Contrast Adaptation Decreases Complexity in Retinal Ganglion Cell Spike Train *

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The difference in temporal structures of retinal ganglion cell spike trains between spontaneous activity and firing activity after contrast adaptation is investigated. The Lempel–Ziv complexity analysis reveals that the complexity of the neural spike train decreases after contrast adaptation. This implies that the behaviour of the neuron becomes ordered, which may carry relevant information about the external stimulus. Thus, during the neuron activity after contrast adaptation, external information could be encoded in forms of some certain patterns in the temporal structure of spike train that is significantly different, compared to that of the spike train during spontaneous activity, although the firing rates in spontaneous activity and firing activity after contrast adaptation are sometime similar.

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Contrast adaptation is one of the important properties of visual system in response to changing environment.[1] Electrophysiological results show that in visual neurons, the process of contrast adaptation is characterized by reduced firing rate in response to prolonged contrast stimulus. The firing activity after contrast adaptation is very similar to spontaneous firing, in a sense that the neurons fire action potential at a low and steady rate in both the cases.[2] However, whether or not the firing pattern is similar to each other for these two cases, which is important for the understanding of information coding, remains unclear.

With the development of nonlinear science and its application, new insights have been provided for the investigation of the temporal properties of neural activities.[3,4] Rapp and coworkers classified neuron activities according to the dynamical structure of their spike trains, and found that the complexity index of neural spike trains increase during focal seizures.[3] Szczepański *et al.* used Lempel–Ziv complexity to discriminate the activity of single neuron in response to different kinds of stimulus.[4] Complexity measurement provides a feasible tool to reveal the dynamic properties of neural activity, which can hardly be detected using linear methods.

In this Letter, we start with the knowledge that information can be partly encoded by the temporal structure of inter-spike interval (ISI) series.[5] Using a multi-channel recording system to record the activities of chick's retinal ganglion cells before and after contrast adaptation, we employ Lempel–Ziv complexity[6] in combination with surrogate data sets to analyse the temporal structure of the ISI series. The results show that the complexity of neural spike trains decreases after contrast adaptation, which implies that the behaviour of neurons becomes ordered, which may carry relevant information about the external stimulus.

The isolation of retina and recording of ganglion cell spike trains are performed as previously described.[7] Light stimulus is generated using a computer monitor, and is focused to form a 0.71×0.71 mm square image on the isolated retina via a lens system. The stimulus is full-field light with its intensity being renewed every 50 ms (20 Hz) following a pseudo-random binary sequence with high value of $I_{\max}$ and low value of $I_{\min}$. The contrast is defined as $(I_{\max} - I_{\min})/(I_{\max} + I_{\min})$ and the mean intensity is $(I_{\max} + I_{\min})/2$.[2,7] In the present study, the contrast level is chosen to be 100% with a medium mean intensity ($I_{\max} = 1.39\,\mathrm{mW/m^2}$, $I_{\min} = 0$), and the stimulus sequence lasts for 250 s. Multi-unit photo-responses from ganglion cells are simultaneously recorded from the multi-electrode array (MEA) electrodes and are amplified with a 60-channel amplifier. The selected channels of recording, along with one channel of stimulus signal, are digitized with a commercial multiplexed data acquisition system (MCRack) and stored in a Pentium-based computer. The data are sampled at a rate of 20 kHz, plotted on screen instantaneously, and stored on the hard disk for off-line analyses.

Spike events recorded from each electrode are detected and classified into neuronal activities based on the methods previously described,[8] the inter-spike interval (ISI) series are then derived from the firing sequences.

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Lempel–Ziv complexity[6,9] analyses the temporal structure of sequences composed of finite alphabets that are transformed from original data based on a coarse-graining partitioning. It has been applied for the analyses of electrocardiograph[10] and neural firing activities.[4] The complexity counter $c(N)$ measures the number of distinct patterns contained in the sequence investigated.

Before the application of the Lempel–Ziv complexity analysis, the ISI series $u_i(i = 1, 2, \ldots, N)$ must be transformed into a symbolized sequence U and the subsequent calculations depends crucially on the procedure of symbolizing the original ISI sequence. An inappropriate partitioning will lead to spurious results. Following Rapp and co-workers,[3] the ISI series is transformed into a 0–1 string by partitioning about the median of data: If an interval is shorter than the median, it is assigned as the symbol 0, otherwise 1 is assigned. The Lempel–Ziv complexity analysis is therefore performed as follows.[6]

Let S and Q denote, respectively, subsequences of the symbol sequence $U = s_1, s_2, s_3, \ldots, s_N$, and SQ be the concatenation of S and Q, while sequence $SQ\pi$ is derived from SQ after its last character is deleted (π means the operation to delete the last character in the sequence). Let $v(SQ\pi)$ denote the vocabulary of all different subsequences of $SQ\pi$. Initially, $c(N) = 1$, $S = s_1$, $Q = s_2$, and $SQ\pi = s_1$. Suppose $S = s_1, s_2, \ldots, s_t$, $Q = s_{t+1}$ and $SQ\pi = s_1, s_2, \ldots, s_t$; if $Q \in v(SQ\pi)$, then Q is a subsequence of $SQ\pi$, not a new sequence. S need not change and now renew Q to be s_{t+1}, s_{t+2}, then judge if Q belongs to $v(SQ\pi)$ or not, and continue until $Q \notin v(SQ\pi)$, now $Q = s_{t+1}, s_{t+2}, \ldots, s_{t+i}$ is not a subsequence of $SQ\pi = s_1, s_2, \ldots, s_t, s_{t+1}, s_{t+2}, \ldots, s_{t+i-1}$, so increase $c(N)$ by one. Thereafter, combine S with Q and S is renewed to be $S = s_1, s_2, \ldots, s_t, s_{t+1}, s_{t+2}, \ldots, s_{t+i}$, at the same time take Q as $Q = s_{t+i+1}$. Repeat these procedures until Q is the last symbol. At this time, the number of different subsequences is $c(N)$, namely, the measure of complexity. This algorithm uses only two simple operations, comparison and accumulation, which makes the computation of $c(N)$ easy to implement.

In order to obtain a complexity measure that is independent of the sequence length, a normalized complexity measure $C(N)$ is calculated.[6,9] Suppose that the number of different symbols in a symbol set A is a and the length of sequence is $l(U) = N$. Hence,

$$\lim_{N\to\infty} c(N) = b(N) = \frac{N}{\log_\alpha(N)}. \tag{1}$$

For a 0–1 sequence, $a = 2$, therefore

$$b(N) = N/(\log_2(N)), \tag{2}$$

and $c(N)$ can be normalized by this limit,

$$C(N) = c(N)/b(N). \tag{3}$$

In the present study, the normalized complexity measure is employed.[6,9]

In order to validate that the temporal structure of ISI sequence contributes significantly to the normalized complexity which minimizes the effect caused by the sequence length, complexity measurements are performed on surrogate data that are derived from the original sequence. In the present study, surrogate data are generated using three algorithms, i.e. random shuffled (RS), Fourier shuffled (FS) and amplitude-adjusted Fourier transformed (AAFT), to test various hypotheses concerning the structure of the experimentally observed time series of neuronal firing activities.[11]

RS surrogate data are generated by shuffling the original sequence randomly with the null hypothesis that ISI sequence is independent, and identically distributed (IID). FS surrogate algorithm is applied with the null hypothesis that the ISI sequence is linearly correlated random sequence. According to the null hypothesis, the surrogate data can be constructed by randomizing the phases of the Fourier transform of the original ISI sequence with the power spectrum unchanged. AAFT surrogate algorithm is used with the null hypothesis that the ISI sequence comes from monotonic nonlinear transform of a linear Gaussian random sequence. AAFT surrogate data can be generated as follows. First, generate a Gaussian-distributed time series G_0 following the rank order of the original sequence. The FS surrogate of G_0 results in a new sequence G_1. Next, AAFT surrogate data are obtained by rearranging the original ISI sequence following the rank order of the surrogate G_1.

Let $C_{\rm orig}$, $\langle C_{\rm surr}\rangle$ and $\sigma_{\rm surr}$ denote the complexity measurement obtained from the original series, the average and the standard deviation of the complexity measurement obtained from surrogate data sequences, respectively. The significance T of the distinction between the original data and surrogates can be calculated by[3,11]

$$T = |C_{\rm orig} - \langle C_{\rm surr}\rangle|/\sigma_{\rm surr}. \tag{4}$$

In the present study, we assume that the complexity measures for the surrogates generated using each algorithm are normally distributed (numerical experiments indicate that this is a reasonable approximation for our data that are not shown). Therefore, a value of $T > 1.96$ corresponds to a probability $p > 95\%$ that the original data and surrogates have different normalized complexity measure and the null hypothesis can be rejected; otherwise the null hypothesis is accepted. Note that Eq. (4) is equivalent to applying a one-sided hypothesis test.

Adaptation to stimulation begins from the retina in visual pathway. In our experiments, it was observed that quite a portion of the retinal ganglion cells fired actively at the onset of stimulation and the firing rate was progressively reduced in response to prolonged contrast stimulation. The firing rate remained relatively steady after contrast adaptation was finished, when stimulus was maintained. In our experiment, 10 ganglion cells were recorded and analysed. These ganglion cells consisted of ON and ON-OFF subtypes. A typical example (ON-OFF ganglion cell) is shown in Fig. 1. Spontaneous activity was detected at a relatively low level during pre-stimulation period, while the firing rate of the neuron increased rapidly to a high level at the onset of the contrast stimulation and it took about 40 s for the neuron to adapt to the contrast stimulation. After the neuron adapted to the prolonged stimulation, the firing rate remained at a relatively steady level while the stimulation was still presented. Here we investigate the differences in the temporal structure of retinal ganglion cell spike trains between the firing sequences after contrast adaptation and during spontaneous activity.

Because instantaneous responsiveness is an essential property of biological systems, normalized complexity calculated on the data with the same length of time duration may be an index better than the complexity calculated on the ISI strings with the same length.[6] The calculation results of normalized Lempel–Ziv complexity $C(N)$ based on fixed time duration data sets (60 s and 160 s) for firing activity after contrast adaptation and during spontaneous activity are listed in Table 1. The result shows that in most cases, the firing rate after adaptation is somewhat higher as compared to the spontaneous activity, while this is not always the case. On the other hand, the normalized Lempel–Ziv complexity decreases after contrast adaptation in all neurons.

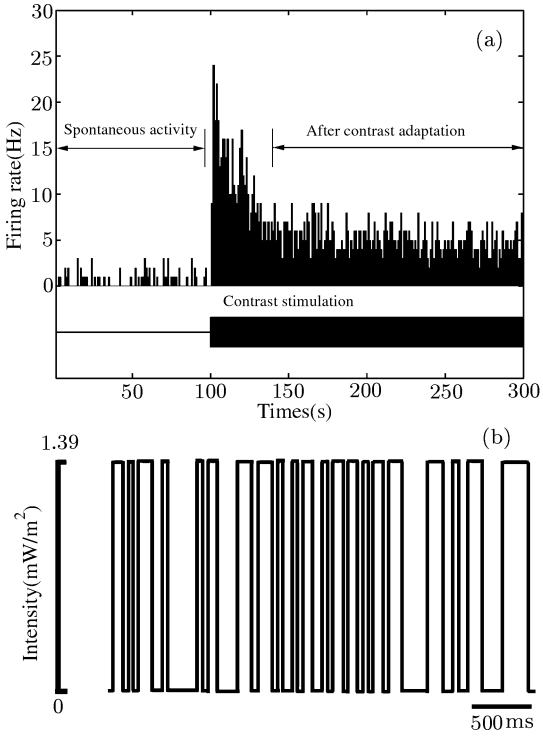

Fig. 1. Ganglion cell activity changes in adaptation to contrast stimulation: (a) Responses of a ganglion cell to contrast stimulation. It took about 40 s for the neuron to adapt the contrast stimulation. The firing rate is presented in 1 s time bin. The lower trace indicates the contrast stimulation. (b) Temporal pattern of intensity changes of the stimulation in (a) shown in an expanded time scale.

Table 1. Average firing rate and normalized Lempel–Ziv complexity of spontaneous firing (SF) and firing after contrast adaptation (FACA).

Neuron	Average firing rate (Hz)		Complexity 60 s		Complexity 160 s	
	SF	FACA	SF	FACA	SF	FACA
1	0.4382	0.7087	1.3373	1.0842	1.1854	1.1177
2	0.3828	3.8518	1.0458	0.9343	1.0564	0.5224
3	0.7251	0.7510	1.4361	1.2619	1.2087	1.1388
4	0.6402	0.5287	1.1724	0.8805	1.0387	0.9375
5	0.6757	4.7382	1.3552	0.7301	1.0189	0.8907
6	0.4396	0.8824	1.5283	1.1459	1.2962	1.0067
7	0.4591	0.9913	1.4463	1.3303	1.2587	1.0403
8	0.9209	2.0940	1.2059	1.0936	1.0686	1.0039
9	0.1822	0.1091	1.4089	1.2925	1.5076	1.0135
10	0.2811	0.4366	1.5000	1.3373	1.2839	1.0962

In order to investigate whether the complexity decrease is related to the temporal structure of the string, the normalized complexity measurement was calculated on surrogate data generated using relevant algorithms. Comparisons between the original and surrogate data sequences (160 s) for the significance T are given in Table 2. In this study, 100 surrogates were generated using each algorithm, for firing sequences during both spontaneous and adapted activities. RS surrogate algorithm was used to examine whether the complexity is related to the temporal structure of the strings with the null hypothesis that there are no temporal correlations in the spike train. The result is that the value of significance T is larger than 1.96

for all the 10 neurons investigated, therefore the null hypothesis is rejected and it can be concluded that the structure of spike trains contributes significantly to the measurement of Lempel–Ziv complexity. FS and AAFT surrogate algorithms were used to test the null hypotheses whether the spike trains are similar to linearly correlated random sequence or to linearly correlated random sequence transformed by a static and monotonic nonlinearity, respectively. The values of the index T for these neurons are all larger than 1.96, therefore these two null hypotheses are rejected, and it can be concluded that the spike trains were not derived from linearly correlated random sequences or to linearly correlated random sequences transformed by a monotonic nonlinearity.

Table 2. Significance comparisons between the original data and surrogate data. Each data set lasts for 160 s.

Neuron	T_{RS} SF	T_{FS} SF	T_{AAFT} SF	T_{RS} FACA	T_{FS} FACA	T_{AAFT} FACA
1	5.27	4.73	3.68	17.66	15.68	12.16
2	4.19	3.38	2.49	29.88	27.67	27.17
3	16.62	12.88	8.64	17.58	16.34	16.18
4	12.58	9.56	5.98	16.98	13.83	12.47
5	12.27	8.73	7.89	33.79	29.56	23.57
6	7.12	5.22	4.35	19.89	18.73	16.47
7	7.36	5.66	3.25	21.93	19.42	16.77
8	17.78	14.94	9.56	23.66	21.07	18.29
9	2.26	2.21	1.98	3.79	3.78	3.09
10	2.58	2.55	2.01	5.67	5.02	3.65

The phenomenon that retinal ganglion cells reduce discharge rates during contrast adaptation and remain a relatively steady firing after contrast adaptation is distinct and interesting. In order to investigate the difference in the temporal structure of retinal ganglion cell spike trains between spontaneous activity and firing activity after contrast adaptation, we employ the normalized Lempel–Ziv complexity measure $C(N)$, which reflects the arising rate of new patterns along with the series. In this study, the result of normalized Lempel–Ziv complexity analyses shows that the complexity of the neural spike trains decreases after contrast adaptation. Given the properties of normalized Lempel–Ziv complexity, the result suggests that the arising rate of new patterns along with the spike train after contrast adaptation is lower than that during spontaneous firing. Therefore, it leads to the inference that the behaviour of the neurons becomes ordered during the response to sustained stimulation that may carry relevant information about the external stimulus. Thus, during the neuron activity after contrast adaptation, external information could be encoded in forms of some certain patterns in the temporal structure of spike train that is significantly different as compared to that of the spike train during spontaneous activity, although the firing rates in spontaneous activity and firing activity after contrast adaptation are sometimes similar.

Complexity calculation is not limited to binary symbol string. Similar results are also obtained in complexity analyses with multiple symbol strings applied to our data (not shown). Using RS surrogate algorithm, our result demonstrates that the structure of spike trains is important in complexity calculation.

Employing FS surrogate algorithm and AAFT surrogate algorithm, we have validated that the temporal structure of the spike trains cannot be explained by either a linearly correlated random sequence or a linearly correlated random sequence transformed by a static monotonic nonlinearity.

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