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Introduction

Retinal spike response to stimuli is constrained, on one hand by short range correlations (receptive field overlap) and on the other hand by lateral connectivity (cells connectivity). This last effect is difficult to handle from statistics because it requires to consider spatio-temporal correlations with a time delay long enough to take into account the time of propagation along synapses. Although MaxEnt model are useful to fit optimal model (maximizing entropy) under the constraints of reproducing observed correlations, they do address spatio-temporal correlations in their classical form (Ising or higher order interactions but without time delay). Binning in such models somewhat integrates propagation effects, but in an implicit form, and increasing binning severely bias data [1]. To resolve this issue we have considered spatio-temporal MaxEnt model formerly developed e.g. by Vasquez et al. [2]. The price to pay, however is a huge set of parameters that must be fitted to experimental data to explain the observed spiking patterns statistics. There is no a priori knowledge of which parameters are relevant and which ones are contributing to overfitting. We propose here a method of dimension reduction, i.e. a projection on a relevant subset of parameters, relying on the so-called Susceptibility matrix closely related to the Fisher information. In contrast to standard methods in information geometry though, this matrix handle space and time correlations.

We have applied this method for retina data obtained in a diurnal rodent (*Octodon degus*, having 30% of cones photoreceptors) and a 252-MEA system. Three types of stimuli were used: *spatio-temporal uniform light*, *white noise* and a *natural movie*. We show the role played by time-delayed pairwise interactions in the neural response to stimuli both for close and distant cells. Our conclusion is that, **to explain the population spiking statistics we need both short-distance interactions as well as long-distance interactions**, meaning that the relevant functional correlations are mediated not only by common input (i.e. receptive field overlap, electrical coupling; spillover) but also by long range connections.

Methods

Recordings: Extracellular recording of the electrical activity of retinal patches from 4 healthy, young individuals of the rodent species *Octodon degus* were performed *ex vivo* using a Multielectrode Array (USB-MEA256 from Multichannel Systems, MCS GmbH).

Stimuli: (i) **Photopic spontaneous activity (PSA)**: A uniform spatio-temporal invariant full field (15 mins); (ii) **White noise (WN)**: Binary checkerboard pattern (20 mins); and, (iii) **Natural Movie (NM)**: recorded in the animal's natural environment (30s movie, 40 repetitions).

PSA WN NM

The images were projected using a conventional DLP LED projector at 60fps and registered at 20KHz. Sorting was done using Offline Sorter®by Plexon Inc, and the spatio-temporal receptive fields were computed using STA in WN stimulus.

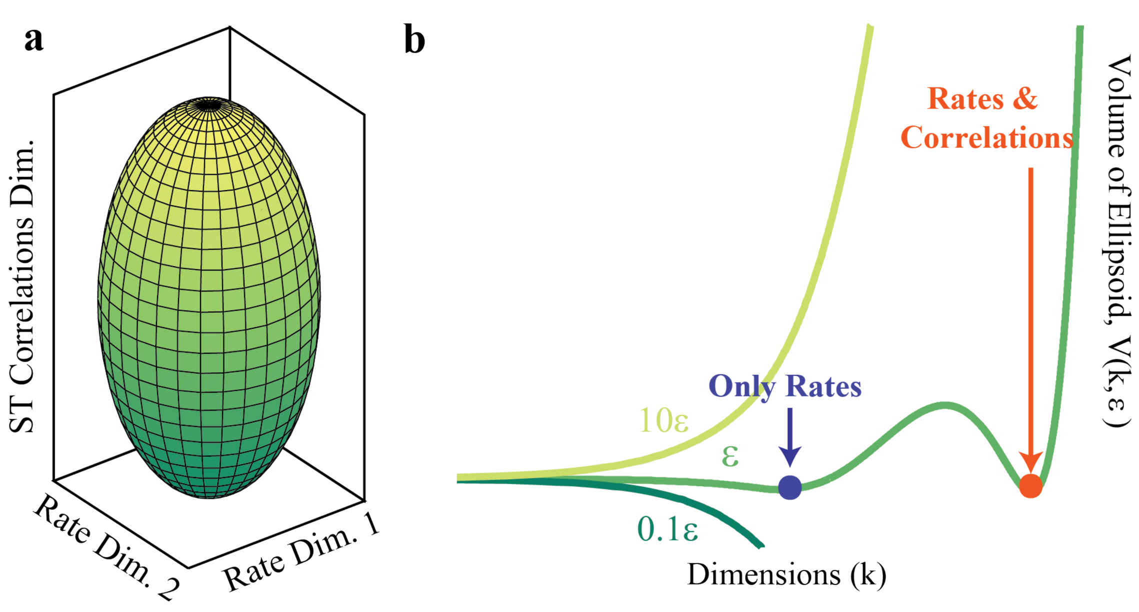
Analysis: A binary raster ω of $N = 50$ neurons with a bin size of 5ms were used, where $\omega_n(t) = 1$ if neuron n spikes at time t, 0 otherwise. The goal is to fit the empirical distribution of ω with a MaxEnt model (eq. 1) and compute its corresponding **Susceptibility matrix** χ (eq. 2):

$$\mathcal{H}(\omega) = \sum_{l=0}^{L} h_l m_l(\omega) \quad (1), \qquad \chi_{ll'} = \frac{\partial \mu[m_l]}{\partial h_{l'}} \quad (2)$$

where m_ls are the observables, h_l the free parameters to fit, l is parameter label. t ranges from 0 to $R-1$, where the integer $R \geq 1$ is called the *range* (i.e. memory) of the potential $\mathcal{H}$, in this case, $R = 2$.

The ***Susceptibility matrix*** (eq. 2) tells us how much a slight change on one parameter (h_l) changes the estimation of the observables probabilities (m_l). χ depends on stimuli, increasing their entries as the stimuli complexity increases.

DimRed: Geometric Intuition



The set of indistinguishable distributions around the optimal set of parameters defines an ellipsoid on the parameter space (see **a**) with a volume $\mathcal{V}$ satisfying:

$$\log \mathcal{V}(k) = \frac{1}{2} S_{\mathcal{H}}(k) - \log \Gamma\left(\frac{k}{2}+1\right) + \frac{k}{2}\log\left(\frac{2\pi\epsilon}{T}\right), \quad (3)$$

$$S_{\mathcal{H}}(k) = -\sum_{i=1}^{k} \log \lambda_i \quad (4)$$

where λ_is are decreasing χ eigenvalues; $\log\Gamma(\frac{k}{2}+1)$ is purely combinatoric; $\log\left(\frac{2\pi\epsilon}{T}\right)$ characterizes the effect of precision accuracy (ϵ) and finite sampling. Minimizing eq. (1) is yields the optimal set of parameters given a finite sample size (T) with accuracy ϵ.

(a) illustrates model composed by the Rates of two neurons (Rate Dim. 1 and 2) and the spatio-temporal correlations between both (z axis). The ellipsoid is more elongated on the sloppy eigendirections (correlations) and less elongated on the stiff eigendirections (rates).
(b) shows the value of the volume, $\mathcal{V}(k,\epsilon)$ as the degrees of freedom (k) increases. The volume reaches a minimum (dots) for certain k named as k_c. Increasing k upon k_c makes the volume explode.

Acknowledgements

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ENAS software (https://enas.inria.fr/) was used for the computation of χ.

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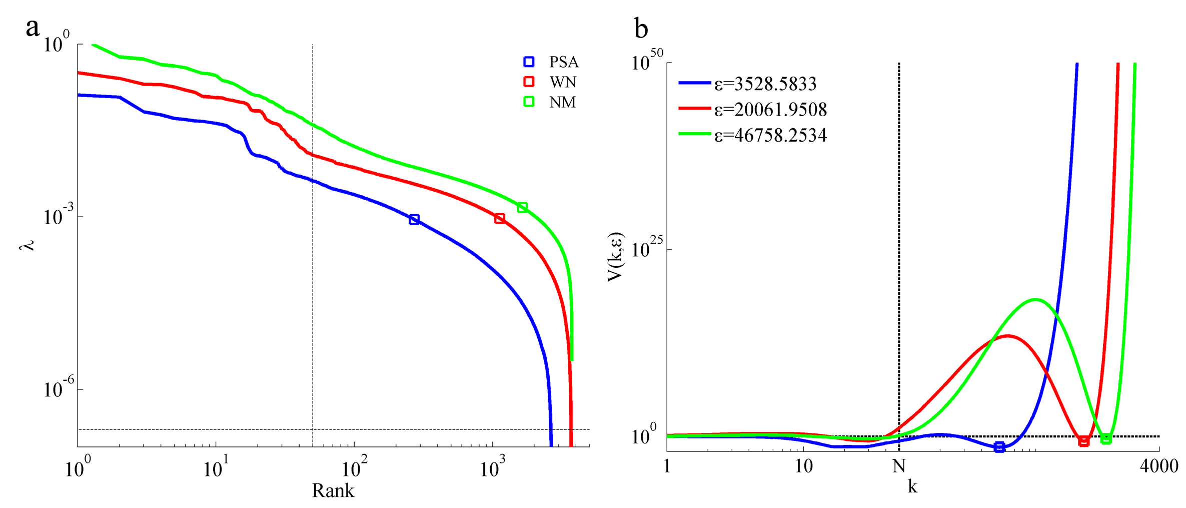
χ Spectral Properties Under Different Stimuli

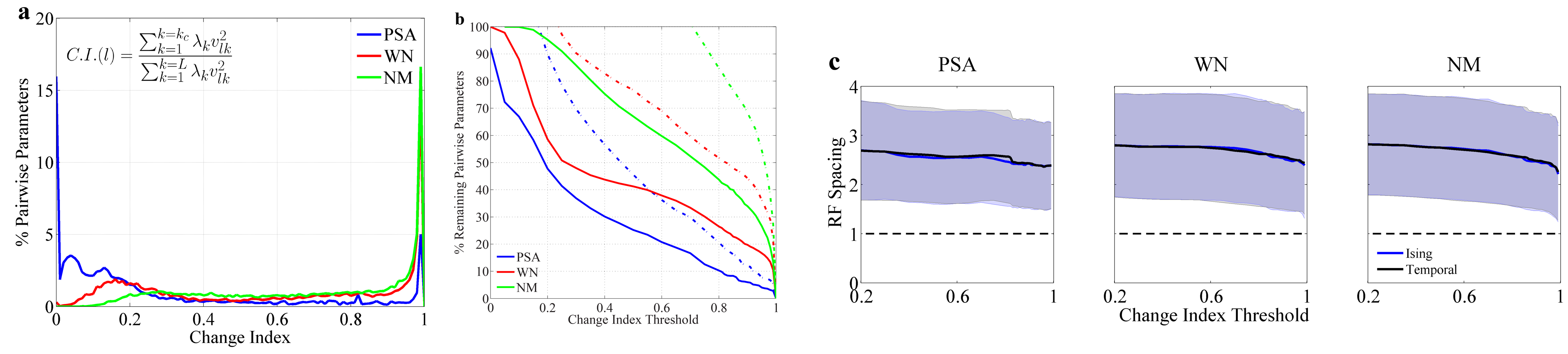


(a) The χ eigenvalue spectrum obtained for PSA, WN and NM stimuli. The graphs shows two cut-offs: The first cut-off, close to the network size N represented as a vertical dashed line, is mainly to the effect of individual firing rates. The second cut-off is associated to the information contained on spatio-temporal pairwise interactions. Minimizing eq. (3), we obtain different values of k_c which are represented as squares on each curve.

(b) Volume $\mathcal{V}(k,\epsilon)$ obtained for PSA, WN and NM stimuli. In the three cases, k_c minimizing $\mathcal{V}(k,\epsilon)$ is represented with a square. The number of relevant dimensions k_c, exceeds the firing rates meaning that spatio-temporal pairwise interactions are needed for the optimal value of $\mathcal{V}(k,\epsilon)$.

Remark: The number of optimal dimensions k_c required to fit the empirical distribution increases with the stimuli high-order correlations.

From χ to Network Properties



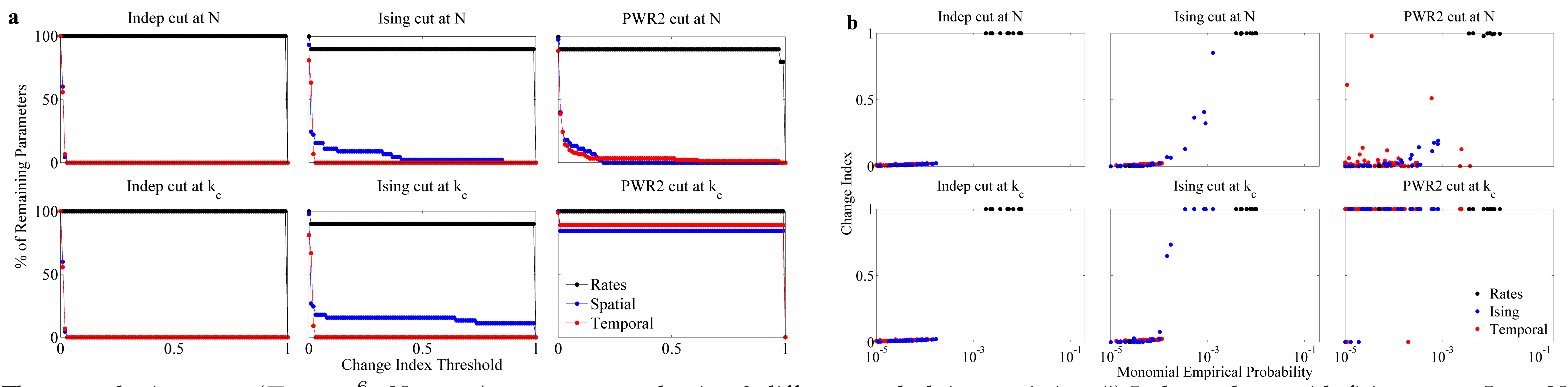
The effect on the estimation of slight changes in the lth parameter is computed as $\sum_{k=1}^{k=K} \lambda_k v_{lk}^2$, where v_{lk} is the lth entry of the eigenvector $\vec{v_k}$ and λ_k is corresponding eigenvalue. The Change Index (C.I. equation on **a**) is the ratio of the effect before ($K = L$) and after filtering ($K = k_c$). C.I.=1 means no filtering effect and C.I.=0 means full filtering effect. **C.I. summarizes the effect of filtering on the direct influence of h_l on m_l estimation and all the indirect influences (h_l acts on m'_l which modifies m_l)**

(a) shows the distribution of C.I. values for the pairwise parameters, where PSA shows two modes, one close to 0 and other to 1. WN and NM shows one big mode close to 1. Thus, **static stimulus (PSA) shows much more pairwise parameters affected by filtering than dynamic ones.**

(b) shows the % of the remaining pairwise spatial (solid) and temporal (dashed) parameters as the C.I. threshold increases. Temporal interactions are more abundant than spatial ones for all stimuli at all thresholds. PSA shows less remaining pairwise parameters than dynamic stimuli for all thresholds. Then, **the number of spatio-temporal parameters required to optimally fit the empirical distribution increases with the stimuli high-order correlations.**

(c) shows the Receptive Field (RF) Spacing (<1 overlap; $=1$ adjacency, horizontal dashed line; >1 no overlap) as the C.I. threshold increases for spatial (blue) and temporal (black) parameters. Lines are medians and shaded area the interquartile range. We see the same behaviour for all cases: the RF spacing slightly decreases with C.I. threshold, showing that **the optimal set of parameter includes both short-range (i.e. RF overlap) and long-range (no overlap) pairwise interactions for all stimuli.**

Synthetic Data: Firing Rates on N First Dimensions, Correlations on First k_c



Three synthetic rasters ($T = 10^6$, $N = 10$) were generated using 3 different underlying statistics: (i) **Independent**, with firing rates, $L = N$; (ii) **Ising**, firing rates and spatial correlations, $L = N(N-1)/2$; (iii) **Pairwise R=2** (PWR2), with firing rates and spatio-temporal correlations, $L = N(N-1)/2 + N^2$. For each raster a PWR2 MaxEnt model was fit. The respective χ matrices were filtered with $k_c = 10, 15$ and 127, respectively (see eq. 1 and 2). Then, the C.I. was computed for each parameter in order to link relevant dimensions with relevant parameters.

(a) By construction the Indep. raster shows no pairwise parameters at thresholds as small as 0.03, while Ising raster, at the same threshold, shows only firing rate and spatial correlations parameters. PWR2 shows a small reduction on the % of remaining spatio-temporal parameters for $k_c = 127$ but keeping most of them, whereas using $k_c = N$ removes all the pairwise parameters at very low thresholds.

(b) The monomials probabilities show a non-linear relationship with C.I.. Monomials with low probabilities are likely to show low C.I. values. The Indep. raster shows only firing rates parameters with C.I. ~ 1; Ising raster shows firing rates and spatial correlations parameters with C.I. ~ 1, but none related to temporal correlations shows high C.I.; Almost all PWR2 parameters show C.I.~ 1 when filtering with k_c, but filtering with $k_c = N$, reduces the C.I. of most of the spatio-temporal parameters at values ~ 0.2, while most firing rates parameters remain unchanged.

The first N dimensions contains mainly information about firing rates, while the next $k_c - N$ concentrates information about spatio-temporal correlations.

Conclusions

(i) The first cut-off of χ spectrum contains mainly information about individual neuron firing rates, while the second cut-off contains information about spatio-temporal correlations. If $k_c = N$, there is no relevant information about spatio-temporal correlations on the data and it can be optimally explained by a model which takes into account only neuron firing rates.
(ii) All tested stimuli requires spatio-temporal interactions to optimally fit the evoked retinal population activity. So, as other works have shown on different species (salamander [2,3,5]; monkey [4]; guinea pig[3]), retinal population activity presents significant spatio-temporal interactions. Moreover, the stimuli high-order correlations increases the number of relevant spatio-temporal interactions on the network.
(iii) *The optimal set of pairwise parameters, which implies a pair of neurons, includes neurons with overlapped receptive fields as well as distant neurons for all tested stimuli, with small differences between stimuli. Short range correlations can be explained via stimulus correlation and receptive field overlap whether long range more presumably reflect lateral connectivity effects.*