Comparing Kurtosis Score to Traditional Statistical Metrics for Characterizing the Structure in Neural Ensemble Activity.

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Abstract. This study investigates the range of behaviors possible in ensembles of spiking neurons and the effect of their connectivity on ensemble dynamics utilizing a novel application of statistical measures and visualization techniques. One thousand spiking neurons were simulated, systematically varying the strength of excitation and inhibition, and the traditional measures of spike distributions – spike count, ISI-CV, and Fano factor – were compared. We also measured the kurtosis of the spike count distributions. Visualizations of these measures across the parameter spaces show a range of dynamic regimes, from simple uncorrelated spike trains (low connectivity) through intermediate levels of structure through to seizure-like activity. Like absolute spike counts, both ISI-CV and Fano factor were maximized for different types of seizure states. By contrast, kurtosis was maximized for intermediate regions, which from inspection of the spike raster plots exhibit nested oscillations and fine temporal dynamics. Brain regions exhibit nested oscillations during tasks that involve active attending, sensory processing and memory retrieval. We therefore propose that kurtosis is a useful addition to the statistical toolbox for identifying interesting structure in neuron ensemble activity.

Introduction

With the multi-electrode recording techniques available today, it is possible to discern spiking activity from dozens or even hundreds of neurons simultaneously from awake, behaving animals [1]. In the first half of the twentieth century, it was discovered that electrical activity in the brain oscillates in characteristic ways (see [2] for a review at the time), and now these new recording techniques have allowed the examination of neural ensemble spiking activity, and how it relates to local field potential (LFP) recordings which characterise brain oscillations. It can be seen that simulated populations of neurons also display synchronous and oscillatory behaviour (see Figure 1), and theoretical work has shown how this behaviour can be supported by the individual firing regimes of sparsely connected neurons [3].

There are numerous methods for measuring regularities in spike trains (e.g. power spectra, spike-count distributions). Two of the most popular are the Fano Factor [4] and the coefficient of variation of the interspike interval (ISI-CV) [5]. These two measures are maximised for super-synchronous seizure-like spike trains, and in simulations of coupled networks of neurons, are themselves closely correlated with the total number of spikes generated by the network in a given time. Hence, they do not provide a measure of the structure in realistic spike trains with typical intermediate levels of activity. The new metric presented here, called the *Kurtosis Score*, more clearly reveals the nested oscillatory patterns of activation found in simulated spike trains, where bursts of high frequency appear at the peaks of lower frequency oscillations.

With desktop computing power available today, it is becoming practical to use *parameter sweeps* across multi-dimensional spaces as a tool for investigating the behaviour of complex systems. If system behaviours can be quantified with one or more metrics, these metrics can be displayed as graphs called *heat maps* that can reveal relationships between parameters and between metrics that may otherwise remain hidden. In the following sections, heat maps are used to compare Kurtosis Score, total spike count, Fano Factor and ISI-CV for their effectiveness at identifying simulated spike trains with varying characteristics. The chapter concludes with a discussion of when it may be best to use Fano Factor or ISI-CV, and when Kurtosis Score may be the more appropriate metric.

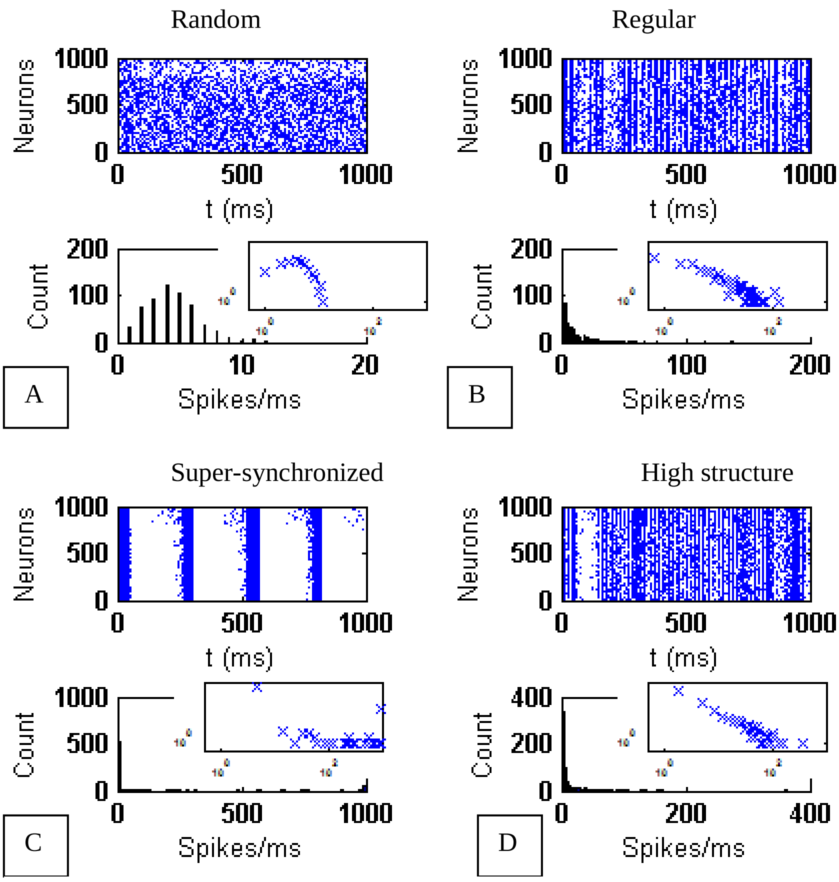
Methods

Kurtosis Score is defined as the fourth cumulant divided by the square of the variance of the spikes per millisecond distribution, simultaneously recorded or simulated for a large number of neurons. Fano Factor [4] is the variance divided by the mean of the spikes per millisecond distribution. ISI-CV [5] is the standard deviation divided by the mean of the interspike interval (interspike intervals are calculated for each neuron separately, and then all calculated intervals are combined for the ISI distribution).

In order to compare these metrics, Kurtosis Score, spike count, Fano Factor and ISI-CV were calculated for simulated spike train data. This data was obtained by simulating networks of Izhikevich model neurons [6]. Each network was fully connected, contained 800 pyramidal cells and 200 interneurons and was run for 1000 ms of simulated time. The metric calculations excluded the first 400 ms of each trial to give the networks time to settle from their initial conditions; the metrics were than calculated for the time period 401 to 1000 ms. The excitatory weights in the networks were distributed (uniform random) between zero and a maximum weight w^{+}_{max} that varied from trial to trial. w^{+}_{max} varied systematically between zero and a value large enough for approximately four presynaptic neuron spikes to alone cause a spike in a postsynaptic neuron (typical cortical synaptic efficacies require 10 to 40 presynaptic spikes to activate a postsynaptic neuron, which is approximately in the middle of the range over which w^{+}_{max} varied). The maximum inhibitory synaptic weight w^{-}_{max} varied between zero and twice the maximum excitatory weight (i.e. $w^{-}_{max} = -2w^{+}_{max}$). All weights were subject to short term depression with exponential recovery [7]. The excitatory and inhibitory weight variation between trials created networks that behaved very differently across different regions of this parameter space, and the spike trains thus generated ranged from uncorrelated activity to super-synchronous seizure-like states. Each neuron received zero-mean Gaussian input, with standard deviation of 5 for pyramidal cells and 2 for interneurons [6]. Because the network input and connections are stochastic, 50 to 100 instances of the networks were simulated at each testing point in parameter space and the calculated metrics averaged to obtain a picture of the mean network behaviour at each parameter space point. The averaged metric scores were plotted on 2-dimensional graphs called heat maps for visualisation of how the metrics change over the parameter space, with excitatory weight on the abscissa and inhibitory weight the ordinate.

Results

Simulations of the network with varying excitatory and inhibitory connection strengths showed a variety of behaviours (see Figure 1). In these examples, Fano Factor and ISI-CV were maximal for super-synchronised spike trains, while Kurtosis Score was maximal for spike trains containing bursts of gamma wave activity nested within slower oscillations. By systematically varying the parameters for the excitatory and inhibitory connection strengths, a picture of how these metrics change and relate to each other can be constructed (see Figure 2; full color version available online). When Kurtosis Score was mapped across the entire tested parameter space, a region of high kurtosis where spike trains exhibit high structure became apparent (Figure 2D – light blue to white regions). When compared with ISI-CV, Fano Factor and the total number of spikes generated in the simulation period, Kurtosis Score can be seen to be high in regions of parameter space adjacent to high ISI-CV and Fano Factor, where the total number of spikes also begins rising dramatically (Figure 2A, B and C). Clearly high Fano Factor and ISI-CV primarily indicate super-synchrony (which also tends to generate more total spikes), while Kurtosis Score is quite low in these super-synchronous regions of weight space. Instead, Kurtosis Score is high when the spike train contains fine but unpredictable temporal structure, rather than either fully predictable or completely random.



	Kurtosis	Fano	ISI-CV	# Spikes	(Excitation,Inhibition)
A	0.4	1.0	0.5	4500	(0, 0)
B	24.7	23.4	0.5	9300	(1, 2.75)
C	5.4	834.8	5.2	120000	(2, 2.75)
D	70.1	58.4	0.6	11000	(2, 10)

Fig. 1. Characteristic behaviors from different regions of parameter space. Spike raster plots from four simulated networks show the same 100 neurons fully connected with different synaptic strengths, resulting in very different network dynamics in each case. Below each raster plot is the spike count distribution. *(A)*: Random. No connections between neurons gives a Kurtosis Score close to 0, a Fano Factor close to 1, indicating a near Poisson distribution, and a low ISI-CV. *(B)*: Regular. Intermediate excitation and inhibition gives a moderately high Kurtosis Score, a higher but still relatively small Fano Factor and a low ISI-CV. *(C)*: Super-synchronized. Strong excitation and intermediate inhibition gives a low Kurtosis Score but Fano Factor and ISI-CV are maximized by this super-synchronized activity. *(D)*: High structure. Strong excitation and strong inhibition strengthens the fast oscillations and 'fine' temporal dynamics, and hence maximizes the Kurtosis Score, while Fano Factor and ISI-CV are reduced. *(Insets)*: The spike count distributions plotted on log-log axes (see Discussion).

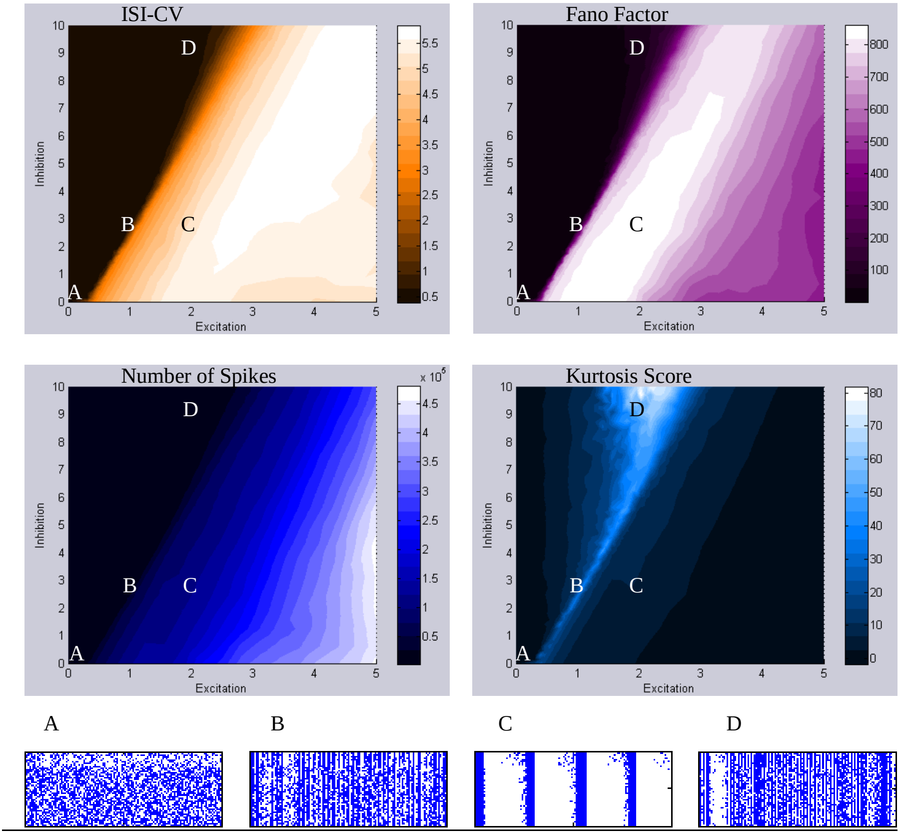


Fig. 2. Different measures of spike train characteristics, plotted across the excitatory and inhibitory weight space. The legend at right of each graph shows the shade correspondence to the displayed metric. The four networks from Figure 1(A-D) are placed in context on this graph. *(Top Left)*: ISI-CV is the standard deviation of the interspike interval divided by the mean. This value is maximized when the network is in a fully synchronized (seizure) state. This state is comprised predominantly of short periods of no activity punctuated by very long bursts of activity when all neurons fire almost simultaneously. *(Top Right)*: Fano Factor is similar in shape and analysis to ISI-CV except that its value is maximized when the network is in a seizure state comprised of *long* periods of no activity punctuated by very *short* bursts when all neurons fire almost simultaneously. *(Bottom Left)*: The total number of spikes generated by the network correlates with both Fano Factor and ISI-CV. *(Bottom Right)*: The Kurtosis Score identifies those regions in parameter space where slow oscillations predominate but are punctuated by short periods of fast oscillations (in the sampled networks, these fast oscillations occur at the slow oscillation peaks but this doesn't affect the score calculation – see Discussion). The slow oscillations give fewer spikes per millisecond and cause the peak of the distribution close to zero. The fast oscillations that cause many simultaneous or near-simultaneous spikes create the long tail. The combination of tall peak and long tail increases the kurtosis and, because the distribution is heavily skewed to the right (see histograms in Figure 1B and D) also increases the skewness. Seizure-like spike trains do not have this characteristic since they are comprised of two quite distinct peaks in the distribution, dramatically lowering the kurtosis.

Discussion

Fano Factor and ISI-CV are both ratio metrics with the mean as the divisor. Thus these values are maximized as the mean approaches zero, as long as some variance is maintained. For Fano Factor this maximization occurs in a seizure-like state where bursts of activity are short and 'rest' periods long, while for ISI-CV it occurs also in seizure but when bursts are long and rest times short. If the Fano Factor and ISI-CV graphs from Figure 2 are rescaled so that the shade transitions occur in the region where Kurtosis Score is highest, it can be seen that ISI-CV actually decreases, while Fano Factor increases monotonically towards the seizure state throughout the region of high kurtosis (see Figure 3). The clear implication is that Fano Factor and ISI-CV are not good measures of spike train structure; rather they give slightly different accounts of the closeness of a spike train to super-synchrony.

High Kurtosis Score occurs in a region of weight space immediately adjacent to seizure-like activity (Figures 2 and 3). Thus to operate in a high Kurtosis Score regime the nervous system needs to maintain tight control over excitation and inhibition. Slightly too much of the former or slightly too little of the latter will tip the network into seizure. Given the lifetime prevalence of epilepsy of 2-5% in the general population [8], the failure of the brain to maintain this tight control may not be an uncommon problem. Continuous electro-encephalogram (EEG) recordings are available from epileptic patients before, during and after seizures, and it would be interesting to calculate these metrics on EEG data recorded prior to and during seizures to test for any diagnostic or predictive capabilities.

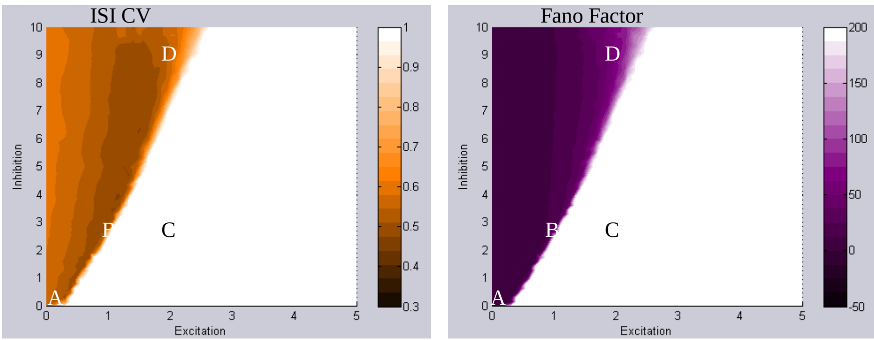


Fig. 3. ISI-CV and Fano Factor graphs from Figure 2 rescaled to reveal characteristics in the region of high kurtosis. ISI-CV decreases, while Fano Factor increases monotonically towards the seizure state throughout the region of high kurtosis.

The power spectra of EEG traces over long time frames demonstrate a power law distribution [9]. The mammalian cortex also appears to be wired using small world connectivity principles, so that it simultaneously minimises path lengths and the required number of connections (see [10] for a synthesis of ideas on this topic). It seems the brain is using scale-free principles for both physical structure and macro-scale dynamics. Is it possible that micro-scale spiking behaviour may also be governed by similar principles? Intriguingly, it has been said that kurtosis should be thought of as the scale-free movement of probability from the shoulders of a distribution to the centre and tails [11]. Spike count distributions plotted on log-log axes show a tendency to straight lines for those spike trains with high Kurtosis Score (see Figure 1 insets: compare the curve of Figure 1A inset showing low Kurtosis Score with the more linear relationship in Figure 1D inset with the highest Kurtosis Score). While a linear relationship on a log-log graph is not sufficient to demonstrate a scale-free distribution, it is consistent with one, and it remains as future work to investigate the potential link. Note that for any scale-free distribution, the kurtosis will increase as the exponent in the power law (i.e. the slope of the line in the log-log plot) increases, whereas a true power law regression should be independent of slope.

Because Kurtosis Score is based on the spike count distribution, it omits all information about the *order* of the events in the spike train. An alternative spike train to that shown in Figure 1D, where the events are sorted in increasing number of spikes per millisecond, shows very different structure (see Figure 4). This spike train has the same Kurtosis Score as in Figure 1D because it has the same spike count distribution. Therefore to say that the Kurtosis Score identifies nested oscillations is incorrect; but in the context of spike events in networks of neurons, highly kurtotic distributions are much more likely to be generated by nested oscillations such as illustrated in Figure 1D than by spike trains like that shown in Figure 4. Also, true scale-free behaviour should be scale-free over a broad range of timescales (Figure 1D) rather than being dependent on the chosen sampling start and end times (Figure 4).

Just as the Fano Factor was developed in the context of the statistical properties of ionising radiation [4], yet is applicable in diverse domains, so too is Kurtosis Score. Events in any domain that occur discretely in time or space are amenable to Kurtosis Score calculation, and it will be particularly relevant where a power law relationship is hypothesised or known to exist. This includes graph and queuing theory, medicine and epidemiology, physics, geology, economics, ecology and sociology to name a few [12]. We also suggest that the technique used in this study of performing parameter sweeps across multi-dimensional spaces and displaying the results as heat maps can be a great aid for visualisation and understanding of complex system behaviour, and with the computing power now available this technique can be successfully applied to the simulated neural network domain.

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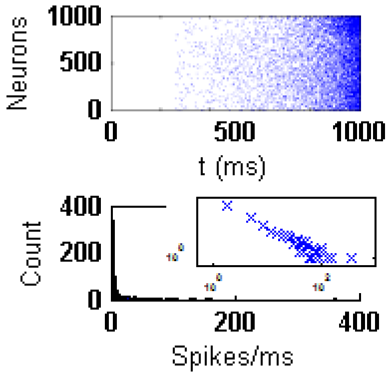

Fig. 4. A transformed spike train with the same Kurtosis Score and Fano Factor as Figure 1D. This spike train was obtained by dividing the raster plot of Figure 1D into 1 ms time slices, and sorting the slices according to spike count. The Kurtosis Scores for the original and transformed raster plots are the same since the spike count distribution is unchanged by the sorting process. The difference in the spike trains also shows that the Kurtosis Score gives very different information to a spectrum analysis.

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