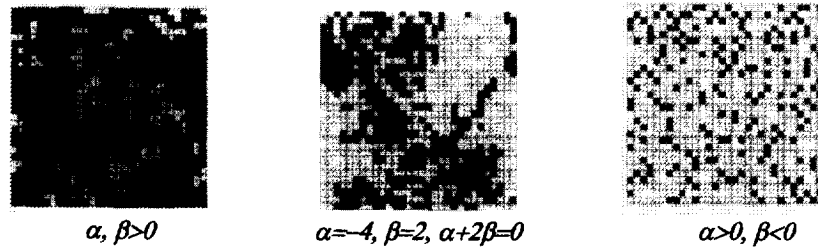


FIGURE 1. Examples of typical configurations and their estimated parameters of MRF. Black checkers correspond to simulated spikes, white to the absence of them. As the particular values of the parameters depend on the size of the lattice we give signs of α and β rather than their immediate values: (a) strong strength of coupling w , almost all nearest neighbors are generating synchronous spikes, $\alpha, \beta > 0$; (c) weak strength of coupling w , synchronicity of the nearest neighbors is insignificant, $\alpha > 0, \beta < 0$; (b) the case of the phase transition configuration-coexistence of two distinctly clustered phases $\alpha = -4, \beta = 2, \alpha + 2\beta = 0$.

influence the values of α and β . A second goal was the determining of how typical configurations of the network's activity are reflected by the values of α and β . See legend to Figure 1 which demonstrates various configurations for different values of α and β .

3.2. Experimental data analysis

Simultaneous recordings of complex spikes (CS) from crus 2a Purkinje cells in rat cerebellum were obtained using the multiple electrode technique (Llinás & Sasaki, 1989; Sugihara, Lang & Llinás, 1993; Welsh, Lang, Sugihara & Llinás, 1995). The recordings were obtained from rats conditioned to lick with sound stimulus. The earlier findings on the morphology of the cerebellum and its functional role in the organization of movement made it imperative, given the complexity of the data, that a non-standard method such as Markov Random Fields (MRF) be used for their analysis.

The activity of inferior olive (i.o.) neurons is represented by its spatial and temporal components. In addition the exact spatio-temporal mapping of the activity of the i.o. cluster to the Purkinje cell layer was carefully determined. Thus, the experimental results demonstrate that the activities of the two structures are fully synchronized (Llinás, 1991).

The regular geometric organization of the cerebellum has been viewed as uniquely capable of implementing an internal representation of external geometry integrating it with temporal organization (Pellionisz & Llinás, 1985; Llinás, 1991). But the geometric organization must also be reflected in the spatial organization of activity. This has been one of our goals in using the MRF method.

We have constructed an MRF by accumulating, (during given time bins), the spikes registered by given electrodes in the corresponding nodes of a rectangular lattice mapped from the electrode matrix. To choose the appropriate bin size was not an easy task. We decided a priori to start with the minimum time bin and check the outcome parameters for reliability (see below) and repeated the procedure until a satisfactory result for the reliability was reached. It was important that the bin size

not be longer than is the characteristic time of the system, that is, the average time of system transition to a different state. In order to check the accuracy of our results in the sense of statistical reliability, we randomized the original pattern, and then recomputed β_{mix} . The procedure was repeated 50 times. After that a mean (and standard deviation) of β_{mix} were compared with β estimated for the original pattern. In most cases, owing to the low level of background activity due to the absence of movement, such an estimate was similar to β_{mix} . However, this was not the case during movement. Indeed the computed parameters for neuronal activity differed remarkably between the no movement state (background) and during the movement execution. Therefore, special attention was paid to the latter case. The bin size was varied from 30 to 100 ms. It was also found useful to slide the bin using a shift smaller than the bin size to determine gradual changes occurring within the bin size time. The

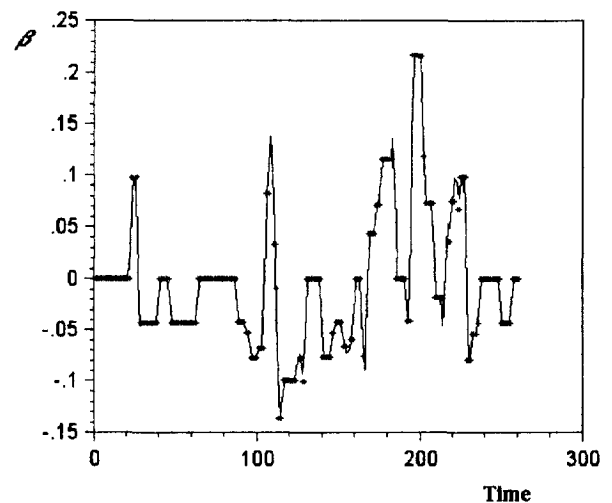


FIGURE 2. A typical behavior of estimated β vs time (in bins) during a single course of movement. Each point on the plot presents β for a separate MRF. The change of the parameter means that the strength of coupling is not staying the same during the movement. With $\beta(t_0) > 0$ the nearest neighbors are synchronized, $\beta < 0$ the nearest neighbors are not synchronized. When $\beta = 0$ configuration has a random character.

total number of patterns we have processed amount to $\sim 15 \cdot 10^3$; this includes, mostly, those observed during movement.

Significant results were found regarding the specific behavior of β , which is related to the spatial coupling of the activity (Figure 2). The fact that the coupling is strongly variable suggests that the effect of de- and re-synchronization takes place during the movement. Figure 3 shows the corresponding regions for trajectories during background (no movement) and during movement execution. The first and clearest condition to be derived from such calculations was that of a strong dependence between distinct activity components at the time of movement execution. From this we may conclude that during the movement phase the neurons of the inferior olive act not as a set of individual elements, but, rather, as a well coordinated synchronous ensemble. Indeed the value of β represents a quantitatively unambiguous measure determining activity coupling in such an ensemble in an unquestionable fashion. Detailed analysis of the time dynamics for β brought to our attention an important point, namely, that the neuronal coupling has a well specified dynamic character and that such dynamics change quickly (within 10 ms), which is the minimum time shift we used for the analysis. Furthermore, the ensemble activity mode evolves in a self-organized manner from the background activity at the onset of movement. During the movement phase itself values of β corresponding to regularized patterns are intermitted by zero values, pointing to transient onset of spatial chaos (Figure 2). This can be a consequence of the

non-continuous nature of movement execution assumed to be one of the basic features of movement performance (Llinás, 1991). The alteration between regular and chaotic modes of spatio-temporal dynamics of ensemble activity may be regarded as a necessity for effective dynamic adaptation of the neuronal system to the constantly changing environment. It must be stressed that different levels of coupling may correspond to the same overall level of activity and conversely, that similar levels of coupling may correspond to different levels of the activity. This finding indicates that the informational capacity of the total signal in the synchronized neuronal ensemble depends not only on the number of neurons which are constituting the configuration, but also on the interaction between them. In terms of the abstract geometric interpretation of these patterns, we observed alteration of a number of degrees of freedom, which the system is probably using to create an internal representation (Pellionisz & Llinás, 1985).

We also found that during movement, the trajectory on the α - β plane showed a tendency to run along the line $\alpha + 2\beta = 0$, the one along which the phase transition region is located (Figure 4). This trend needs further study because the matter has a complex theoretical basis (Besag, 1974; Kirillov & Makarenko, 1991) and very important practical implications. Namely, it suggests that the pattern of the overall activity is most sensitive to the smallest fluctuations and that it may be swiftly rearranged, suggesting that a specific control connection may be most effectively organized during such a stage. In addition, having estimated the parameters during the movement, one may consider a time series in further analysis.

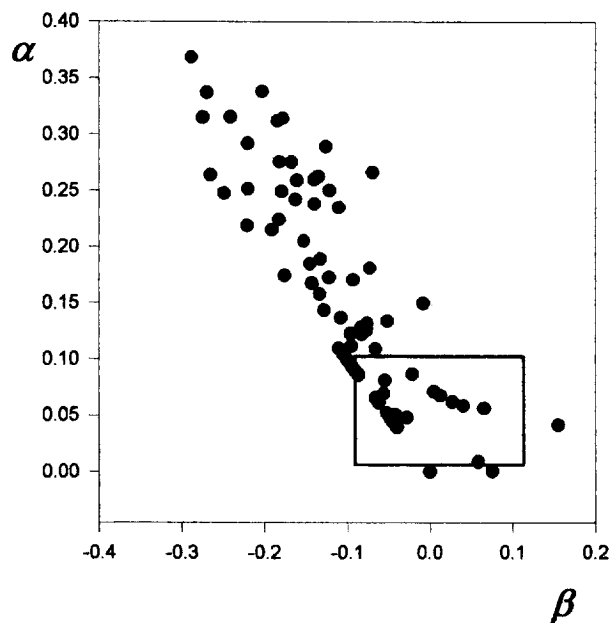


FIGURE 3. This is an example of the region of the background activity (small box on the figure) prior to movement mapped into the region of the activity during the movement on the phase plane α, β . The value of β in the background is close to zero and points to the random character of the activity.

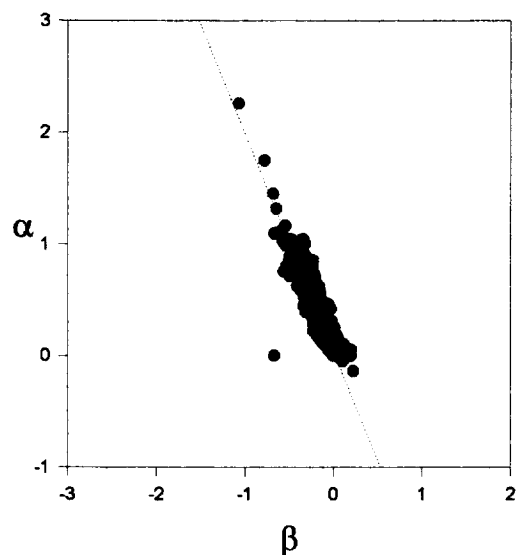


FIGURE 4. Plot on the α, β phase plane. The MRF parameters during four movement periods are accumulated to demonstrate the trend of the parameter's values to be close to the straight $\alpha + 2\beta = 0$. It is not the case for the background activity.

4. CONCLUSIONS AND PERSPECTIVES

The MRF method was successfully applied to model as well as experimental neuronal data and provided unique information on the regularity of the spatio-temporal organization of overall activity and its local features. It afforded the remarkable ability to interpret data obtained through direct observation over spatially distributed systems. This computational ability is urgently needed today and with respect to neuronal ensembles the approach is particularly important given a recent interest in the problem of synchronous regimes as a collective behavior effect. Such a problem cannot be solved without taking into account the spatial component of the system. We also hope that the method will be useful in considering neural network modeling where, as in the inferior olive, the coupling parameter may change in a dynamic manner. The method may also be useful in the solving of problems such as thalamocortical temporal binding of neuronal ensembles as separate structural units (columns). On the other hand, recent findings on the molecular biological level demonstrate the presence of fine spatial organization structurally as well as functionally. One such example is the calcium channel clustering in the presynaptic active zone in the squid giant synapse and the issue of concentration microdomains (Llinás, Sugimori & Silver, 1995). Finally, the appropriate use of the method may considerably enhance our understanding of presently available neurophysiological data and introduce an additional estimate for assessing the consistency of models to their biological counterparts.

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NOMENCLATURE

Σ	summation
$\exp()$	exponent
Π	product
\in	to belong to