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Neurocomputing 58–60 (2004) 13–18
NEUROCOMPUTING
www.elsevier.com/locate/neucom

When does interval coding occur?

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Abstract

During the stationary portion of neuron's spiking response to a stimulus, the stimulus could be coded in the average rate and, more elaborately, in the statistics of the sequence of interspike intervals. We use information processing theory to explicitly define when interval coding occurs and quantify the coding gain beyond rate coding provided by the interval code. We explicitly find the interval distribution commensurate with average rate coding. When we analyzed optomotor neural responses recorded from the crayfish eye, we found little interval coding occurring despite stimulus-induced changes from a unimodal to a bimodal interval distribution.
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Keywords: Interval coding; Rate coding; Kullback-Leibler distance

1. Introduction

When a stimulus is presented, the responding neuron usually produces a transient response, which can be followed by a sustained, relatively constant rate of discharge. When present, the sustained rate usually depends on the stimulus, with larger stimuli producing greater rates. The encoded stimulus may not affect only discharge rate, but also the probability distribution of the interspike intervals and their statistical dependence structure [5]. Determining what aspects of a sustained response encode the stimulus is difficult to discern. For example, if the average rate solely encodes the stimulus, average rate variations must entail a change in the interval distribution and possibly a change in the dependence structure as well.

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doi:10.1016/j.neucom.2004.01.016

Our information processing theory rests on studying how neural responses change with the stimulus [2]. In practice or in theory, we compute the Kullback–Leibler distance between responses to measure how well the response encodes the stimulus change: the larger the distance, the more effective the encoding. This approach applies to both the transient and sustained responses; we concentrate on the sustained response here and ask the question "How should the response statistics—interval distribution and dependence structure—change to accommodate a pure rate encoding?" We derive the statistical structure commensurate with rate changes that result in the *minimal* Kullback–Leibler distance. If the measured distance exceeds this minimum, additional features of the discharge pattern also encode the stimulus. If not, only the average rate encodes the stimulus.

2. Results

The framework of information processing theory rests on investigating how the response changes between two stimulus conditions. In this approach, we compute the Kullback–Leibler distance between the probability distributions $p_{\mathbf{X}}(\mathbf{x};\alpha_0)$ and $p_{\mathbf{X}}(\mathbf{x};\alpha_1)$ that describe the response $\mathbf{X}$ to stimulus conditions parameterized by α_0 and α_1, respectively.

$$\mathscr{D}(p_{\mathbf{X}}(\mathbf{x};\alpha_1)\|p_{\mathbf{X}}(\mathbf{x};\alpha_0)) = \int p_{\mathbf{X}}(\mathbf{x};\alpha_1)\log\frac{p_{\mathbf{X}}(\mathbf{x};\alpha_1)}{p_{\mathbf{X}}(\mathbf{x};\alpha_0)}\,\mathrm{d}\mathbf{x}.$$

In this expression, α_0 represents the reference stimulus condition. We use natural logarithms for the Kullback–Leibler distance in subsequent derivations. For simplicity of presentation, assume first that the sustained response consists of a sequence of statistically independent, identically distributed interspike intervals. Thus, the data are well-described as a renewal point process and the interval distribution $p(\tau)$ captures all response characteristics [1]. The Kullback–Leibler distance between two interval distributions would be

$$\mathscr{D}(p_\tau(\tau;\alpha_1)\|p_\tau(\tau;\alpha_0)) = \int_0^\infty p_\tau(\tau;\alpha_1)\log\frac{p_\tau(\tau;\alpha_1)}{p_\tau(\tau;\alpha_0)}\,\mathrm{d}\tau.$$

For a given reference response $p_\tau(\tau;\alpha_0)$ and a second response having measured average interval $\bar{\tau}_1$ when the stimulus was α_1, we seek the *minimal distance* interval distribution: what interval distribution based the first response's statistics is *needed* to achieve the observed rate change? Mathematically,

$$\min_{p_\tau(\tau;\alpha_1)} \mathscr{D}(p_\tau(\tau;\alpha_1)\|p_\tau(\tau;\alpha_0)) \quad \text{subject to} \quad \int_0^\infty \tau p_\tau(\tau;\alpha_1)\,\mathrm{d}\tau = \bar{\tau}_1.$$

Somewhat surprisingly, this constrained optimization problem has a closed-form solution. Kullback [3] showed a simple solution solves a very general class of problems that includes the one we have here,

$$\min_{p_{\mathbf{X}}(\mathbf{x};\alpha_1)} \quad \mathscr{D}(p_{\mathbf{X}}(\mathbf{x};\alpha_1)\|p_{\mathbf{X}}(\mathbf{x};\alpha_0))$$

$$\text{subject to} \quad \mathscr{E}_1[f(\mathbf{x})] = \bar{f} \Rightarrow p_{\mathbf{X}}^{\min}(\mathbf{x};\alpha_1) = K p_{\mathbf{X}}(\mathbf{x};\alpha_0)\mathrm{e}^{af(\mathbf{x})},$$

where K is a constant that gives a unit-area result

$$K = \frac{1}{\int p_{\mathbf{X}}(\mathbf{x};\alpha_0)\mathrm{e}^{af(\mathbf{x})}\,\mathrm{d}\mathbf{x}},$$

$f(\mathbf{X})$ is any function of the random quantity $\mathbf{X}$, a equals a constant that forces the solution to meet the constraint, $\bar{f}$ is the constraining value that the expected value of $f(\mathbf{X})$ must equal, and $\mathscr{E}_1[\,\cdot\,]$ denotes the expected value with respect to the probability function $p_{\mathbf{X}}(\mathbf{x};\alpha_1)$. The minimal Kullback–Leibler distance consistent with the constraint equals $\ln K + a\bar{f}$.

The reason this result is so important is that it specifies how an interval distribution must "morph" just enough to match some response criterion. In our problem, $\mathbf{X} = \tau$, the interspike interval, and the response property we are trying to match is the average interval; consequently, $f(\tau) = \tau$. Using Kullback's result, the minimal Kullback–Leibler interval distribution that has the same average interval as that measured in response to α_1 has the form

$$p_\tau^{\min}(\tau;\alpha_1) = K p_\tau(\tau;\alpha_0)\mathrm{e}^{a\tau}. \tag{1}$$

This minimal Kullback–Leibler interval distribution is related to the reference distribution by multiplication with an exponential function of the interspike interval. To find expressions for the constants a and K, first note that K equals the reciprocal of the moment-generating function of the reference interval distribution

$$K^{-1} = \int_0^\infty p_\tau(\tau;\alpha_0)\mathrm{e}^{a\tau}\,\mathrm{d}\tau \equiv \Phi(a;\alpha_0).$$

To find a, we impose the average rate constraint

$$\int_0^\infty \tau K p_\tau(\tau;\alpha_0)\mathrm{e}^{a\tau}\,\mathrm{d}\tau = \bar{\tau}_1.$$

Simple manipulations show that finding a rests on finding when the derivative of the logarithm of the interval distribution's moment-generating function equals $\bar{\tau}_1$: $\mathrm{d}/\mathrm{d}a \ln \Phi(a;\alpha_0) = \bar{\tau}_1$. Note that the parameter a can be positive or negative: a positive value occurs when $\bar{\tau}_1 > \bar{\tau}_0$ and a negative value occurs in the opposite situation. Furthermore, an average rate change *must* induce a distance between the interval distributions of at least $\ln K + a\bar{\tau}_1$. Any measured Kullback–Leibler distance bigger than this quantity must be due to "extra" interval distribution changes that indicate interval coding is occurring. Furthermore, the additional distance describes how much the interval coding contributes to the ability to discriminate between the two interval sequences.

Because the minimal-Kullback–Leibler-distance "morphing" of the interval distribution is multiplication by an exponential, you can investigate various reference interval distributions analytically to determine how they change. For example, gamma distributions, which have the form $p_\tau(\tau;\alpha_0) \propto \tau^m \mathrm{e}^{-k\tau}$, morph into a gamma distribution having the same value for the parameter m. If the interval distribution is (approximately) Gaussian, multiplication by an exponential amounts to simply changing the mean: the distribution is shifted left or right with no change in variance. Thus, if a stimulus change causes the response's interval distribution to change from a gamma distribution to some other form, interval coding in addition to rate coding is occurring.

Coding by interval patterning—varying the statistical dependence betweeen successive intervals—can also be analyzed with Kullback's result. Here, the reference probability distribution is the joint probability function for successive intervals $p_{\tau_{n-1},\tau_n}(\tau_{n-1}, \tau_n; \alpha_0)$. This quantity captures the dependence of an interval's duration on the previous interval's duration. The joint probability function for the second response having the same average interval as that measured but closest to the measured reference joint probability function is easily shown to be

$$p^{\min}_{\tau_{n-1},\tau_n}(\tau_{n-1}, \tau_n; \alpha_1) = K p_{\tau_{n-1},\tau_n}(\tau_{n-1}, \tau_n; \alpha_0) \mathrm{e}^{a\tau_{n-1}} \mathrm{e}^{a\tau_n},$$

where K is again a normalization constant and a is found to satisfy the average-interval constraint. The exponentials multiplying each other are reminiscent of the joint probability function for independent random variables. Exploring several examples shows, however, that the dependence of successive intervals (as measured by the correlation coefficient) can be smaller or larger than that of the reference. In any case, the presence of interval patterning can be explored using the Kullback–Leibler distance: a measured Kullback–Leibler distance between joint probability functions larger than the minimal value $\ln K + 2a\bar{\tau}$ can be due to interval coding and/or interval dependence coding. Calculating the excess distance for the marginal interval distribution $p_\tau(\tau; \alpha_1)$ can help discern whether dependence coding is also present. Note that the value of K, but not a, differ in the marginal and joint probability function cases.

3. Data analysis

These elegant theoretical results do not lend themselves well to dealing with empirical distributions. First of all, despite the existence of fast algorithms to compute the moment-generating function (chirp-z transform) [4], finding the parameters from data this way is complicated. Instead, we note that finding the scaling parameter K is easy once we know a. We established an iterative procedure (Newton–Raphson) to estimate the parameter a from the reference interval histogram and the average-rate constraint provided by the second response. We found this to converge quickly. Fig. 1 shows the result of applying this algorithm to data recorded from a crayfish motoneuron. Here, the recordings were made from on optomotor neuron responding to a spatial wavelength (λ) variations of a sinusoidal grating. The increase in Kullback–Leibler distance for intermediate values of spatial wavelength reflect the fact that the discharge rate increased, which led to a greater discrepancy between the reference interval distribution and that obtained when the stimulus changed. The confidence intervals include the minimal Kullback–Leibler distance in all but the two smallest spatial wavelengths. Note that despite the fact the reference interval histogram is unimodal, the minimal Kullback–Leibler interval distribution is bimodal in the $\lambda = 22°$ and $30°$ cases and that these distributions match well with those measured. For the cases that have a larger Kullback–Leibler distance than required for the rate change ($\lambda = 5°, 11°$), the excess distance can be traced to the presence of more short intervals than necessary for a pure rate change. The difference in the measured and minimal Kullback–Leibler distance is

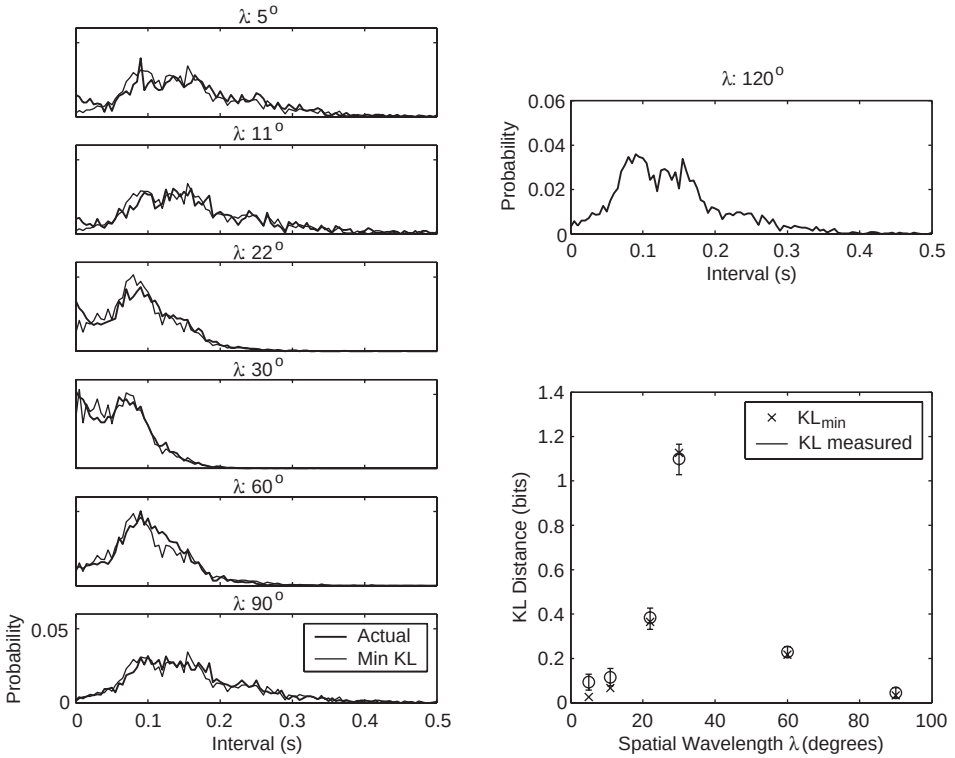


Fig. 1. The left column shows the interval histograms of a crayfish visual motoneuron responding to variations in spatial wavelength of a sinusoidal grating. The solid line is the measured interval histogram and the thin line is the minimum Kullback–Leibler distribution derived from the reference interval histogram shown in the right column. The reference stimulus had a wavelength of 120°. The bottom plot in the right column compares the measured and minimal Kullback–Leibler distances for the measured interval histograms. For each stimulus condition, the circle indicates the bootstrapped estimate of the Kullback–Leibler distance between the two measured interval histograms and the error bars denote 90% confidence intervals for the estimate. The × symbol marks the value of the minimal Kullback–Leibler distance consistent with the measured average interspike interval.

not large, indicating that this interval coding, while statistically significant, does not contribute greatly to the overall distance.

4. Conclusions

The Kullback–Leibler distance characterizes how well two responses can be distinguished by an optimal classifer [2]. Kullback's result allows teasing apart components of a measured distance into those required for a rate change and those that might be required to reflect an interval distribution change and a dependence change. Thus, an *objective* measure can be made not only of the efficacy of a neural code, but also of

what response attributes contribute to it. That rate coding amounts to multiplying a basic interval distribution by an exponential does *not* mean that the encoding neuron mechanistically employs this change. The analysis described here quantifies how well the response encodes the stimulus and what response aspects contribute to the coding. Identifying these response attributes does not mean that the receiving neuron employs them in its processing, but they do contribute to distinguishing the responses. If not employed, subsequent processing is suboptimal.

Because of the generality of this result, any response attribute that can be expressed as an expected value can be analyzed in this way. Several response attributes can be examined systematically in this approach, with the each attribute's contribution to the neural code quantified.

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