On the Asymptotic, Near-Equilibrium Sensory Response

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The asymptotic, near-equilibrium neural response of the sensory periphery can be derived exactly using information theory, asymptotic Bayesian statistics and a theory of complex systems. Almost no biological knowledge is required. The theoretical approach shows good agreement with experimental data across different sensory modalities and animal species. The theory is reminiscent of statistical physics.

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INTRODUCTION

Sensory transduction is the process whereby sensory stimuli are converted to neural responses. The sensory system is the gateway to the brain and transmitting information its most important task. The precise mathematical relationship between information and the peripheral sensory response is a topic of current interest.

This paper attempts to show that the asymptotic, near-equilibrium response of a peripheral sensory neuron can be characterized exactly using a single equation of information with no detailed knowledge of the underlying physiology. The basis of this approach is that the sensory system undergoes a measurement process involving the estimation of a sensory signal. The entropy of this estimate is then attributed to the response of the neuron. This is all that is required to understand the behaviour of a sensory neuron at its most elementary level.

The theory presented here concerns the problem of intensity coding. However, the methodology is general so that it can be applied to other types of biological information acquisition as well. Intensity coding is the process by which neurons encode information about the sensory stimulus strength. Increasing magnitudes of stimuli typically induce higher rates of response (in terms of action potentials per unit time). Also, the response of a neuron to a steady signal drops monotonically over time, a process known as adaptation.

This paper is a continuation of a series of papers detailing an information or entropy approach to sensory processing [1, 2]. From this theory, over 150 years of sensory science can be unified using a Boltzmann or Shannon measure of uncertainty together with a few auxiliary assumptions. This approach was later extended to neurophysiology [3, 4]. Despite the use of entropy, the exact connection to physics has not been thoroughly explored. This is the topic of the current paper where it is demonstrated that the asymptotic, near-equilibrium sensory response can be derived using ideas from information theory, asymptotic Bayesian estimation and complexity theory. Ultimately, the aim of this approach is to explore the generic principles of sensation and its relationship to physics.

DERIVATION OF MAIN EQUATION

Let $\theta$ denote the parameter estimated by the sensory system. In the case of intensity coding, $\theta$ refers to the magnitude of sensory stimulation. The sensory receptor draws repeated, independent samples $X$ from an unknown distribution, i.e. $X_1, X_2, ..., X_m \sim p(x|\theta)$. Given the prior distribution $\pi_0(\theta)$ (representing the uncertainty in $\theta$ before any measurements), after $m$ samples the posterior distribution takes the form

$$
\pi(\theta) = p(\theta|X_1, ..., X_m) \propto p(X_1, ..., X_m|\theta)\pi_0(\theta)
$$

(1)

In the limit of large $m$, and under most conditions observed in nature, the posterior distribution is asymptotically normally distributed with mean parameter equal to the maximum likelihood value $\hat{\theta}$ and variance proportional to $\text{var}(X)/m$,

$$
\pi(\theta) \xrightarrow{d} \mathcal{N} \left( \hat{\theta}, \frac{\text{var}(X)}{m} \right)
$$

(2)

where $\text{var}(X)$ is the variance of the sensory signal. The form of the asymptotic distribution is independent of the choice of the prior. This result is discussed in greater detail below.

Stimulus samples are processed with limited resolution. We assume the error to be normally distributed with zero mean and variance $R$. The entropy is calculated from the mutual information obtained from the posterior and the error distributions. Taking the entropy of the convolution of the two distributions and subtracting the equivocation gives

$$
H = \frac{1}{2} \log \left( 1 + \frac{\text{var}(X)}{mR} \right)
$$

(3)

This is simply the Shannon-Hartley law for an additive white Gaussian noise channel with signal-to-noise ratio equal to $\text{var}(X)/mR$ [5].
Equation (3) was first derived in the context of sensory processing over forty years ago \([1\). The original derivation made use of the central limit theorem to derive the asymptotic form of the distribution of uncertainty in \(\theta\). In this paper, we use instead a Bayesian approach which makes clear the role of the prior distribution. The derivation of the posterior distribution in (2) requires a number of steps. Following (6), the asymptotic form of the posterior distribution for \(m \to \infty\) can be shown to have mean equal to \(\theta\) and variance equal to the reciprocal of the Fisher information of \(\theta\). In the case where \(X\) belongs to the one-parameter exponential family (which includes most of the well-known random variables observed in nature) and \(\theta\) is a natural parameter of the family, there exists an efficient estimator of \(\theta\) which achieves the Cramèr-Rao lower bound \([7\). In this case, the reciprocal Fisher information equals \(\text{var}(X)/m\). For the sensory problem considered here, \(\theta\) is the signal magnitude, and the sample mean obtained from \(X_1, X_2, \ldots, X_m\) is an efficient estimator of \(\theta\). Thus, implicit in this approach is the idea that the sensory receptor averages to estimate intensity.

By itself, (3) has already many of the characteristics required to describe mathematically the process of sensory transduction. Given a constant sensory signal, an increase in the number of samples or measurements results in a monotonic reduction of uncertainty \(H\). Recall that during adaptation the sensory response to a steady input also falls monotonically. This suggests that entropy \(H\) can be related to the sensory response through the equation

\[
F = kH
\]

where \(F\) is the firing rate or spike response of a neuron and \(k\) is a positive constant with units of spikes per second. The fall in neural response during adaptation can be interpreted as a gain in certainty in the sensory signal. When the uncertainty vanishes, there is no response. The association of firing rate with uncertainty also permits the testing of theory with experimental data. For extensive discussion and the origins of this equation see (2).

The postulate in (4) fundamentally changes our view of sensation. At its core, this equation suggests that sensation quantifies measurement uncertainty. When (4) is combined with (3), we see that the peripheral neural response must increase monotonically with signal variability. Is this prediction supported by experimental observation? For example, the phenomenon of brightness enhancement (aka the Brücke-Bartley effect, e.g. \([8\)) shows that the apparent brightness of a flickering light can change depending on the frequency of flicker. The time-average luminance remains constant. However flickering contributes to temporal variations in the signal resulting in the enhancement in apparent brightness. Other experiments involving the stabilization of an image on the retina show that prolonged exposure to a fixed image leads to the fading of the visual percept, e.g. \([9\]). In each case, we observe that the sensory response is coupled to variations in the signal. There have been other theoretical approaches that have similarly postulated that sensation is coupled to variation or changes in the signal, e.g. \([10, 11\). However, neither of the above experiments probes the exact relationship between variance and firing rate. Instead a new experimental test can be proposed to test this assumption directly. Light exhibits very different statistical behaviour depending on whether it is in the classical or quantum limit. Photon bunching is the phenomenon whereby the statistics of the photon count deviates from a Poisson distribution (e.g. \([12\]). If a photoreceptor is stimulated with such a signal, the resulting neural response can be recorded to test the dependency of firing rate on variance with mean held constant.

Yet it is clear that the neural response is related to the mean of the signal. An increase in mean generally results in an increase in neural response. As such, we expect the dependency of \(F\) to be on \(E(X)\) and not \(\text{var}(X)\). How can this discrepancy be resolved? Some recent work has shown that many complex systems exhibit a power-law relationship between mean and variance. The fluctuation scaling law was first discovered in ecology through animal population studies and is known also as Taylor’s law \([13\). A compelling explanation for the fluctuation scaling law was recently proposed \([14\). The family of probability distributions known as the Tweedie distributions exhibits a power law relationship between the mean and the variance. A convergence theorem has been established suggesting a reason for the ubiquity of the power law in complex systems \([15\).

Let us assume for now the applicability of the fluctuation scaling law to sensory signal statistics. Introducing \(\text{var}(X) = \epsilon \mu^\rho\), where \(\epsilon\) and \(\rho\) are positive constants and \(\mu = E(X)\) and defining a new constant \(\beta = \epsilon/R\), we obtain

\[
H = \frac{1}{2} \log \left(1 + \frac{\beta \mu^\rho}{m}\right)
\]

(5)

The response is now a monotonic increasing function of the mean. See \([11\) for the original derivation of this equation.

The signal mean consists of both external and internal sources. The external source is the sensory signal itself and any other external environmental signals. Internal sources may include other signals generated internally including thermal noise, self-generated signals, etc. We model the signal mean as a sum of the two components \(\mu = I + \delta I\) where \(I\) is the total magnitude of external sources and \(\delta I\) the sum of internal sources. \(\delta I\) will be small relative to the external input for almost the entire range of \(I\).
Next we consider the role of time in the sensory response. Sample size increases with the number of measurements taken. Hence \( m \) is a function of time and \( \frac{dm}{dt} \) refers to the sampling rate. It is reasonable to assume that sampling does not occur ad infinitum: when the number of samples attains the optimal value, sampling stops. Sampling is thus a function of the difference between the current sample size \( m \) and the optimal value \( m_{eq} \). That is,

\[
\frac{dm}{dt} = g(m - m_{eq}) \tag{6}
\]

where \( g \) is some function with the condition \( g(0) = 0 \) (sampling stops when \( m = m_{eq} \)). Near equilibrium, we take a Taylor expansion around \( m = m_{eq} \) to obtain

\[
\frac{dm}{dt} \approx g(0) + \dot{g}(0)(m - m_{eq}) = -a(m - m_{eq}) \tag{7}
\]

Since the number of samples \( m \) must be less than \( m_{eq} \) and \( \frac{dm}{dt} \geq 0, a = -\dot{g}(0) \) is a positive time constant. Solutions of \( m \) are used to calculate \( H \) from (5) given a choice of \( m_{eq} \).

One final step is required before the derivation is complete. The determination of an optimal sample size \( (m_{eq}) \) will depend on the precise condition for optimality. In the Appendix, it is shown that if the response variability (i.e. firing rate) is constrained then the optimal sample size must grow as a function of stimulus intensity in the form

\[
m_{eq} = (I + \delta I)^{p/2} \tag{9}
\]

That is, the sample size must grow as a power function of intensity.

Summarizing, we have

\[
F = kH \tag{10}
\]

\[
H = \frac{1}{2} \log \left( 1 + \frac{\beta (I + \delta I)^p}{m} \right) \tag{11}
\]

\[
\frac{dm}{dt} = -a(m - m_{eq}) \tag{12}
\]

\[
m_{eq} = (I + \delta I)^{p/2} \tag{13}
\]

As we shall see, these equations give a good description of the neural response to most time-varying sensory inputs up to physiological saturation levels (e.g. see [3,4]).

DISCUSSION

The derivation above requires the use of a Tweedie distribution with \( \text{var}(X) = \epsilon E(X)^p \). Tweedie distributions belong to the exponential family. They exist for all real values of \( p \) except \( 0 < p < 1 \) [15]. This turns out to have important consequences for the growth of the neural function. Compression is an essential property of sensory neurons since sensory signals can range over several orders of magnitude (e.g. for light intensity the ratio is approximately \( 10^5:1 \)) while the dynamic range of a peripheral neuron is far more limited.

In the asymptotic limit of large sample size where \( m = m_{eq} \), one can easily derive from Eqs. (10-13) the result

\[
F = \frac{k\beta}{2} (I + \delta I)^{p/2} \tag{14}
\]

A compressive response involves a power exponent less than one. Since \( p \) itself is positive, and no such Tweedie model exists for \( 0 < p < 1 \), this implies that the only possible range of exponents lies within \( p \in [1,2) \). Such Tweedie models are known as compound Poisson-gamma models [15]. A compound Poisson-gamma model can be generated via a sum of gamma-distributed random variables, with the number of summed terms itself Poisson distributed.

Fluctuation scaling would thus imply that the interaction between signal and receptive field is well-characterized by a Poisson-gamma model when the response is compressed relative to the range of input. In the olfactory system, for example, odourant molecules bind with receptor sites on the cilia in the epithelial layer [16]. At steady-state, the number of binding events per unit interval of time is likely Poisson distributed. The number of receptor sites activated is a cluster and cluster sizes are often modelled by gamma distributions. It would appear that the Poisson-gamma model provides not only a reasonable model for olfaction, but for other modalities as well. For sensory modalities where the range of stimuli is more limited (e.g. mechanoreception or stretch sensing), the neural response may not necessarily be compressive. When \( p > 2 \), this would imply that \( X \) has a distribution belonging to the family of positive stable distributions [19].

PREDICTIVE SCOPE OF THEORY

Time-independent inputs

The equations governing sensory entropy can be solved for different inputs or experimental configurations. We will consider a number of examples involving piece-wise constant inputs. First consider the solution for a step input illustrated in Figure 1. We divide the solution into three distinctive regions: Region I \( (t < 0) \) where the stimulus is off, II \( (0 \leq t < t_0) \) where stimulus is turned on, and III \( (t \geq t_0) \) where the stimulus is turned off.

Next the relevant response is solved assuming that the neuron is equilibrated (i.e. fully adapted) prior to \( t < 0 \). In this case the sample size \( m(t) \) can be solved from (12)
and to give
\begin{align}
m_1 &= m_{eq1} \\
m_{II} &= m_{II}(0)e^{-at} + m_{eq2}(1 - e^{-at}) \\
m_{III} &= m_{III}(t_0)e^{-a(t-t_0)} + m_{eq3}
\end{align}
(15)
where \(m_{eq1} = m_{eq3} = \delta I^{p/2}\) and \(m_{eq2} = (I + \delta I)^{p/2}\). Continuity ensures that \(m_{II}(0) = m_{I}(0)\) and \(m_{III}(t_0) = m_{II}(t_0)\). Substituting \(m\) and \(I\) into (10)-(11) gives the response of the neuron \(F\) in all three regions. Other inputs (e.g. a double-step input in Figure 1b) can be solved similarly.

The challenge in evaluating (10)-(13) is to find an experimental situation which allows for the robust determination of five unknown parameters. Unlike fundamental physics, these parameter values are not predetermined and are specific to receptor type, as well as to individual units. To avoid overfitting, we make use of the idea that multiple experiments conducted on the same unit should obey the same set of parameters. This is a stringent test of the theory as it greatly reduces the number of degrees of freedom allowed to the equations.

Next we compare theory with experimental data.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{schematic_inputs.png}
\caption{A schematic illustration of sensory inputs commonly used to probe the response of sensory fibres. In all figures, the ordinate shows firing rate and the abscissa time. (a) A step input is used to measure adaptation. (b) Double-step function. (c) A ramp-and-hold stimulus. (d) Sinusoidally modulated intensity superimposed on a constant background.}
\end{figure}

\textbf{Auditory adaptation and driven activity}

Figure 2 shows data from two sources: an adaptation experiment (constant \(I\), duration \(t\) is varied) and an intensity-rate experiment (constant \(t\), \(I\) is varied) [17]. Data was recorded from the same auditory fibre of an anesthetized Mongolian gerbil. In the adaptation experiment, the number of spikes counted in a 960 \(\mu\)s interval was converted to a firing rate and observed as a function of time. An averaged firing rate was obtained over 91 trials. Figure 2a (jagged line) shows the response to a 39 dB SPL tone presented at the characteristic frequency of the fibre (2.44 kHz). In the intensity-rate experiment, the maximal firing rate during a one millisecond interval was recorded as a function of different sound intensities. Figure 2b shows the intensity-rate response curve (open circles). After 40 dB, the response saturates and is not shown in Figure 2b.

The expression for \(F\) used to fit the data was derived from the sample size in Region II, i.e. (16), and is given by
\[
F = \frac{1}{2} k \log \left[ 1 + \frac{\beta (I + \delta I)^p}{\delta I^{p/2} e^{-at} + (I + \delta I)^{p/2} (1 - e^{-at})} \right]
\]
(18)
Since both experiments were conducted on the same auditory fibre, a common set of five parameters was used \((k = 4.1 \times 10^2, \beta = 3.8 \times 10^{-2}, p = 1.3, \delta I = 3.4 \times 10^{-4}, a = 5.1 \times 10\text{Hz})\). Stimulus intensity in dB was calculated from rms pressure relative to 20 \(\mu\)Pa. An additional parameter was required for the rate-intensity experiment \((t' = 1 \times 10^{-1} \text{ ms})\) representing the average recording duration. Thus a total of six parameters was used for two separate experiments. Figure 2 shows good compatibility between theory and data.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{firing_rate_response.png}
\caption{Firing rate response recorded from the auditory fibre of a Mongolian gerbil [17]. Data in both figures recorded from the same fibre. Smooth curves show the predictions of using a common set of parameters for both figures. (a) Firing rate measured as a function of sound duration for a 39 dB tone (jagged line). (b) Peak firing rate measured as a function of sound intensity in decibels (open circles).}
\end{figure}

\textbf{Auditory double-step input}

In [18], the firing rate was measured to a series of double-step inputs from the auditory nerve of guinea pigs. A schematic illustration of the input is shown in Figure 1b. The initial response was elicited with a sound of intensity -4, 2, 8, 14, or 20 dB SPL followed by a 6 dB increase in the second pedestal (see Figure 3 open circles). The solid line in Figure 2 shows the predictions with 5 adjustable parameters \((k = 3.1 \times 10^2, \beta = 5.7 \times 10^{-2}, p = 1.4, \delta I = 5.2 \times 10^{-4}, a = 8.8 \times 10^{-1})\).
Hz). The match is not perfect although the theoretical curves capture largely the behaviour observed physiologically (filled circles).

![Graphs showing auditory neural responses](image1)

**FIG. 3.** Auditory neural responses measured from a double-step input in the guinea pig ear [18]. Initial pedestal with intensity −4, 2, 8, 14 or 20 dB, followed by a second pedestal 6 dB higher. Firing rates indicated by open circles. Smooth curves show the predictions of the neural entropy equation solved for a double-step input using a common set of parameters for all five graphs.

### Peak versus steady-state response

In the same study, peak responses of the adaptation curve were compared to steady-state responses over a range of intensities. These results can be used to test a key component of the theory: that the optimal sample size grows with intensity following [9]. In an attempt to reduce the number of parameters in [18], we approximate the equation by taking the large intensity limit. This is achieved by ignoring the ‘1+’ term in [18] and taking internal noise to be small (i.e. $I \gg \delta I$) to obtain

$$F = \frac{1}{2} k \log \left[ \frac{\beta I^p}{\delta I^p/2 e^{-at} + I^p/2 (1 - e^{-at})} \right]$$

(19)

The peak response is calculated by setting $t = 0$ and the steady-state response with $t \to \infty$:

$$F_{\text{peak}} = \frac{1}{2} k \log (\beta I^p) - \frac{1}{2} k (\delta I^p/2)$$

(20)

$$F_{\text{steady-state}} = \frac{1}{2} k \log (\beta I^p/2)$$

(21)

Plotting these values against the logarithm of intensity (or decibel) will yield two lines with slope differing by a factor of two. Figure 3 shows the predictions together with the experimental results from [17].

![Graph showing peak and steady-state response](image2)

**FIG. 4.** Responses recorded from the guinea pig ear showing peak activity (open circles) and steady-state activity (crosses) from an adaptation curve [18]. Solid lines show the predictions of the theory. The two lines are expected to differ by a factor of two in slope.

### Multiple olfactory adaptation

The adaptation response in the sugar receptors of blowflies was measured for three different concentrations (0.01, 0.1 and 1 M) [19]. The experiment was conducted in the region where the adaptation was not fully complete. The concentrations are sufficiently high such that $\delta I$ can be ignored. As such, we used a simpler version of [18] by taking $\delta I = 0$ and evaluating the first order Taylor series expansion for $t \ll 1/a$ in the denominator to obtain

$$F = \frac{1}{2} k \log \left[ 1 + \frac{\beta' I^p/2}{t} \right]$$

(22)

where $\beta' = \beta/a$.

This equation holds special significance as it is the original form of the equation governing sensory response. First published in 1977, it was the first attempt to use entropy to connect together various empirical sensory laws and appeared in a number of publications (e.g. [1][2]). The simultaneous fit shown in Figure 5 was first published in 1991 [20]. In total, 3 curves were fitted using 3 unknown parameters ($k = 1.1 \times 10^2$, $\beta' = 1.5 \times 10^3$ and $p = 1.3$).

### Time-varying inputs

Hitherto, we have considered responses to inputs that are piece-wise constant. In general, analytical solutions for time-varying inputs are not possible due to the presence of the exponent in [9]. However, numerical solutions can be easily obtained by either solving the differential equation in [12] with Euler’s method or through numerical integration.
Muscle ramp-and-hold

In this example, the response of a cat muscle fibre was recorded to a ramp input [21]. The fibre was elongated linearly and then held fixed at its final length. A schematic representation of the input is shown in Figure 1c. The stimulus in this case is a time-varying function. The solution for the sample size was obtained by solving (12) numerically. In an attempt to reduce the number of parameters, the small intensity limit of (11) was adopted by taking the approximation \( \log(1+x) \approx x \). \( k \) and \( \beta \) combine to become a single parameter. In total, 4 parameters were used for 3 experimental regions \((k\beta = 0.23, \delta I = 3.0 \times 10^{-4}, p = 4.3 \) and \( a = 1.2 \text{ Hz} \)).

Sinusoidal variation and adaptation response in mechanoreception

Recordings taken from the slit sense organ of a hunting spider [22]. Two different adaptation responses were recorded together with the response to a sinusoidal input from the same type of mechanoreceptor unit. (Both were recorded from slit 2 of the lyriform organ of the leg tibia although there is no indication of whether the recordings were made from the same receptor unit or not.) The mechanoreceptor responded only to the positive half of the sinusoidal input, which is typical for mechanoreception. Adaptation responses were calculated using (18) with input intensity 0.0975° and 0.395°, while the sinusoidal input was evaluated through a numerical solution of (12) with a 0.38 Hz sinusoidal input with peak value 0.25°. Five parameters were used for three different experiments \((k = 34 \text{ Hz}, \beta = 0.40, \delta I = 6.7 \times 10^{-3}, p = 4.9 \) and \( a = 1.3 \times 10^{-3} \text{ Hz} \)).

Square pulse versus sinusoidal responses in muscle spindle

The response of spindle afferents to repeated square pulse stimulation was compared to the response from sinusoidal stimulation in the soleus muscle of cats. The amplitude of the square pulses was matched to the amplitude of the sinusoidal stimulation (following the usual mathematical definition of sinusoidal amplitude). The firing rate responses together with the theoretical predictions are shown in Figure 4 \((k = 20 \text{ Hz}, \beta = 1.1, \delta I = 15, p = 1.5 \) and \( a = 1.0 \text{ Hz} \)).

The square pulse response in particular illustrates the mechanism by which the theory works. Equation (11) shows that firing rate is essentially a monotonic function of the ratio of intensity and sample size. Intensity changes abruptly but sample size always remain continu-
ous. When the stimulus is turned on, this ratio becomes large but falls as sample size grows to match the input \((m \text{ approaches } m_{eq})\). At the termination of the input, the ratio falls to near zero before returning to steady-state values as sample size decreases to match the input. Such behavior is typical of adaptation/de-adaptation responses and we observe it mathematically in the equations.

\[
\frac{\sigma}{m} = \frac{1}{\pi} \log C_1^2 \left(\frac{\omega}{a}\right) \sin(\omega t + \phi) Y
\]

where

\[
C_1(\omega) = \sqrt{\frac{1/4 + \omega^2/a^2}{1 + \omega^2/a^2}}
\]

\[
C_2(I) = \frac{p}{2} \left(1 + \frac{\beta (I + \delta I)^{p/2}}{\phi}ight)
\]

\[
\phi = \arctan \left(\frac{\omega/a}{1 + 2\omega^2/a^2}\right)
\]

Thus the steady-state response is itself sinusoidal.

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**Figure 8.** The response of a cat muscle spindle to repeated stimulation. (a) Response to sinusoidal stimulation compared to (b) response to square pulse stimulation. The amplitude for both inputs are identical. Five parameters were used to predict both experiments from a numerical solution of \([10-13]\).

**Response amplitude as a function of modulation frequency in retinal ganglion cells**

When light intensity is varied sinusoidally, the resulting neural response will be periodic. Figure 8 shows an example of a sinusoidally modulated input. The modulation index or modulation depth is defined as \((I_{\text{max}} - I_{\text{min}})/(I_{\text{max}} + I_{\text{min}})\). When the index is small, the neural entropy equation can be solved analytically for an input of the form \(I + \Delta I \sin(\omega t)\). The solution will have both a transient and a steady-state component. We are interested in the steady-state component.

We begin by defining \(Y = \Delta I / (I + \delta I)\). \(Y\) is equal to the modulation index when \(\delta I = 0\). In the limit of small \(Y\), a linear expansion gives

\[
F_{SS} = \frac{1}{2} k \log \left(1 + \beta (I + \delta I)^{p/2}\right)
+ kC_1(\omega)C_2(I) \sin(\omega t + \phi) Y
\]  

\(2kYC_1(\omega)C_2(I) \exp (-\omega^2 \sigma_{jitter}^2/2)\)  

Finally, the width of the time jitter can be shown to be related to the time constant of adaptation in the manner of \(\sigma_{jitter} = 1/2a\) similar to the time-frequency bandwidth tradeoff \([25]\). Thus, response amplitude becomes

\[
2kYC_1(\omega)C_2(I) \exp (-\omega^2/8a^2)
\]  

In the large intensity limit, this is an equation of four adjustable parameters which can be compared with experimental data. Figure 9 shows the response amplitude of a cat ganglion cell measured to a signal with modulation index 0.5 \([17]\). This violates the condition under which \([23]\) was derived. Nevertheless, we will attempt a comparison of theory with data. Out of the four adjustable parameters, one parameter can be constrained using the mean firing rate (which was provided as 49 Hz). The values of the three remaining parameters were obtained \((k = 27, p = 1.5\) and \(a = 32)\) and \([28]\) is plotted along side the data in Figure 9. Despite having only three adjustable parameters, the entire characteristic shape of the response curve is reproduced, including the inflection observed at low frequencies.

**FINAL REMARKS**

The theory developed in this paper has a particular mathematical simplicity because we have restricted the analysis to the asymptotic, near-equilibrium limit. The situation is more difficult if we considered the non-equilibrium case (small \(m\), far from \(m_{eq}\)). In such situations, the response may depend strongly on the initial prior distribution \(p_0(\theta)\) from \([1]\) or on the precise mathematical form of the sampling rate function \(dm/dt\) in \([6]\). Despite this, we have shown that the equations hold enormous predictive power across all time scales, for almost all sensory modalities and different animal species.
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Appendix: The optimal sample size

The determination of the optimal sample size depends on the condition of optimality. Since the fluctuation scaling law posits that the variance of a signal increases with the magnitude of the signal, one approach is to have sample size grow to keep the standard error in the mean constant. Following this argument, one can see that the optimal size must grow as a function of signal intensity in the manner

$$m_{eq} \propto (I + \delta I)^p$$  (31)

An entirely different answer can be obtained if we instead consider response variability as the criterion of optimality. When the sample size $m$ is finite, it is more proper to think of $H$ in [3] a function of the sample variance $s^2$. Thus in the limit of large $m$,

$$H = \frac{1}{2} \frac{s^2}{mR}$$  (32)

where $\text{var}(X)$ is replaced by the sample variance $s^2$. Moreover, if the distribution for $X$ has kurtosis $\kappa$, the sample variance can be shown to have mean and variance equal to

$$E(s^2) = \text{var}(X)$$  (33)
$$\text{var}(s^2) = \frac{\text{var}(X)^2}{m} \left( \kappa - 1 + \frac{2}{m - 1} \right)$$  (34)

in the asymptotic limit [26]. Using $F = kH$, we have for large $m$,

$$E(F) = \frac{k}{2mR} \text{var}(X)$$  (35)
$$\text{var}(F) = \frac{k^2 (\kappa - 1)}{4m^3 R^2} \text{var}(X)^2$$  (36)

In statistics, the dispersion index is a normalized measure of variation defined as the ratio between the variance and the mean, i.e. a noise-to-signal ratio. The dispersion ratio for neural response can be calculated from the mean and variance of the firing rate. Setting the dispersion ratio constant with respect to intensity would allow for the decoding of intensity by the nervous system to be independent of the magnitude of the signal. The dispersion ratio is similar to the Fano factor which has been observed to be constant for various modalities (e.g. [27] [28]).

Using $\text{var}(X) = c\mu^p$, the dispersion ratio can be expressed as

$$\frac{\text{var}(F)}{E(F)} = \frac{k (\kappa - 1) \text{var}(X)}{2R \frac{m^2}{m^2}}$$  (37)
$$\propto \frac{(I + \delta I)^p}{m^2}$$  (38)

At equilibrium ($m = m_{eq}$), we impose the condition that this ratio is constant with respect to changes in signal intensity. Therefore,

$$m_{eq} = c(I + \delta I)^{p/2}$$  (39)

where $c$ is a constant. The optimal sample size must grow as a function of intensity for the dispersion index.
to remain constant. For simplicity, we set \( c = 1 \) as it can be incorporated into \( \beta \) in [3]. Equation (39) is the expression for optimal sample size used in the theory.

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