

Testing the Efficiency of Sensory Coding with Optimal Stimulus Ensembles

Christian K. Machens,^{1,*} Tim Gollisch,^{2,3}
Olga Kolesnikova,² and Andreas V.M. Herz²

¹Cold Spring Harbor Laboratory
One Bungtown Road
Cold Spring Harbor, New York 11724

²Institute for Theoretical Biology
Humboldt-University Berlin and
Bernstein Center for Computational Neuroscience
10099 Berlin
Germany

Summary

According to Barlow's seminal "efficient coding hypothesis," the coding strategy of sensory neurons should be matched to the statistics of stimuli that occur in an animal's natural habitat. Using an *automatic* search technique, we here test this hypothesis and identify stimulus ensembles that sensory neurons are optimized for. Focusing on grasshopper auditory receptor neurons, we find that their optimal stimulus ensembles differ from the natural environment, but largely overlap with a behaviorally important subensemble of the natural sounds. This indicates that the receptors are optimized for peak rather than average performance. More generally, our results suggest that the coding strategies of sensory neurons are heavily influenced by differences in behavioral relevance among natural stimuli.

Introduction

Sensory systems exhibit an astounding diversity in form and function—from the chemosensation of archaeobacteria to mammalian vision—and are often exquisitely adjusted to the natural environment of the specific organism (Hauser, 1996). Although their functional organization reflects the particular evolutionary adaptations, their design may also be guided by general principles that hold across sensory modalities and species. A prominent candidate for such a general principle is the "efficient coding hypothesis," which was first formulated by Barlow more than 40 years ago (Barlow, 1961; Simoncelli, 2003). The hypothesis asserts that sensory systems seek to provide an efficient representation of the complex and dynamic signals occurring in an animal's natural environment. To achieve this goal, single sensory neurons should strive to fully employ their information capacity in response to natural stimuli, and different neurons should aim to operate as largely independent encoders.

Various experimental findings support the efficient coding hypothesis. For example, it has been demonstrated that single neurons can use their full output ca-

capacity by precisely matching their tuning curve to the statistics of natural stimuli (Laughlin, 1981). On the system's level, the hypothesis has helped to elucidate the topological and functional organization of early visual cortex (Olshausen and Field, 1996; Bell and Sejnowski, 1997; Hyvärinen and Hoyer, 2000) and the time-frequency trade-offs of the cochlear filter bank (Lewicki, 2001). There is also substantial evidence that sensory systems convey far less information about simplified artificial stimuli than about signals that share salient statistical properties with behaviorally relevant stimuli (Rieke et al., 1995; Attias and Schreiner, 1998; Machens et al., 2001; Reinagel, 2001; Vinje and Gallant, 2002; Chacron et al., 2003; Escabi et al., 2003). Recent studies even suggest that adaptation shifts the tuning curves of neurons dynamically to keep up with slow variations in the statistics of environmental stimuli (Wainwright, 1999; Stemmler and Koch, 1999; Brenner et al., 2000; Fairhall et al., 2001).

The efficient coding hypothesis leaves open how the ensemble of natural stimuli is defined. This poses a severe problem, as any specific prediction derived from the hypothesis depends crucially on the measured (or assumed) distribution of natural stimuli. In particular, natural stimuli vary in their behavioral relevance, and the set of behaviorally relevant stimuli often differs from species to species, even for animals living in the same habitat. Studies that are based on a heuristic collection of natural stimuli may thus undersample or even completely miss features that are of utmost importance for the investigated species. Furthermore, a sensory system may efficiently process stimuli that are not even encountered in nature. For instance, animals often prefer artificially enhanced ("supernatural") communication signals over those of potential mating partners (Hauser, 1996). Accordingly, sensory systems may not seek an efficient representation of natural stimuli per se; rather, their optimization may be heavily biased toward those natural stimuli that are behaviorally most relevant.

In order to investigate if and in which way a given sensory system is optimized with respect to its environment, we here perform a systematic online search for the ensemble of stimuli that are encoded best, using the live responses of receptor neurons as a guide. The attributes of the determined optimal stimulus ensemble can then be compared to the stimuli of the organism's natural environment. This procedure provides an independent test of the efficient coding hypothesis and may ultimately lead to a better understanding of the general principles that underlie the functional design of neural systems. To do so, we use a search technique that *automatically* finds optimal stimulus ensembles under well-specified constraints. For concreteness, the quality with which stimuli are encoded will be quantified in terms of the mutual information between stimulus and neural response.

Finding optimal stimulus ensembles requires sufficient knowledge of the (probabilistic) stimulus-response relation of the system under study. Although the mathe-

*Correspondence: machens@cshl.edu

³Present address: Department of Molecular and Cellular Biology, Harvard University, Cambridge, Massachusetts 02138.

mathematical framework is straightforward, the high dimensionality of behaviorally relevant stimulus spaces seems to preclude any such attempt in neurobiological experiments, as it is impossible to completely cover the stimulus-response relation. Using a recently developed online algorithm (Machens, 2002), we demonstrate that optimal stimulus ensembles can nevertheless be approximated through an iterative process.

We perform our studies on the auditory system of grasshoppers, for which much is known about the importance of specific signals in the acoustic environment. Grasshoppers use species-specific acoustic communication signals for mate selection and mate localization (von Helversen and von Helversen, 1994; Stumpner and von Helversen, 2001). These “calling songs” feature cues on time scales that range from a few seconds down to a few milliseconds. Correspondingly, the auditory receptors of grasshoppers exhibit tonic activity for long-lasting stimuli as well as precise locking of spikes to a sound’s amplitude modulation (Römer, 1976; Machens et al., 2001). The cells are therefore well suited for tackling questions of coding efficiency and read-out mechanisms on different time scales. In addition, grasshopper receptor neurons can be recorded for long time periods and allow reliable spike detection, two key prerequisites for the implementation of online algorithms. Taking advantage of these characteristics of the grasshopper auditory system, we focus on the coding properties of single receptors, determine the optimal stimulus ensembles, and compare them with the behaviorally relevant acoustic environment.

Results

The Efficient Coding Hypothesis and Optimal Stimulus Ensembles

The efficient coding hypothesis asserts that neurons match their coding strategy to the ensemble of natural stimuli. A simple example of such a matching is shown in Figures 1A–1C (see also Laughlin, 1981; Stemmler and Koch, 1999). Given a distribution of stimulus intensities in the world (Figure 1B), how should a neuron choose its input-output function to encode these intensities? Note that a neuron has only a finite range of responses. To avoid loss of information, the neuron should therefore set its sensitivities such that most of the encountered intensities fall above threshold and below the saturation level. Information theory provides a rigorous solution to this problem: for a noiseless system, the neuron needs to construct its input-output function such that all response levels are used with equal frequency. This can be achieved if the neuron’s input-output curve corresponds to the cumulative probability distribution of the stimuli (Figure 1C). This way, the neuron uses its response range to obtain a high resolution of common events, without reserving large portions for improbable events.

This concept of efficient coding is invertible. Instead of taking the distribution of natural stimuli as given and ask what the optimal input-output function is, we can also take a neuron’s input-output function as given (Figure 1C) and then infer the distribution of stimuli that lets the neuron perform as an efficient device (Figure 1B). We will call this distribution the *optimal stimulus ensemble* (OSE) of the neuron. The efficient coding hypothesis suggests that the OSE should approximately match the natural stimulus ensemble. In Figures 1D and 1E, we illustrate this idea for grasshopper auditory receptor neurons. Figure 1D (blue line) shows the average firing rate of a neuron as a function of the sound intensity of a pure tone. To obtain the OSE, we simply take the derivative of this input-output function (Figure 1E, blue line).

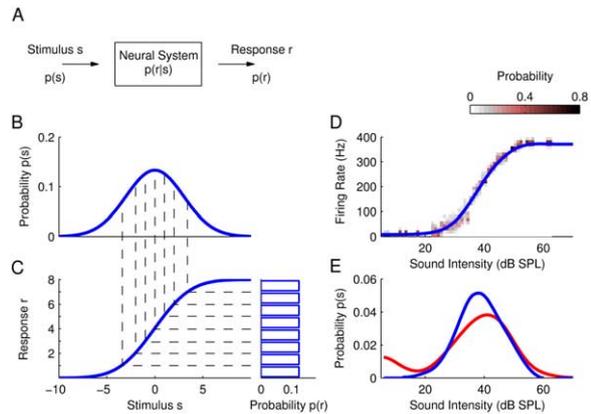


Figure 1. Efficient Coding Hypothesis and Optimal Stimulus Ensemble

(A) A sensory neuron processes stimuli s that occur with probability $p(s)$ in the animal’s environment. For a given stimulus s , the neuron reacts with response r whose conditional probability is described by the stimulus-response relation $p(r|s)$. Summed over all stimuli, each weighted by $p(s)$, this results in the response probability $p(r)$.

(B and C) Optimal coding strategy of a neuron. Given a distribution of stimulus values (B), the neuron should choose its input-output function (C) such that all responses are used with equal frequency. (D) Tuning curve of a typical grasshopper auditory receptor. Shown are the mean input-output function (blue line) and the full input-output relation $p(r|s)$ as a color-coded background plot. The stimuli were pure tones (each of a duration of 80 ms) whose frequency matched the receptor’s best frequency (5 kHz). Each stimulus was repeated ten times.

(E) Optimal stimulus ensemble (OSE). The blue curve shows the OSE for the mean input-output function from (D). The red curve shows the OSE when neural response variability is taken into account. For stimuli that are drawn randomly from this ensemble, the receptor neuron conveys the maximum amount of information in its firing rates. Note that most stimuli fall into the rising part of the neuron’s tuning curve.

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So far, the calculation neglects that the number of spikes in response to a particular sound varies from trial to trial due to intrinsic noise sources. If some responses are more reliable than others, then information theory prescribes to use the reliable responses more often than the unreliable and ambiguous responses. In this case, the OSE needs to be computed numerically (see the Supplemental Experimental Procedures available online). The solution is shown in Figure 1E (red line). If the receptor neuron were to encounter sound intensities with these relative frequencies, then its firing rates would transmit the maximum amount of information possible, which is also called the information capacity of the neuron (Cover and Thomas, 1991). Note that some of the probability has been shifted from stimuli around 30–40 dB SPL (sound pressure level) to stimuli that fall below the threshold of the cell (<20 dB SPL).

These stimuli trigger the response “no spikes,” which, in the absence of spontaneous activity, is produced with high reliability. To exploit this excess reliability, the OSE features increased probabilities for stimuli with low intensities.

These results demonstrate several important issues. First, the OSE is the result of a compromise. On the one hand, it should be designed such that the neuron generates all response symbols with equal probability; on the other hand, it should be designed such that the neuron avoids the production of noisy response symbols. Second, the OSE is not unique. Since stimuli falling below threshold (<30 dB SPL) generate no spikes, we can replace them by stimuli that are even quieter, e.g., by shifting the leftward bump 10 dB to the left. The resulting ensemble is just as optimal as the ensemble shown in Figure 1E. We call this property an *invariance* of the OSE. In this context, we also note that the detailed shape of the OSE only marginally influences the transmitted information. Whereas the OSE (red curve in Figure 1E) yields an information rate of $I_{\text{opt}} = 29.3$ bits/s, the blue ensemble is almost as good with $I = 28.4$ bits/s. That does not make the OSE arbitrary, however: the bulk of the probabilities must fall between 25 and 55 dB SPL, i.e., into the rising part of the neuron’s input-output function; other probability distributions would yield much lower bit rates. Third, we note that grasshoppers have several receptor neurons with different thresholds. Accordingly, the OSE of one neuron captures only a part of the stimulus region that the peripheral auditory system is optimized for. In summary, the properties of this single receptor neuron, together with the efficient coding hypothesis, suggest that grasshoppers expect to encounter sound intensities between 25 and 55 dB SPL in their natural environment.

While these results appear reasonable, there are two implicit assumptions that we have made so far. We have assumed that the grasshopper’s environment is restricted to sounds of constant intensity, and we have assumed that the neuron encodes information into its firing rate. Both assumptions are not plausible from a biological point of view: acoustic stimuli vary in time, and the precise timing of spikes conveys important information about song signals used by grasshoppers (Machens et al., 2001, 2003).

In the remainder of this paper, we take a two-step approach to analyze the OSE under biologically more realistic conditions. In a first series of experiments, we estimate the OSEs for time-varying stimuli while retaining the assumption that neurons convey information in their firing rates. In a second series of experiments, we use time-varying stimuli and consider the additional information due to the precise timing of spikes. In these latter experiments, we make full use of a neuron’s potential to convey information and therefore approximate a neuron’s true information capacity. This two-step process allows us also to investigate potential OSE differences for the two different read-out modes.

Online Determination of Optimal Ensembles for Time-Varying Stimuli

When moving from constant to arbitrarily fluctuating sound intensities, it becomes technically impossible to map the stimulus-response relation for *all* stimulus-

response pairs. There are simply too many combinations. To circumvent this problem, we describe the stimulus ensemble by a small set of parameters. As the key step of our approach, we then use an iterative online procedure (Machens, 2002) to determine the parameter values that come closest to the OSE. This approach is explained in detail in the [Supplemental Experimental Procedures](#).

For the present study, our stimuli are 80 ms sound snippets consisting of bandwidth-limited random amplitude modulations of a sine-wave carrier (Figure 2). We characterize each snippet by its sample mean and standard deviation. Figure 2B shows ten such snippets with different means and standard deviations, as well as the elicited responses. We assume that the OSE can be approximated by a Gaussian distribution over mean and standard deviation of the snippets. To keep the graphics as simple as possible, we represent this Gaussian by a single contour line (an ellipse that is a single standard deviation from the center of the Gaussian) in the two-dimensional plane spanned by the sample mean and standard deviations of the snippets (Figure 2A).

One step of the iterative algorithm on a single receptor neuron is presented in Figures 2A–2C. Starting with some initial choice for the Gaussian stimulus ensemble (ellipse in Figure 2A), a set of snippets is drawn and the neuron’s responses to several stimulus repetitions are measured ($n = 10$, cf. Figure 2B). We then estimate the contribution of each snippet to the information rate, as visualized by the size of the dots in Figure 2C. Using this knowledge, we update the parameters of the Gaussian stimulus ensemble and move it into those regions of the stimulus space that contribute most to the information rate. The updated ensemble results in an improved estimate of the relevant stimulus regime and is used to draw new, additional snippets. Results for the entire experiment are depicted in Figures 2D and 2E. With each iteration of the procedure, a better Gaussian stimulus ensemble is obtained (ellipses in Figure 2D) until the best Gaussian fit of the OSE is reached (black ellipse). Figure 2E illustrates the corresponding growth in information rates. After about 20 iterations, the information rates converge to a value of $I \approx 48$ bits/s.

Optimal Stimulus Ensembles—Firing-Rate Code

In a first series of experiments, we investigated the stimulus information encoded in the firing rate of the receptor neurons, which we determined in 80 ms windows. For a single neuron, the results of the online procedure are shown in Figure 3. Final estimates of the OSEs, obtained from the same neuron in different runs of the algorithm, are depicted as ellipses in Figure 3A. In all cases, the iterative procedure converged to rather similar information rates ($I \approx 47.4$ bits/s). While the resulting stimulus ensembles are therefore all valid estimates of *optimal* stimulus ensembles, they are not unique and thus reveal invariances in the neural input-output mapping.

To understand the properties of the OSEs, we compare them to the neural tuning curves, shown as contour lines in Figure 3A. Along the x axis (mean of the stimulus snippets), each OSE is located such that it

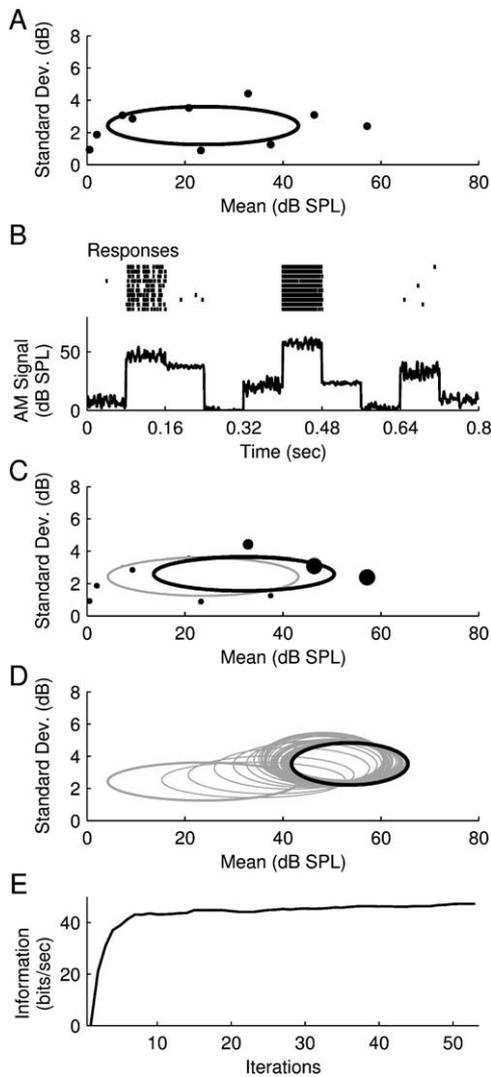


Figure 2. Iterative Tracking of the Optimal Stimulus Ensemble in a Grasshopper Auditory Receptor

We use an online procedure to find a parameterized fit of the OSE in higher-dimensional spaces. (A and B) The stimuli are ten 80 ms-long snippets of white-noise amplitude modulations of a sine-wave carrier whose sample mean and standard deviation (dots in [A]) are drawn from a two-dimensional Gaussian distribution, represented by an ellipse that outlines the standard deviation of the Gaussian. (B) The stimuli are played repeatedly, resulting in the shown raster of spike train responses. (C) Using the responses from several trials, the contribution of each stimulus to the mutual information is estimated; this contribution is depicted by the size of the dots representing the individual snippets. The contributions are taken as weights that are used to update the parameters of the Gaussian distribution, which is thus shifted toward the more important stimuli (black ellipse). The updated stimulus ensemble is then used to draw new, additional test stimuli. (D) For a longer sample run, intermediate estimates of the OSE (gray) rapidly move toward the most informative region in stimulus space where they converge to the final estimate of the OSE (black). (E) Accordingly, the information rate initially grows rather fast with each iteration until it saturates after about 20 iterations.

covers almost the full range of firing rates. Hence, the ensembles make use of all response symbols. As noted above, the OSE should stay away from stimulus regions

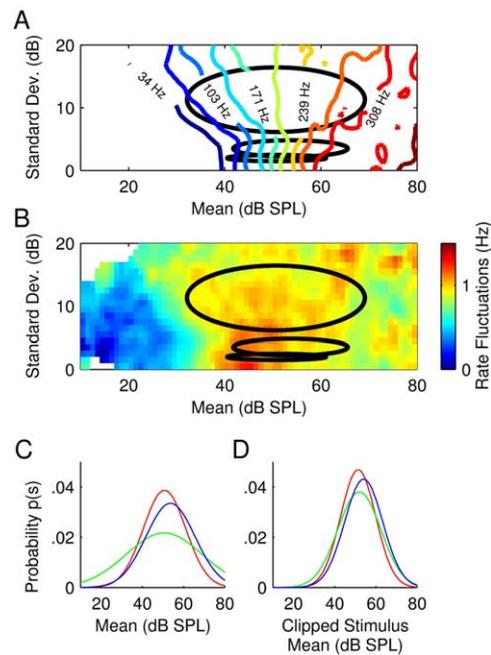


Figure 3. Optimal Stimulus Ensembles and Underlying Structure of the Stimulus-Response Relation

Shown are data from the same cell as in Figure 2. (A) Gaussian fits to the OSEs (black ellipses) together with iso-firing rates (colored lines), projected onto the two-dimensional plane spanned by the sample mean and standard deviation of the 80 ms-long snippets. Similar to Figure 1, the OSEs cover almost the complete range of firing rates, which determines position and extent of the OSEs along the horizontal axis. The position and width of the ensembles along the vertical axis is largely arbitrary due to the invariance of the neuron's stimulus-response mapping with respect to the standard deviation of the stimulus snippets. (B) Reliability of neural responses. For each stimulus, the reliability was measured as the standard deviation of the elicited firing rate. The reliability varies only slightly within the range of stimuli covered by the OSEs. (C) Projection of the OSEs from (B) onto the mean of the stimulus snippets. The OSEs differ because the iso-firing rates in (A) diverge for higher standard deviations of the stimuli. (D) Illustration of the OSE invariances. Once the OSEs are redrawn with respect to the clipped stimulus mean, they are almost equal in this new coordinate.

with unreliable stimulus-response pairs. Here, this principle has little influence on the position or width of the OSEs along the y axis (standard deviation of the snippets), since the reliability of the responses, as measured by the standard deviation of the firing rates, varies only slightly along the lines of equal firing rate (Figure 3B). This observation suggests that the temporal fine-structure of the stimulus, given by the fluctuations around the stimulus mean, does not contribute much to the transmitted information under the rate-code paradigm.

The analysis demonstrates that there can be invariant directions in stimulus space, along which the OSE is not uniquely determined, such as the standard deviation of the stimulus snippets in the present setting. The observed invariances are a result of the dimensional reduction of the input-output mapping, from a high-dimensional stimulus space into the one-dimensional firing rate. That does not mean that the OSE is arbitrary, however, since there can also be *variant* directions

along which the OSE is uniquely determined. Within the presently assumed read-out mode, the stimulus mean could be a candidate for defining such a variant direction. However, the differences in the probability distributions in Figure 3C demonstrate that the OSEs are not uniquely determined along the mean of the stimulus snippets either. In fact, a simple transformation of the stimuli yields a much better approximation of the variant direction for the investigated receptor neurons: given the threshold and saturation point for a cell, we clip the snippets at these two values, i.e., we set all stimulus values below threshold to the threshold value and all stimulus values above the saturation point to the value of the saturation point. For each snippet, we can then calculate the mean intensity after this transformation, which we call the “clipped stimulus mean.” When we recompute the Gaussian fits using these clipped stimulus means, the three distributions become nearly identical (Figure 3D). Despite the high dimensionality of the stimulus space, the OSEs for the rate-code paradigm can therefore be condensed into a one-dimensional distribution over the clipped stimulus means.

The efficient coding hypothesis thus suggests that the auditory receptor neuron expects to encounter a distribution of sounds whose clipped representation coincides with Figure 3D. Whether the amplitudes of these sounds are relatively constant or strongly fluctuating does not matter for the firing-rate read-out.

Optimal Stimulus Ensembles—Spike-Timing Code

The results of the previous section were based on the assumption that the information conveyed by the receptor spike trains is integrated over a time scale of ≈ 80 ms by some downstream read-out neurons. In the next step of our analysis, we relax this restriction and consider the contribution of precise spike timing to information transmission. The OSEs estimated in these new experiments therefore approximate the true information capacity of the investigated receptor neurons. To account for temporal correlations between the spikes, spike times were binned in 2 ms time intervals, and ten successive bins were assembled into a string (Strong et al., 1998); accordingly, every 20 ms-long neural response is represented by a string with ten zero/one entries. The chosen temporal resolution reflects the neurons’ absolute refractory period and thus allows at most one spike per 2 ms bin, and the 20 ms strings well encompass the neuron’s integration time and response correlation (Gollisch and Herz, 2005; Schaette et al., 2005). This approach increases the number of possible output patterns; to obtain reliable estimates of the stimulus-response relation, we therefore used 25 repetitions of every stimulus (see the Supplemental Experimental Procedures for the reliability of these estimates).

An example for an OSE thus obtained is shown in Figure 4. This OSE focuses on stimulus snippets with relatively large standard deviations (≈ 10 dB) and with means around 48 dB SPL. Moreover, the OSE is much narrower along the x axis (mean of the stimulus snippets) than before, clinging to a regime of intermediate firing rates ≈ 200 –300 Hz. These findings were reproduced in all investigated cells. Hence, the OSEs for a timing read-out differ strongly from the OSEs for a rate-based read-out.

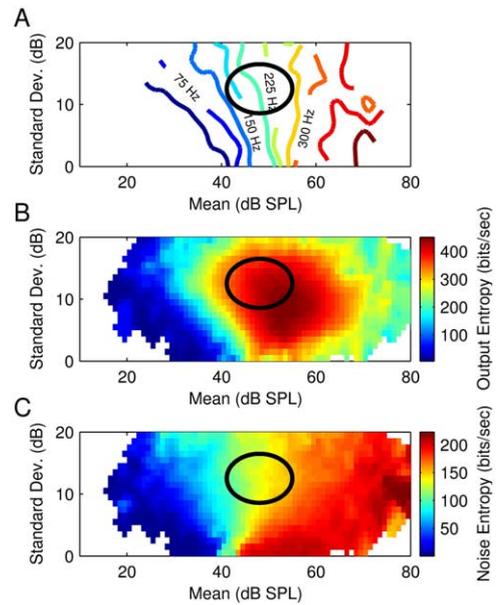


Figure 4. Optimal Stimulus Ensemble for a Spike-Timing Readout (A) Gaussian fit of the OSE (black ellipse) and iso-firing rates (colored lines), projected onto the two-dimensional plane spanned by the sample mean and standard deviation of the snippets (as in Figure 3A). The OSE focuses on intermediate firing rates (≈ 200 –300 Hz) and stimuli with high standard deviation.

(B) Local response entropy. This measure quantifies the entropy of the response symbols obtained when stimuli are restricted to a particular mean and standard deviation. The red region indicates a stimulus regime where almost all of the possible response symbols are generated by the neuron.

(C) Local noise entropy, defined in the same manner as the local response entropy. The red region indicates a stimulus region where the neurons fire almost completely at random. The OSE seeks to avoid a high noise entropy (random firing) while keeping a high output entropy (large number of output symbols).

To understand the position and extent of the OSE, we show that it can be understood as a compromise in which the neuron employs as many response symbols as possible yet avoids noisy and ambiguous responses. In order to generate many different responses, stimulus ensembles need to increase a neuron’s response entropy. To illustrate this aspect, Figure 4B shows the local response entropy, i.e., the response entropy for snippets with a given sample mean and standard deviation. The large red region in Figure 4B represents the region in stimulus space leading to a large diversity of responses and therefore a high response entropy. This demonstrates that stimuli that fluctuate strongly (standard deviation ≈ 10 dB) achieve a high response entropy. To drive the neuron reliably, the optimal stimulus ensemble should also lead to a low noise entropy, which quantifies the average variability in response to the exact same stimulus and therefore serves as a measure of the trial-to-trial variability. Figure 4C shows the local noise entropy for snippets with a given mean and standard deviation. Accordingly, the noise entropy varies mostly with the mean of the stimulus snippets: low means lead to reliable responses, high means lead to unreliable responses. On the basis of these characteristics of the stimulus-response relation, the algorithm has

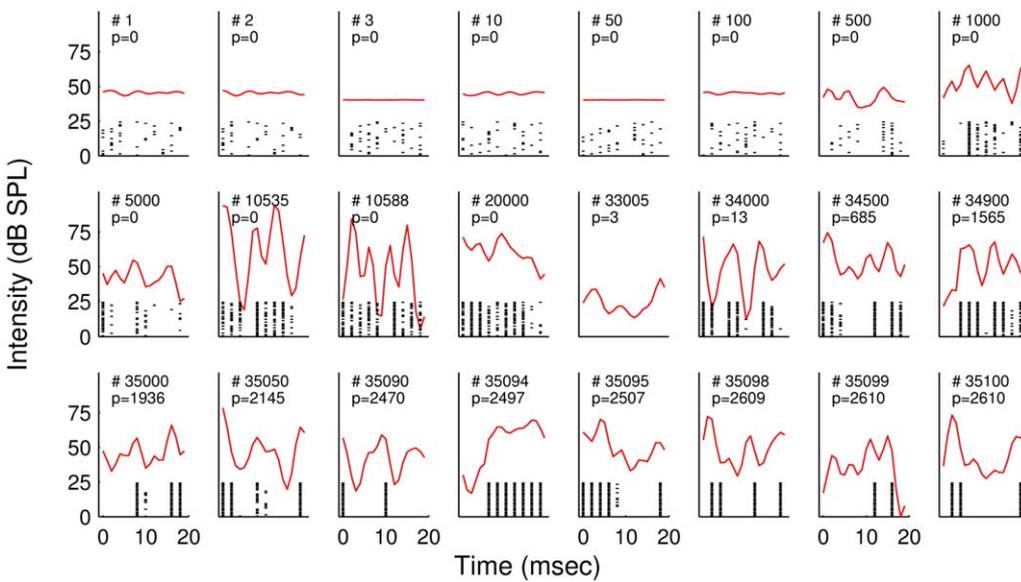


Figure 5. Examples of Snippets s Sorted According to Their Probabilities $p(s)$ and the Respective Responses

The OSE assigns a probability $p(s)$ to every snippet tested. This probability is indicated in ppm by the second number in each panel. The first number specifies the rank of each stimulus when sorted by its probability. Accordingly, the snippets in the top row do not contribute to the OSE, as also suggested by the highly unreliable responses (spike rasters, spikes binned at a resolution of 2 ms). The snippets in the bottom row (and hundreds of others not shown) are distinguished by the high reliability (small noise entropy) and mutual distinction (leading to a high response entropy) of the respective responses. Whereas the snippets in the bottom row fluctuate more strongly than those in the top row, strong stimulus fluctuations are not sufficient to produce reliable spiking, as illustrated by the examples in the middle row.

found a stimulus regime that reliably triggers a large variety of spike patterns at high temporal precision. In the optimal ensemble, stimuli have strong intensity fluctuations (standard deviation ≈ 10 dB) and mean intensities that cover a range of intermediate firing rates.

Sample snippets are shown in Figure 5, sorted by the probabilities $p(s)$ assigned to them in the OSE. The first row contains examples with unreliable spiking and correspondingly small probabilities $p(s)$. In the last row, some examples led to exactly the same spike pattern in all 25 trials and are therefore associated with large probabilities $p(s)$. While large-intensity fluctuations are necessary for such high spiking reliability, they are by no means sufficient: the middle row shows some counterexamples of stimuli with large fluctuations that do not lead to reliable spiking. These snippets have mean intensities around 50 dB SPL and therefore fall into stimulus regions with high noise entropy (red region in Figure 4C). Furthermore, a detailed analysis of the OSE shows that response symbols corresponding to repetitive firing at the maximum rate are used less frequently. These symbols are less reliable, most likely due to spontaneous failures and fatigue of the spike generator.

The OSE for the spike-timing read-out leads to information rates of nearly $I \approx 420$ bits/s. Compared to the values for a rate code ($I \approx 48$ bits/s), this more than 8-fold increase signifies the large additional information conveyed in the precise timing of spikes. To make use of their full coding capacity, receptor neurons therefore need to encounter time-varying stimuli with strong amplitude fluctuations, centered around a particular mean sound intensity.

Population Data and Comparison with Natural Stimuli

Population data from experiments with at least ten iterations of the optimization algorithm (Figures 6A and 6B) confirm the results from the examples shown in Figures 3 and 4. To compare the OSEs independent of the firing thresholds of the cells, we represent the Gaussian OSE fits relative to the stimulus mean for each cell. For the rate read-out, the optimal stimulus ensembles (r-OSEs) fully cover the receptor's dynamic range of around 20–30 dB, which is given by the rising part of the tuning curve (Figure 6A). For higher standard deviations, the r-OSEs broaden along the axis of stimulus means. This broadening reflects the broadening of the neuron's tuning curve for stimuli with larger standard deviation, as shown by the larger spread of the iso-firing-rate lines in Figure 3A. Note that these changes in the neuron's tuning curve are not caused by adaptation mechanisms, but by an invariance in the neuron's input-output mapping. For the timing read-out, we find that the optimal stimulus ensembles (t-OSEs) are narrower along the axis of the stimulus means (Figure 6B), with only small variability across neurons. The t-OSEs avoid regions in stimulus space with standard deviations < 10 dB, despite the fact that most experiments started with stimulus ensembles whose initial standard deviations were between 3 and 5 dB. No preferred position along the y axis was found for standard deviations > 10 dB. This comparison shows that the OSEs exhibit significant differences for the two read-out modes.

In the final step of our analysis, we compare the OSEs with the acoustic environment of grasshoppers.

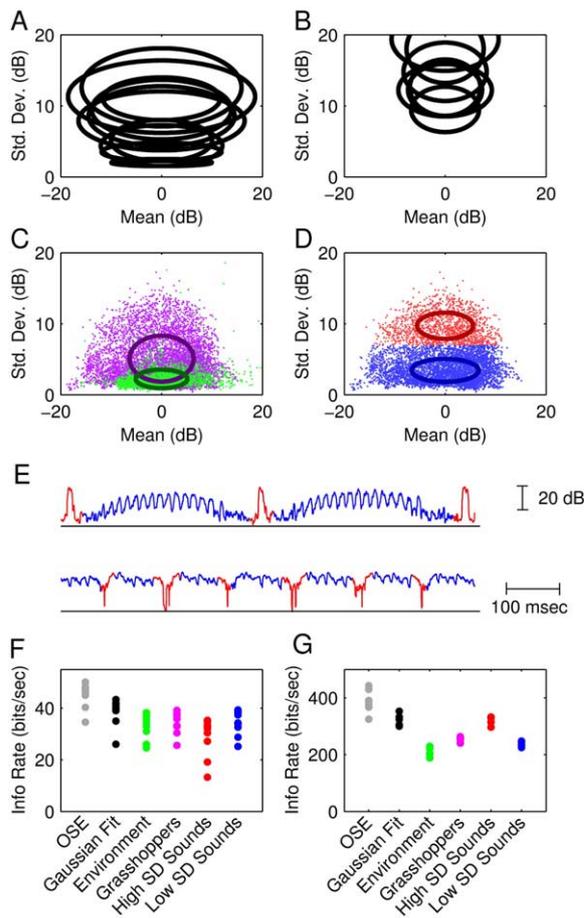


Figure 6. Comparison of OSEs and Natural Sounds

(A) Gaussian fits of OSEs for a rate read-out (r-OSEs). The width of the ensembles along the x axis (mean of the stimulus snippets) is determined by the spread of the neuron's iso-firing rate lines; there is no preferred width or position with respect to the standard deviation of the stimulus (y axis). For stimuli with larger standard deviations, the iso-firing rate lines widen and lead to a corresponding widening of the ellipses.

(B) Gaussian fits of the OSEs for a timing read-out (t-OSEs). The width of the ensembles along the stimulus mean is much narrower than in (A) because the t-OSEs focus on intermediate firing rates. Since large stimulus fluctuations trigger reliable spikes, the t-OSEs are positioned in stimulus regions with large standard deviations.

(C) Natural stimulus ensemble: grasshopper songs (magenta) and environmental (noncommunication) sounds (green). The dots correspond to randomly chosen, 20 ms-long sound sections. The ellipses show Gaussian fits to the respective dots.

(D) Subdivision of grasshopper songs, same format as in (C). We extract a sub-ensemble of grasshopper songs (red) whose statistics come close to those of the t-OSE.

(E) Amplitude modulation of two grasshopper songs, *Ch. mollis* (top) and *Ch. biguttulus* (bottom). The color code indicates whether stimulus sections fall into the range of the t-OSEs (red) or not (blue). The red sections mark the on- and offsets of rhythmic subpatterns (called syllables) which are of specific behavioral relevance.

(F) Information rates for the rate read-out. Shown are the information rates for six different stimulus ensembles, each data point corresponds to measurements from one cell. The labels "Environment" and "Grasshoppers" refer to the natural sound ensembles in (C), the labels "High SD Sounds" and "Low SD Sounds" to the natural sound ensembles in (D).

(G) Information rates for the timing read-out, same format as in (F), but note the different scale on the y axis. Among the natural stimu-

Since vertebrates rarely vocalize in the frequency range covered by the investigated auditory receptors (4–10 kHz), most of the acoustic stimuli that extend into this range are either environmental sounds (such as rustling grass) or insect communication signals (such as grasshopper or cricket calls). In Figure 6C, we show the mean and standard deviations of a random sample of 20 ms-long sections from an ensemble of environmental sounds (green) and an ensemble of grasshopper songs (magenta). The ellipses denote the contours of Gaussian fits to these ensembles. While both ensembles partially match the r-OSEs, there is a clear mismatch with the t-OSEs. Hence, neither ensemble in itself provides the stimulus statistics required to fully employ the information capacity of the receptor neurons.

The choice and design of the two stimulus ensembles is, of course, a somewhat arbitrary division of natural sounds. Rather than focusing on predetermined stimulus ensembles, we can also ask which particular natural stimuli match the statistics of the t-OSEs. For each sample segment of the natural sounds, we can determine how well it matches the parameters of the OSE. We therefore split the natural stimulus snippets into two sub-ensembles, one of which closely matches the statistics of the t-OSEs (Figure 6D, red ensemble) while the other contains all the remaining sound segments (Figure 6D, blue ensemble). In turn, we can take a closer look at the natural sound segments that are covered by the t-OSEs. Since almost all of these sound segments come from grasshopper songs, we show their occurrence in these songs in Figure 6E. Here, stimulus segments that fall into the range of the t-OSEs are colored red; all other stimulus segments are colored blue. In the examples shown, the red sections usually mark the transient onsets of song "syllables" whose behavioral relevance is well established (von Helversen and von Helversen, 1994; Stumpner and von Helversen, 2001; Balakrishnan et al., 2001). Thus, the receptor neurons seem to be optimized for the encoding of strong transients in the natural sounds, but can still provide considerable amounts of information about other stimuli. A detailed comparison of the information rates for the different stimulus ensembles is presented in Figures 6F and 6G for the rate and timing code, respectively.

Discussion

The measurement of information rates of neural systems has a long history (Eckhorn et al., 1976; Rieke et al., 1997; Strong et al., 1998). However, only recently has the dependency of information rates on stimulus ensembles been analyzed (Rieke et al., 1995; Machens et al., 2001; Vinje and Gallant, 2002; Borst, 2003). Here we have set out to investigate the properties of stimuli that fully utilize the information capacity of a specific model system, the auditory periphery of grasshoppers.

Among the natural stimulus ensembles, the ensemble of environmental sounds (green) leads to the smallest information rates, while the red sub-ensemble of grasshopper sound sections leads to the highest information rates, which are similar to those reached by the Gaussian fits to the t-OSEs (black).

These optimal stimulus ensembles can be calculated from the stimulus-response relation. If the recording time does not suffice to measure the full stimulus-response relation, OSEs can be approximated from the system's responses by use of an iterative online algorithm.

The OSE can subsequently be compared to the ensemble of natural stimuli and thereby allows us to identify the aspects of the natural world that the sensory neurons encode best. In general, this comparison will be subject to assumptions made about the neural code, i.e., the context in which a sensory neuron is embedded. Here, this context is given by the read-out mechanism of potential downstream neurons. If we assume that downstream neurons make full use of a neuron's information capacity, then we need to rely on a spike-timing read-out. The higher information rates for the timing code, as opposed to the rate code, are in accord with previous studies on auditory receptors that have shown that the spike timing of grasshopper auditory receptors conveys large amounts of information about the detailed temporal structure of conspecific songs (Machens et al., 2001, 2003).

The spike-timing-based read-out leads to characteristic OSEs with a distribution of mean intensities limited to an intermediate range and comparatively large fluctuations on short time scales. This is in clear contrast to the natural sounds in the grasshoppers' environment, most of which exhibit only small fluctuations on short time scales in the relevant frequency bands. Within the ensemble of natural sounds, the species-specific acoustic communication signals used by the grasshoppers to attract mating partners come much closer to the parameter values of the OSEs. But even within this restricted and behaviorally relevant part of the natural acoustic environment, some features may be of greater importance than others for localizing the source of the sound, for identifying to which particular species the calling grasshopper belongs, and for assessing the individual fitness of the potential mating partner (Machens et al., 2003). This is supported by the finding that those parts of the communication signals that more accurately fit the OSE have characteristic features such as the transitions between "syllables" and "pauses" and short gaps, which have been shown to be of particular importance in behavioral experiments (von Helversen and von Helversen, 1994).

Hence, instead of maximizing the average information gained about natural stimuli, the receptors appear to maximize the information gained about specific, but less often occurring aspects of the stimuli. This result suggests that an organism may seek to distribute its sensory resources according to the behavioral relevance of the natural stimuli, rather than according to purely statistical principles. For instance, if a few important stimuli within the natural environment need to be encoded with high precision, a large part of a system's coding capacity could be designated to encode these stimuli. Consequently, it may well be that even small sub-ensembles strongly influence the coding strategy of sensory neurons. In this case, the optimal stimulus ensemble will not match the ensemble of all natural stimuli encountered by the particular species.

At least some of the recorded receptor neurons are

optimal for even higher standard deviations than those occurring at the particular features of the communication signals. Accordingly, the parameter values of some OSEs exceed the naturally occurring range. Since several animal species are known to prefer supernatural communication signals to those of potential mates (Hauser, 1996), our observation raises the hypothesis that it may be possible to find neural correlates of this preference already at early stages of the system. Whether female grasshoppers prefer male songs with supernatural syllable on- and offsets remains a question for further investigation.

We therefore suggest that the coding strategy of sensory neurons is not matched to the statistics of natural stimuli per se, but rather to a weighted ensemble of natural stimuli, where the different behavioral relevance of stimuli determines their relative weight in the ensemble. Similar neuroethological considerations may hold in other animals as well. For instance, Reinagel and Zador (1999) show that the statistics of randomly sampled visual scenes differ from the statistics of visual scenes actually encountered by the eye—here it is the active sampling of images by saccades that weights stimuli and needs to be taken into account. Our approach presents a systematic way to uncover such potential mismatches between the statistical properties of the natural environment and the coding strategy of sensory neurons. In turn, these discrepancies might improve our understanding of the evolutionary design of the specific sensory system.

This interpretation of the OSEs is subject to several assumptions that will be made explicit and discussed in the following. The efficient coding hypothesis asserts that sensory systems strive to fully utilize their capacity in response to natural sounds. In accordance with the hypothesis, the successive stages of a sensory system could be matched better and better to the statistics of the natural stimuli. For the investigated receptors, the frequency tuning curves are adapted to the frequency content of the communication signals (Meyer and Elsner, 1996); a better match to the amplitude modulations of natural sounds may be achieved at a later stage of the system. Note that we do not claim that receptor neurons have evolved to match the statistics of certain features of the acoustic communication signals. In fact, the qualitative features of the OSEs (high standard deviations) are similar to those found in simple model neurons (Johnson, 1996; Schneidman et al., 2000; Machens, 2002). It is far more likely that the acoustic communication signals and the auditory receptor neurons have coevolved (von Helversen and von Helversen, 1994). Our observation can therefore also be formulated to state that certain features of the grasshopper songs are matched to the coding strategy of the receptor neurons.

A further constraint may arise from considerations of energy consumption (Levy and Baxter, 1996; Schreiber et al., 2002). High firing rates are energetically more expensive, and the true objective for the system might thus be a combination of high information transfer for certain natural stimuli and low overall energy consumption. This problem can be addressed by modifying the maximization objective. For instance, one could include energy constraints in the objective function or seek to

maximize information in bits/spike rather than bits/s. The latter approach faces difficulties, though, since stimulus snippets that produce no spikes at all, for example because they fall below the spiking threshold, would obtain unusually high weights. Most likely, a maximization of the objective bits/spike will therefore lead to rarer and rarer spikes and drive the firing rate down to zero. In the present system, energy consumption due to receptor activity is not expected to be a major constraint, as its effect is likely to be negligible compared to the highly energy-expensive production of the communication signals.

A general issue for information-theoretic investigations is the control of bias from limited sampling (Treves and Panzeri, 1995). In order to save time during the online experiments, we have chosen to work with naive estimates of the entropies that are based on counts of response patterns and can be quickly calculated. In the Supplemental Experimental Procedures, we show that while the actual information values are biased due to small sampling rates, the parameters of the OSE are robust with respect to the amount of available data. In the future, however, it may be possible to include bias-correction techniques (Strong et al., 1998; Paninski, 2003; Hsu et al., 2004) within the online analysis.

Furthermore, the large amounts of required data often limit information-theoretic approaches to single-cell analysis, even more so in an iterative procedure as presented in this study. For the investigated grasshopper auditory receptor neurons, it was shown that the responses of single cells indeed contain enough information to reconstruct naturalistic sound signals (Machens et al., 2001). It remains uncertain, however, whether the OSE for the population of neurons is well described by lumping together the OSEs from single neurons. Future experiments should test this possibility and may thereby also shed light on the population code and putative relevance of spike synchrony (Ronacher and Römer, 1985).

We have shown in this work that, for a specific neural system, OSEs can be obtained from electrophysiological recordings under in vivo conditions. The OSEs provide a testing ground for the efficient coding hypothesis and allow us to assess whether the statistics of natural stimuli are indeed matched to the coding strategy of sensory neurons. This approach thus complements classical investigations, which explicitly tested whether natural stimulus ensembles are encoded better than certain nonnatural ensembles. The concept of the OSE, as introduced in this paper, provides an alternative perspective on neural information processing, which may be pursued to study efficient coding as well as other aspects of neural function.

Experimental Procedures

Electrophysiology and Stimulus Design

Experiments were performed on adult *Locusta migratoria* as explained in detail elsewhere (Gollisch et al., 2002). In short, the animals were waxed to a Peltier element; head, legs, wings, intestines, and the dorsal part of the animal were removed, and the left and right auditory nerves, which are located in the first abdominal segment, were exposed. Each nerve contains the axons from the approximately 80 receptor cells at each ear. Intracellular recordings

from single axons were obtained with standard glass microelectrodes filled with a 1 M KCl solution.

The acoustic stimuli ("snippets") consisted of 80 ms-long samples of white-noise amplitude modulations ($f_c = 250$ Hz) of a sine tone at the characteristic frequency of each cell. Stimuli were presented as 800 ms-long concatenations of ten snippets, each with different mean intensity and standard deviation as explained in the main text. Stimuli were separated by pauses of 250 ms and repeated ten (for the rate-code paradigm) or 25 times (for the timing-code paradigm). Spikes were detected via the custom-made Online Electrophysiology Laboratory (OEL) software and used for online analysis of information rates. After each block of stimulus presentations, all available data were used to update the parameters of the stimulus ensemble. The algorithm employed to optimize the parameters has been described in Machens (2002); its specific application to the receptor neurons is detailed in the Supplemental Experimental Procedures. Briefly, we run the Blahut-Arimoto algorithm (Cover and Thomas, 1991) on the conditional probabilities $p(r|s)$, which are obtained from histogram estimates of the data. The input probabilities $p(s)$ obtained from this algorithm are then used to fit the parameters of the Gaussian stimulus ensemble $G(s)$ via a weighted maximum likelihood fit, $\log L = \sum_s p(s) \log G(s)$. New snippets are then drawn from the updated Gaussian stimulus ensemble, iterating the algorithm.

Data Presentation

In Figures 3A and 4A, stimuli were first projected onto the plane given by the sample mean μ_s and sample standard deviation σ_s . The average rate for each stimulus, $r(\mu_s, \sigma_s)$, was then computed using a kernel estimate where the kernel was given by a Gaussian with unit standard deviation (1 dB) in all directions. The same procedure was used in Figure 3B with respect to the standard deviation of the firing rate.

In Figures 6C and 6D, environmental sounds were taken from commercially available CDs. Grasshopper songs of various species (*Ch. biguttulus*, *Ch. mollis*, *Ch. brunneus*, *Ch. parallelus*) were recorded with a high-precision microphone (40AC, G.R.A.S Sound & Vibration, Vedbaek, Denmark). Sounds were first band-pass filtered (4–10 kHz) to match the frequency-tuning of the receptor neurons. The amplitude modulation was then determined as the root-mean-square power in sliding 2 ms windows.

Supplemental Data

The Supplemental Data for this article can be found online at <http://www.neuron.org/cgi/content/full/47/3/447/DC1/>.

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