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Point-process modeling of excitatory/inhibitory interactions in LSO neurons

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Point-process modeling of excitatory/inhibitory interactions in LSO neurons

by

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ABSTRACT

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The thesis of this work is that the representation of sensory information in the discharges of single neurons can be characterized by point process models. The work focuses on the encoding of binaural information in the discharges of neurons in the cat lateral superior olivary (LSO). LSO neurons are postulated to be involved in encoding interaural level difference (ILD) and interaural time-of-arrival difference (ITD)—binaural cues for localizing and detecting high frequency signals. These cues are extracted from the binaural inputs by the interaction of the excitatory input (from the ipsilateral ear) with the inhibitory input (from the contralateral ear) and encoded in the discharges of LSO neurons.

I have developed a unifying point process model that describes the temporal and statistical characteristics of the discharges of all three LSO unit types. The model is based on an intrinsic recovery function that is independent of the stimulus conditions and the timing of previous discharges. The effects of the stimulus conditions and the duration of the previous interval are described by operators (e.g. scaling and shifting) that are applied to the intrinsic recovery function. The resulting model successfully predicts the complex effects of the stimulus conditions on the statistical and temporal characteristics of LSO neuron discharges.

Excitatory and inhibitory effects are clearly distinguished and it is concluded that the sustained discharges of LSO neurons convey information about both the average sound level and the ILD. The ILD affects also the relative latency of the excitatory and inhibitory inputs and modulates the tightly distributed timing of the initial discharges to a monaural stimulus. Thus, the model quantifies the representation of
ILD in the timing of LSO neurons; pressing the question of the utilization of information represented in the detailed timing of neural activity as opposed to the general consensus that only the discharge rate is relevant for neural information processing.

Specific implications about the properties of LSO cells membranes are made based on the correlation between the operators used in the model and the effects they describe and can direct the construction of a compartmental model of LSO single-neuron.
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To Aliza and Mordechai Zackenhouse,

Eldad Zackenhouse,

and Sigal

with love
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Chapter 1

Introduction

1.1 The role of the LSO in binaural processing

The auditory system provides a frequency representation of sound irrespective of the spatial location of the sound source: A single pure tone excites the same auditory nerve fibers regardless of its location [36]. Thus, sound location is not mapped directly into a receptor site. The auditory system differs in this sense from the visual system, for example, where the retina maps the direction of the light source as well as its frequency content (color)—only the depth of the light source has to be inferred indirectly. The lack of spatial segmentation in the initial encoding of the auditory stimuli complicates also the task of segmenting the auditory image into different sources, as for example in discriminating signals from noise [81]. Both of these tasks, sound localization and auditory image segmentation, are greatly enhanced by binaural hearing as compared with monaural hearing [28].

There are three basic binaural cues that are relevant for localizing pure tones: The Interaural Time-of-arrival Difference (ITD), the Interaural Phase Difference (IPD), and the Interaural Level Difference (ILD) [36, 74]. The ITD is a reliable cue for localizing both low and high frequency sounds. The IPD is a reliable cue only at low frequencies when the wavelength is greater than head size. In contrast, the ILD is a reliable cue only at high frequencies (wavelength less than head size) where the head shadowing effect and the pinnae directivity produce significant level differences at the two ears. The effect of ILD is frequency dependent and consequently, complex sounds
produce interaural spectral differences. The ILD and ITD cues combine to produce interaural envelope differences in modulated sounds.

The first centers to receive binaural projections are the Lateral Superior Olive (LSO) and the Medial Superior Olive (MSO) [10] (projections to the LSO are shown schematically in Figure 1.1). The ipsilateral projections to the LSO are believed to arise from the spherical/bushy cells in the anteroventral cochlear nucleus (AVCN) and to end on the distal dendrites of LSO principal cells [11, 24]. The AVCN spherical/bushy cells produce primary-like (similar to auditory nerve fiber response) tone burst discharge patterns almost exclusively [8] and receive few, one to two, auditory nerve inputs. LSO input from the contralateral ear arises from the principal/globular cells of the medial nucleus of the trapezoid body (MNTB) that receives contralateral input from the AVCN globular/bushy cells. The projections from the AVCN globular cells terminate as the calyces of Held on the cell body of MNTB principal neurons. The calyces are giant axosomatic terminals that envelope the cell body and contain numerous areas of synaptic contact [10, 71]. Both the globular/bushy and the spherical/bushy cells in the AVCN are considered to “relay” information from the auditory nerve to the MNTB and the LSO, respectively. The projections from the MNTB principal cells end on the perisomatic and proximal dendrites of LSO principal cells with terminals that are believed to contain inhibitory synapses [9]. The MNTB principal cells produce tone burst responses that are primary-like or pri-notch type (primary-like, but with a short 1-2 ms, period of spike suppression following the first spike) [29]. In contrast with LSO principal cells, which do not produce spontaneous activity, MNTB principal cells may discharge spontaneously in the absence of an experimenter-controlled stimulus. Each LSO projects bilaterally to the Inferior Colliculus nuclei, which receive projections from almost all the major divisions of the brainstem auditory system, including the lateral lamniscus, the superior olivary complex (the LSO and MSO), and the cochlear nucleus (dorsal, posterior ventral, and anterior ventral subdivisions).
**Figure 1.1** Diagram of the LSO network
Diagram of the connections from the cochlear to the LSO. Nerve fibers from the cochlear form the major excitatory input to both spherical (S) and globular (G) bushy cells. The spherical cells provide excitatory inputs to the ipsilateral lateral superior olivary nucleus (LSO). The globular cells provide excitatory inputs to the contralateral medial nucleus of the trapezoid body (MNTB). The MNTB projects ipsilaterally to the LSO where the effect is inhibitory. Presumably excitatory inputs are indicated by open terminal symbols, the larger of these representing calyces of Held; presumably inhibitory inputs are indicated by filled terminal symbols [10].
While both the LSO and the MSO receive input from both the ipsilateral and contralateral ears, they differ in their frequency sensitivity: Most LSO neurons are sensitive to mid-to-high frequency sounds while MSO neurons are sensitive to low frequency sounds. Thus, the LSO is the first nucleus in the ascending auditory pathway involved in the binaural processing of mid-to-high frequency (> 1kHz) sounds. LSO units having characteristic frequencies (CFs) greater than 1 kHz are excited by stimulation of the ipsilateral ear and inhibited by simultaneous stimulation of the contralateral ear (E/I neurons) [6, 26, 29]. As the first stage in high-frequency binaural processing, the LSO is believed to play a crucial role in extracting binaural cues relevant for localization and discrimination of high frequency sounds. These cues include the interaural level difference and the interaural time difference between high-frequency transients and between the envelopes of complex high-frequency stimuli.

The potential role of LSO neurons in encoding ILD is suggested by the sensitivity of their discharge rate to ILD [72]. The sustained mean discharge rate increases with the ratio of the sound pressure levels at the two ears (or, equivalently, with the difference between the sound levels expressed in dB). The potential role of LSO units in extracting temporal cues is suggested by their highly structured initial chopping discharge patterns in response to tone burst stimuli [7, 56, 68, 69]. The initial discharges in the response are time locked to stimulus onset and produce peaks in the post-stimulus-onset time histograms (PST histograms defined in Section 1.4) that become wider and eventually obscured with time (Figure 1.2, left column). The high instantaneous discharge rate, marked by the peaks in the PST histograms in Figure 1.2, reflect the high level of synchronization during the initial phase of the responses to different representations of the same stimulus.

The width and spacing of initial peaks in the PST histograms are used to differentiate between two LSO unit types [68]: Slow choppers produce PST histograms with relatively broad and widely spaced peaks (Figure 1.2, upper row), and fast choppers
produce PST histograms with multiple narrow and closely spaced peaks (Figure 1.2, middle row). The discharge rates of the sustained response that follow the initial chopping response are correlated with the unit classes: Slow-choppers respond at low sustained discharge rates (< 300 spikes/sec) and fast-choppers respond at higher rates. While most of the slow and fast chopping units produce unimodal histograms of interspike intervals, some LSO units produce bimodal interval histograms and are therefore classified separately as bimodal units (Figure 1.2, middle column, lower row vs. upper two rows).

1.2 Characterizing binaural processing

A comprehensive understanding of how the LSO processes its binaural inputs to enhance sound localization and segmentation should address the following issues:

- Functional: What information should an optimal processor extract from the binaural stimulus to estimate sound location?

- Neural Network:
  - How can the output from the LSO be best processed by higher centers?
  - How is the auditory space represented in the spatial and temporal distribution of neural activity in the LSO?

- Information processing: How are binaural cues extracted from and encoded in spike trains?

- Neurophysiology: What are the characteristics of the cell-membrane implementing the necessary excitatory/inhibitory interaction?

Within this framework, the study of spike trains is directly related to the issue of information processing by a single LSO cell. Analyzing and modeling spike trains produced by LSO neurons are expected to reveal how the relevant binaural cues are
Figure 1.2 Characteristics of LSO tone burst responses
The characteristics of the response to ipsilaterally presented stimulus at the characteristic frequency of the neuron +25 to +35 dB above unit threshold determine the unit type. PST histograms (left column), interval histograms (middle column, bold), recovery functions (middle column), and conditional mean functions (right column) of a slow chopper (upper row), fast chopper (middle row) and a bimodal unit (lower row). All PST histogram binwidth are 250 $\mu$s. Histograms binwidths are (from top to bottom) 100, 50, and 100 $\mu$s.
encoded in the statistical or temporal structures of the discharges. Such an understanding, in turn, is crucial for investigating the other aspects of the LSO binaural processing network. In particular:

- The encoding scheme implemented by the LSO neurons can be compared to the information that an optimal processor is expected to extract from its binaural inputs. Such a comparison can be used to validate or contradict the assumed role of the LSO or the assumed characteristics of the inputs to the processor.

- The information encoded in the spike trains produced by the LSO determines how LSO outputs have to be augmented to perform sound localization and segmentation at higher centers.

- Based on the information represented in the discharges of a single LSO neuron, a population model can be developed to describe the representation of the auditory space in the temporal and spectral distribution of neural activity in the LSO.

- The analysis of spike trains can also shed light on the mechanisms of spike generation in LSO neurons [50].

Furthermore, the nature of the interaction of the excitatory and inhibitory processes within the LSO is of general interest as it provides insight to a basic component of neural function. Having both excitatory and inhibitory inputs, a LSO neuron may discharge at the same mean rate in response to different combinations of ipsilateral (excitatory) and contralateral (inhibitory) stimulus levels. However, while the discharge rate may be the same, the discharge patterns do depend on the specific input conditions [69, 70]. Thus, these findings question the assumption, underlying previous models of binaural interaction in the LSO, that the inhibitory effect on the membrane potential is symmetrically opposite to the excitatory effect [12, 25]. Chronologically, this research work originated from the challenge to construct a model of LSO unit discharges that differentiates between the effects of increasing inhibitory stimulus level and reducing excitatory stimulus level on LSO neurons discharge patterns.
1.3 Neuronal modeling

Single-neuron models have been developed to investigate different aspects of the behavior of neurons. Point process modeling is put into the general context of neuronal modeling by describing four classes of single-neuron models which differ in the aspect of neuron behavior under investigation.

1. Nerve membrane models.

These models are developed to investigate the biophysical mechanisms underlying spike initiation and describe the electrical properties of active membranes in terms of the characteristics of the ionic channels [19, 33, 67, 80]. Most of these models represent a patch of the membrane by an equivalent electrical circuit with a separate parallel branch for each ionic channel. The electrical properties of each ionic channel are derived from voltage-clamp data. Models of spike initiation have been extended to describe synaptic activation [18, 65], the flow of current in continuous dendritic trees [58], and propagation of action potentials [27]. The power of each model is evaluated by its ability to simulate the time course of the action potential and the modes of spiking activity exhibited by the modeled neuron.

2. Low-order Dynamic models.

These models are developed to investigate the dynamic properties of the behavior of single neurons such as generation of single or burst of spikes and oscillations [35, 46, 1]. The neuron behavior is described by a set of nonlinear differential equations which are motivated by the nerve membrane models described above but are limited to two or three variables to capture the essence of the system dynamics [21]. Phase-plane analysis techniques are used to describe the dynamic behavior of the system and the qualitative structure of the model.

3. Stochastic phenomenological models.

These models are developed to investigate the random nature of the firing pat-
terns, the representation of relevant information (usually stimulus conditions) in the spike trains, and the decoding of the relevant information by "higher center". The random nature of the spike trains is characterized by point process models as described in more details in Section 1.3.1.

4. Stochastic mechanistic models.

These models are developed to test hypothesis about the underlying mechanisms of spike initiation that give rise to the repetitive activity of neurons. In simple cases the output spike train can be described as resulting from an interaction between the different input spike trains [13, 66]. In the general case, a simplified model of spike initiation (usually fire-at-threshold) and cell membrane potential is constructed to relate the random nature of the input spike train and ionic channels dynamics to the random nature of the output spike train [23]. The underlying model of spike initiation and cell membrane potential is motivated by nerve membrane models; The degree of simplification varies from Markov random processes [49] to equivalent electrical circuit [61] and compartmental (segmental) models [2]. The power of each model is evaluated by its ability to match an array of measures of interspike-interval statistics.

1.3.1 Point process modeling

It is generally assumed that only the timing of the neural discharges conveys information while the shape of the action potential during a spike is irrelevant. Hence, from the information processing point of view, a spike train can be represented by the times of occurrence of the spikes, or equivalently by a sequence of Inter-Spike Intervals (ISIs). Realizing that a process that generates sequences of points (e.g. event times) can be modeled as a point process, it is possible to characterize neuronal discharges directly without modeling the underlying spike initiation mechanism. Notwithstanding, notions about spike initiation can motivate the structure of the point process model.
In particular, the point process model can be formulated to differentiate between the effects of the stimulus conditions and the effects of the recovery properties of the spike generation process. Furthermore, the construction of a point process model can shed light on the mechanisms of spike initiation that are dominate in the neuron under study. Point processes have been applied extensively to model and study neural discharges at different levels of complexity [34, 55, 64]:

- Simple Poisson processes where the probability of an event is independent of the history.
- Renewal point processes where the probability of an event depends on the time elapsed since the last event.
- Self-exciting point processes where the sequence of interevent intervals exhibits serial dependence [41, 47, 82].
- Non stationary point processes where the probability of an event vary with time [40, 60, 84]
- Fractal point processes that exhibit long term dependence [44].
- Irregular point processes where there is a probability mass for an event to occur after a specific interevent interval [48].

The point process approach enables one to characterize the spike trains independent of the physiological model. Thus, the characteristics of the intensity function underlying the point process model can be used to simulate spike trains and study their information content and processing at the appropriate abstract level. Furthermore, the effects of stimulus and history on the characteristics of the intensity function can provide insight on the mechanisms of spike generation. In contrast, threshold crossing models of spike generation [12, 25] or compartmental models [61, 80] are limited by the assumptions made about the mechanism of spike generation and are usually built to demonstrate some hypothesized physiological mechanisms.
Point process modeling has been applied successfully to describe LSO neuron discharges to ipsilateral stimulation [41]. The analysis presented there indicates that LSO discharges exhibit negative serial dependence (as is evident by the negatively sloped conditional mean functions, Figure 1.2). To describe this serial dependency, the general approach of self-exciting point processes, with history-dependent intensity functions, was applied. The modeling work initiated by that effort was successful in describing the statistics of the monaurally elicited sustained discharges of slow choppers and slowly driven fast choppers. However, the statistics of the monaurally elicited sustained discharges of bimodal neurons and of fast choppers driven to high rates were not modeled adequately.

The effects of simultaneous stimulation of the contralateral ear and the effects of varying the ipsilateral or contralateral stimulus levels on the statistics of the discharges also were not characterized. Simultaneous stimulation of the contralateral ear results in seemingly complex effects on the statistics of the spike trains that are not consistent across different units. Analyses of binaurally elicited discharges (described in Chapter 4) revealed that there is another process—besides the shifting process—associated with the serial dependence exhibited by LSO unit discharges. It was in this context that the suppress-and-rebound process, presented in Chapter 2, was formulated. Furthermore, analysis and modeling of the initial transient response of LSO neurons, which is expected to be crucial in encoding interaural time-of-arrival differences, had not been attempted previously. Thus, prior point processes modeling has fallen short of describing the characteristics of LSO neuron discharges that are relevant for encoding binaural cues of mid-to-high frequency sounds.

In this work, a comprehensive point process model for the sustained and transient response of LSO neurons to tone-bursts is developed and described. In particular:

- The model of serial dependence developed elsewhere [41] is extended to describe the sustained discharges of bimodal neurons and of fast choppers driven to high rates (Chapter 2).
- The effects of changing the ipsilateral stimulus level on the statistical characteristics of the monaural response are quantified and modeled (Chapter 3).

- The effects of simultaneous stimulation of the contralateral ear on the statistics of the monaurally elicited sustained response are quantified and modeled (Chapter 4).

- The transient chopping response of LSO neurons to both monaural and binaural stimuli is analyzed and modeled (Chapters 3 and 4).

1.4 Data collection and analysis methods

The analysis presented in this work was applied to spike trains recorded by Prof. C. Tsuchitani of The University of Texas Health Science Center at Houston. Extracellular recording from single-units in the LSOs of adult cats anesthetized with sodium pentobarbital were made with gold-plated stainless steel microelectrodes with platinum-backed tips [69]. The location of each of the sixteen LSO units used in this study was verified histologically using electrolyte deposits of the recording electrode. The relevant aspects of the recording procedures (detailed elsewhere [69, 73]) are briefly summarized here: Ipsilateral tuning curves (one-spike-discharge threshold level to 40-ms-duration tone burst as a function of stimulus frequency) were measured for each unit. The frequency to which the unit was most sensitive defined its excitatory characteristics frequency or CF. The contralateral stimulus level that inhibited a one-spike discharge to the CF tone burst defined the contralateral threshold level. Tone bursts, set to the excitatory CF, were presented monaurally to the ear ipsilateral to the recording site, or binaurally to both ears with no interaural onset time delays. In all the examples, the stimulus level is expressed relative to the corresponding (ipsilateral or contralateral) threshold to the CF tone. The tone bursts were 100-400 ms in duration, with 1- to 10 ms rise-fall times and presented at repetition rates of 1 per sec.
to 1 per 6 sec. The voltage recording was band-passed filtered to enhance spike detection and to avoid false triggering. The time at which the voltage crossed a preset threshold level was recorded in digital format (clock quantization of 1 μs) along with the time of the stimulus codes.

Analyses and simulation results are demonstrated in this work for six units, two units from each of the three unit types. These units are referred to as slow chopper-A (unit 128-1A, CF 10.0 kHz), slow chopper-B (unit 157-1F, CF 11.0 kHz), fast chopper-A (unit 93-1A, CF 11.0 kHz), fast chopper-B (unit 176-1F, CF 15.0 kHz), bimodal-A (unit 186-1I, CF 31.5 kHz), and bimodal-B (unit 40-1C, CF 20.3 kHz).

Relevant statistical measures of LSO unit discharges were computed off-line from the digitized data. The PST histogram represents the times of occurrence of discharges relative to the stimulus-onset time under repeated presentations of the same stimulus [38]. The PST histograms are normalized with respect to the binwidth and number of stimulus repetitions and are described as a rate expressed in spikes/s. This normalization procedure reduces the dependency on binwidth and facilitates the comparisons of PST histograms of responses to different numbers of stimuli. The PST histograms were used to select the more stationary, sustained portion of the tone burst response from which interval statistics were computed.

Three measures of the interval statistics were computed from the data: the interval histogram, the recovery function associated with the interval histogram, and the conditional mean function. The interval histogram describes the probabilistic distribution of interspike interval durations: the relative number of interspike intervals having a given duration. The interval histograms are normalized with respect to the binwidth and described as a rate. The recovery function, sometimes called the hazard function, is derived from the interval histogram and describes the probability of an immediate spike occurrence given that no spike has occurred in the elapsed interval [73]. While the interval histogram describes the number of intervals with a given duration relative to the total number of intervals, the recovery function describes the number
of intervals with a given duration relative to the number of intervals having longer durations. The recovery function can be expressed in spikes/s, describing the post-spike discharge rate. The conditional mean function estimates the mean interspike interval as a function of the previous interval's duration. Similarly, the conditional interval histogram and the conditional recovery function derived from it describe the statistics of those intervals that immediately follow a conditioning interval of a specified length. (The relation between the interval histogram and the recovery function is quantified in the next chapter).
Chapter 2

Serial dependence

Point process analyses and modeling have been applied to describe LSO neuron sustained discharges to ipsilateral stimulation [41]. It was demonstrated that LSO discharges exhibit first order negative serial dependence: The mean interspike interval varies inversely with the duration of the preceding interval (see Figure 1.2). Subject to the amount of available data, no significant second order dependence was detected. To accommodate the first order serial dependence observed in LSO unit discharges, the point process model required applying a shifting operation to the unit's recovery process: The conditional recovery following a short interspike interval is a shifted (delayed) version of the conditional recovery following a longer interspike interval. The shifting model successfully describes the recovery of slow choppers and slowly driven fast choppers under ipsilateral (monaural) stimulation. However, the shifting model is not capable of describing the monaurally elicited discharges of bimodal units and of fast choppers driven to high rates. Following a brief review of the relevant point process theory, a complete model for the serial dependence observed in both the monaurally and binaurally elicited responses is described, and the notion of an intrinsic recovery function is presented.

2.1 Spike-trains as realizations of a point process

A point process generates a sequence of event times, which, as descriptors of neural spike trains, mark the times of occurrence of the spikes. It is the times of occurrence of the spikes, rather than their shapes, that encode the information conveyed
by spike trains [34]. Thus, the point process approach extracts and captures those characteristics that are most relevant for studying neuronal information processing.

Generation of event times is governed by an intensity function that, in the general case, may depend on the time and on the history of the realization. Through the explicit dependence on time, the point process model can capture the effects of time-varying stimulus. However, the times of occurrence of the spikes depend also on the recovery properties of the spike generation process—those effects are described by the explicit dependency of the intensity on the history of the discharges.

After a spike has been generated, a neuron takes time to "recover" before it is ready to generate another spike. Consequently, the occurrence of a spike in a response may affect the probability of successive discharges while the neuron, and possibly its inputs, recover. Point processes for which the occurrence of an event has an aftereffect are referred to as self-exciting point processes [62]. The complete characterization of a general self-exciting point process depends on the history of the process and rests on the conditional probability of an event occurring in the interval \([t, t + \Delta t]\) given the process's history:

\[
\Pr\{\text{one event in } [t, t + \Delta t] \mid N_t = n, \mathcal{W} = \mathcal{w}\} = \mu(t; n; \mathcal{w})\Delta t
\]  

(2.1)

The intensity of the process \(\mu(t; n; \mathcal{w})\) depends on the time \(t\), on the counting process \(N_t\) (the number of events up to time \(t\)), and on the vector of event times \(\mathcal{W}\) observed prior to time \(t\). Implicit in the definition of Equation 2.1 are the axioms of a regular point process: The probability of an event occurring in the interval \([t, t + \Delta t]\) is proportional to \(\Delta t\), and the probability of having more than one event in that interval can be made an arbitrarily small fraction of there being one event by choosing \(\Delta t\) sufficiently small. Subject to the amount of data, successive estimates of the intensity, based on increasingly smaller binwidth, reaches a constant value, thereby supporting the assumption that the discharges obey the above assumptions.
The intensity can be expressed more conveniently in terms of the interspike intervals rather than the event times. The \( n \)th interspike interval \( \tau_n \) is given by \( \tau_n = W_n - W_{n-1} \). With \( \tau \) being the vector of interspike intervals corresponding to \( W \), the intensity can be rewritten as:

\[
\Pr\{n + 1st \text{ interval in } [\tau_{n+1}, \tau_{n+1} + \Delta t) \mid N_t = n, \tau\} = \tilde{\mu}(\tau_{n+1}; n; \tau) \Delta t \tag{2.2}
\]

A stationary renewal process, for example, can be characterized by an intensity that depends only on the time since the last spike \( (\tau_{n_t}) \). In this case, the intensity equals what is termed here the recovery function, but is also known as the hazard function, the age-specific failure rate [14], and the spike rate function [75]. The recovery function is directly related to its interval distribution by:

\[
\tilde{\mu}(\tau_{n+1}) = \frac{p_r(\tau_{n+1})}{\int_{\tau_{n+1}}^{\infty} p_r(\alpha) d\alpha} \tag{2.3}
\]

where \( p_r(\tau) \) is the probability density function of the stationary sequence of interspike intervals.

When a first-order serial dependence exists between successive interspike intervals produced by a stationary process, the intensity is equivalent to the first-order conditional recovery function and is related to the first-order conditional interval histogram, wherein the statistics are conditioned on the duration of the previous interspike interval.

\[
\tilde{\mu}(\tau_{n+1}; \tau_n) = \frac{p_{r_{n+1} | \tau_n}(\tau_{n+1} \mid \tau_n)}{\int_{\tau_{n+1}}^{\infty} p_{r_{n+1} | \tau_n}(\alpha \mid \tau_n) d\alpha} \tag{2.4}
\]

Thus, to reveal the underlying structure of processes having first-order serial dependence, as in all LSO discharges, the first-order conditional interval histograms must be measured; the usual interval histogram is not powerful enough. Generalization to higher order serial dependence is straightforward, by replacing the conditioning previous interval \( \tau_n \) by the conditioning vector of previous intervals \( \tau \).

The data processing procedure presented above—measuring a sequence of event times, computing the interval histogram, and deriving the recovery function from it
(equation 2.4)—can be reversed. Given a family of conditional intensity functions, the corresponding family of conditional probability density functions can be derived. For a stationary process exhibiting first order serial dependence this relationship is given by:

$$p_{\tau_{n+1}|\tau_n}(\tau_{n+1}, \tau_n) = \bar{\mu}(\tau_{n+1}; \tau_n) \exp\left(-\int_0^{\tau_{n+1}} \bar{\mu}(\alpha; \tau_n) d\alpha\right)$$  (2.5)

Furthermore, given an intensity function, a simulated spike train can be generated that is characterized by a recovery function having the same shape as the underlying intensity function [41, 53]. Similarly, a simulated spike train exhibiting serial dependence and having the desired conditional recovery functions can be generated by specifying a family of conditional intensity functions. This procedure has been used to generate simulated spike discharges based on models for the intensity underlying a point process description of the spike trains. Comparison between the statistics of these simulated discharges and the statistics of the measured discharges provide a measure of the model’s descriptive power.

2.2 Interaction between the shifting process and deadtime

The shifting model developed elsewhere [41] describes how the conditional statistics change with the duration of the preceding conditioning interval. The shifting model is based on the observation that the first-order conditional statistics of monaurally elicited sustained discharges are shifted toward shorter intervals as the preceding conditioning intervals become longer, but otherwise have the same form. While the shifting model seems to describe well the serial dependence exhibited in the monaurally elicited discharges of slow choppers and of slowly driven fast choppers, it fails to describe the nature of the serial dependence exhibited in the discharges of bimodal neurons and fast choppers driven to high rates. Furthermore, the ability of the shifting model to describe the serial dependence exhibited in the binaurally elicited discharges was not addressed.
Further insight into the nature of the serial dependence exhibited by LSO neurons was gained while studying the inhibitory effect of simultaneous stimulations of the contralateral ear. The effect of the serial dependence not captured by the shifting model can be demonstrated best by studying the conditional statistics of binaurally elicited discharges of fast choppers or bimodal neurons, but is also apparent in the monaurally elicited discharges of these neurons. Conditional interval histograms and conditional recovery functions derived from monaurally and binaurally elicited discharges of a fast chopper and from monaurally elicited discharges of a bimodal neuron are illustrated in Figure 2.1. To facilitate the comparison of their shapes, the conditional statistics associated with the longer conditioning intervals in Figure 2.1 (i.e., those in the two lower rows of Figure 2.1) are presented separately in Figure 2.2 and have superimposed upon them the shifted conditional statistics associated with the shortest conditioning interval of Figure 2.1 (those in the top row of graphs of Figure 2.1). The superimposed conditional statistics of the fast-chopper monaural response (Figure 2.2, left) match well, demonstrating the shifting relationship. However, the constancy of form of the conditional statistics does not hold for the fast chopper binaural discharges (Figure 2.2, middle column) and the bimodal unit's monaural discharges (Figure 2.2, right column). In these examples, the mode of the conditional interval histogram may change with the duration of the conditioning interval (Figure 2.2, middle & right columns) and a unimodal histogram may change to a bimodal or vice versa (Figure 2.2, right column). A closer look at these conditional statistics indicates that the differences occur only during a short interval immediately after the deadtime, with the shapes of the conditional statistics retained at longer intervals.

When the conditional recovery function is shifted toward shorter intervals, it eventually reaches the shortest interspike interval the neuron can produce. This interval—termed here the absolute deadtime—is distinguished from the observed apparent deadtime, or the shortest observed interspike interval, which depends strongly
Figure 2.1  Conditional statistics

The conditional interval histograms and conditional recovery functions are illustrated for a fast chopper and a bimodal unit. Stimulus conditions are indicated in dB above the unit excitatory and inhibitory thresholds, respectively. The conditional interval histogram (thin line) describes the distribution of those interspike intervals that follow a conditioning interval ($\tau_n$) of specified duration and, having been normalized by the binwidth, is expressed as fraction per second (right scale). The conditional recovery function (bold line, left scale) is then derived from the conditional interval histograms. Indicated at the top of each graph is $\tau_n$, the midpoint of the specified conditioning interval duration in ms, and $N$, the total number of conditional intervals in the graph. The conditioning interval duration equals $\tau_n \pm \delta$ with a $\delta$ of 0.6 ms for the fast chopper and 0.75 ms for the bimodal unit. The conditional statistics are computed from the sustained portions of the units’ responses, specifically from the PST intervals (75 – 200 ms) and (50 – 200 ms) with binwidth of 50 $\mu$s and 150 $\mu$s for the fast chopper and bimodal unit, respectively.
Figure 2.2 Shifted and compared conditional statistics

The conditional statistics associated with the shortest conditioning interval in the top graphs of Figure 2.1 are shifted by the time (in ms) indicated in the parenthesis above each graph and superimposed (thin lines) on the conditional statistics that were illustrated in the lower two rows of previous figure (thick lines). Notation is as in Figure 2.1. The fast chopper exhibits the “suppress-and-rebound” phenomenon (middle column) under the binaural stimulation. The “suppress-and-rebound” phenomenon may also occur under monaural stimulation as is illustrated in the discharges of the bimodal unit (right column).
on the stimulus conditions. The examples in Figure 2.2 suggest that shifting as a function of the conditioning interval holds only at intervals longer than the absolute deadtime. Discharge probability is reduced to zero in that portion of the conditional recovery function that is shifted into the absolute deadtime interval. When this effect occurs, the conditional recovery function after the deadtime increases beyond the level expected by a simple shift. Detailed analysis of the shifted conditional recovery functions indicates that the total number of spikes that have been suppressed in the absolute deadtime interval well approximates the additional number of spikes that occur immediately after the deadtime. Thus, a "suppress-and-rebound" process is postulated so that when the discharge probability is suppressed during the absolute deadtime, the discharge probability immediately after the absolute deadtime "rebounds" by a magnitude equal (approximately) to that suppressed.

The "suppress-and-rebound" phenomenon is common for fast choppers: Fast choppers produce high sustained discharge rates, short interspike intervals, and hence a significant probability of discharging immediately after the absolute deadtime interval (Figure 2.2, middle). However, the appearance of this phenomenon is level dependent for some fast choppers; that is, at low ipsilateral stimulus levels that elicit low discharge rates, fast choppers may exhibit a "pure" shift in conditional statistics (Figure 2.2, left). Slow choppers discharge with low sustained rates, generate longer interspike intervals, and tend to exhibit a "pure" shift in conditional statistics. When driven to higher discharge rates, they may also exhibit the suppress-and-rebound phenomenon but to a lesser degree than fast choppers and bimodal units. Bimodal units producing either slow-chopping or fast-chopping discharges are characterized by recovery time constants greater than those of fast choppers i.e., exhibit long refractory periods (Figure 2.1, right; note the time scale). The slowly recovering bimodal units generate both short and long interspike intervals that exhibit serial dependence. Consequently, the conditional recovery function governing discharge probability after long interspike intervals may be shifted into the absolute deadtime interval, thus
evoking the suppress-and-rebound phenomenon. While the discharges produced by both fast choppers and bimodal units exhibit this phenomenon, the longer recovery times of the bimodal units result in a bimodal conditional interval histograms with a prominent mode located at a long interval separable from the mode immediately after the deadtime (Figure 2.1, right).

### 2.3 The intrinsic recovery function

Specifying a family of conditional intensity functions for generating spike trains characterized by the desired serial dependence can, in the general case, be arbitrarily complex. A parsimonious method for specifying a family of first-order conditional intensity functions is described here based on a single underlying intensity function and a set of rules for generating the conditional intensity functions from that function. This single underlying intensity function describes the history independent recovery characteristics of the neuron and is termed the *intrinsic recovery function* [82].

\[
\tilde{\mu}(\tau_{n+1}; \tau_n) = \mu_0 O(r(\cdot); \tau_{n+1}; \tau_n; \mu_0)
\]  

Here, \(O(\cdot)\) is the operator that captures the rules for manipulating the intrinsic recovery function \(r(\cdot)\) given the time elapsed since the last discharge \(\tau_{n+1}\), the duration of the previous interval \(\tau_n\), and the intensity magnitude \(\mu_0\).

Note that while some rules for generating the conditional intensity functions preserve the shape of the intrinsic recovery function (the shifting model being one example), others may introduce distortions so that the resulting conditional intensity functions have different shapes. In the latter case, extracting the shape of the intrinsic recovery function from the measured recovery function or from the measured conditional recovery functions may not be straightforward. Understanding the distortion mechanism helps extract the shape of the intrinsic recovery function in those cases in which distortion prevails under all conditions. In previous work, the shape of the intrinsic recovery function was restricted to the space of non-decreasing, piecewise-
linear functions having at most four segments [41, 82]. Later work [83] was based on further restricting the shape of the intrinsic recovery function to the space of saturating linear functions:

\[
    r(x) = \begin{cases} 
    x/R, & x \leq R \\
    1.0 & x \geq R 
    \end{cases}
\]  

(2.7)

where \( R \) is the saturation interval; at longer intervals the post-spike discharge rate does not increase with time.

It is difficult to assess the length of \( R \) from the measured recovery functions since the number of intervals that are longer than the mode of the interval histogram decreases exponentially with the length of the interval. The measured recovery functions seem to increase linearly at long intervals with possible saturation that may reflect only lack of data. A measure of the recovery function that defines how the width of the bins should be increased at long intervals to keep the variance of the measured recovery function approximately constant has been developed. While the resulting recovery functions are smoother, the conclusions relative to the saturation of the recovery functions are the same. Hence, the measured data provides a lower bound on \( R \), but does not determine it uniquely. The specific value of \( R \), as long as it is larger than that lower bound is arbitrary. The only meaningful physical variable is \( \mu_0/R \)—the rate of change in the post-spike firing rate. The above notation—Equations 2.6 and 2.7—is adopted for compatibility with general intrinsic recovery functions.

2.4 Modeling the rebound phenomenon

2.4.1 Intensity model

Point process models for spike trains are defined by an intensity function, which describes the probability of an immediate occurrence of a spike given the relevant history of the spike train. Because the LSO unit discharges exhibit first-order serial dependence, the intensity function depends on the duration of the preceding interspike
interval as well as the time elapsed since the last discharge. The intensity function can be factored into two functions: A driving function that is related to the acoustic stimulus and an intrinsic recovery function that describes how the probability of discharge varies with the time elapsed since the last discharge. The shifting model developed to describe monaurally elicited LSO discharges [41] accounts for the serial dependence by shifting the intrinsic recovery function with the duration of the preceding interval. For a stationary case, the functional form of the intensity function describing the shifting relationship is

\[ \bar{\mu}(\tau_{n+1}; \tau_n) = \mu_0 r[\tau_{n+1} - d - s(\tau_n)] \]  

(2.8)

where \( \mu_0 \) is the amplitude of the intensity, \( r(\cdot) \) is the intrinsic recovery function, \( d \) is the deadtime, and \( s(\cdot) \) is the shifting function. The intrinsic recovery function should be distinguished from the measured recovery function, which estimates the expected value of the intensity function with respect to the random variable \( \tau_n \). The shifting function determines the shift with respect to the deadtime: Positive values of the shift function correspond to shifting the intrinsic recovery function to intervals that are longer than the absolute deadtime, and vice versa.

When the shifting model applies, the conditional mean function equals the shifting function up to an additive constant [41]. Because the measured conditional mean functions (e.g. Figure 1, [70]) are generally well described by linear relationships, a linear shifting function is adopted:

\[ s(\tau_n) = (a - br_n)u(a - br_n) \]  

(2.9)

The unit function \( u(\cdot) \), \( u(x) = 1, x > 0; u(x) = 0, x < 0 \), restricts the shifting function to positive values. The shifting model is illustrated in Figure 2.3a, wherein a saturating linear conditional recovery function (the solid line) is shifted toward shorter intervals as the duration of the preceding interval increases.

The shifting model is extended here to describe the suppress-and-rebound process evoked when the conditional recovery is shifted into the absolute deadtime interval:
Figure 2.3 Illustration of the suppress-and-rebound process
(a) According to the shifting model, the conditional recovery function governing the probability of a discharge following a conditioning interval $\tau_n$ in the range $\tau_0 < \tau_n \leq \tau_1$ (dashed line) is shifted to the left as the duration of the conditioning interval increases so that $\tau_1 < \tau_n \leq \tau_2$ (solid line). (b) Suppress-and-rebound phenomenon occurs when the conditional recovery function is shifted into the deadtime, as may happen, for example, after long conditioning intervals so that $\tau_2 < \tau_n \leq \tau_3$. The discharge probability during the absolute deadtime is suppressed and a corresponding rebound occurs (grey area) following the absolute deadtime.
The discharge probability is suppressed during the absolute deadtime and a rebound function \( g(\tau_{n+1}; \tau_n) \) is added to the intrinsic recovery function.

\[
\tilde{\mu}(\tau_{n+1}; \tau_n) = \mu_0 \{ r[\tau_{n+1} - d - s(\tau_n)] + g(\tau_{n+1}; \tau_n) \} u(\tau_{n+1} - d)
\]

The suppression of activity during the absolute deadtime \( d \) is enforced by the unit step function \( u(\cdot) \). In particular, the shifting function can take negative values corresponding to shifts to the left and has the form (compare with Equation 2.9)

\[
s(\tau_n) = a - b\tau_n.
\]

When \( s(\tau_n) \) is negative, that part of the conditional recovery function shifted into the absolute deadtime interval is "suppressed" (i.e., probability reduced to zero) and a corresponding rebound in the recovery occurs past the deadtime, as shown in Figure 2.3, left column.

An exponential rebound function describes well the observed rebound in the recovery interval:

\[
g(\tau_{n+1}; \tau_n) = \frac{1}{T} g_0(\tau_n) \exp\left(-\frac{(\tau_{n+1} - d)}{T}\right), \quad \tau_{n+1} > d
\]

where \( T \) is the time constant of the rebound process and \( g_0(\cdot) \) is the area of the rebound. Based on the conclusions drawn from the data analysis presented above, the area of the rebound is constrained by "conservation of spikes". As noted in the context of Figure 2.2, the total area under the conditional recovery function "suppressed" during the absolute deadtime appears to equal the area added by the rebound past the deadtime. Hence, the area of the rebound is set equal to

\[
g_0(\tau_n) = \int_0^d \left\{ \tau_{n+1} - d - s(\tau_n) \right\} d\tau_{n+1}, \quad s(\tau_n) < 0
\]

Assuming this constraint on the area of the rebound, straightforward analysis shows that, at intervals much longer than the rebound time constant, the resulting conditional interval histograms obey the shifting relationship. This result agrees
well with the observations, and supports the selection of the above constraint on
the magnitude of the rebound. Other possible constraints that cannot be detailed
from the measurements include (a) the rebound area being proportional but less
than the area suppressed during the absolute deadtime interval, and (b) a grading
effect reflecting the decaying contribution of the reduced probability of firings to the
magnitude of the rebound. For parsimony, we assume that the area of the rebound
equals the underlying probability of firings suppressed during the deadtime, as stated
by Equation 2.13. Hence, the only additional free parameter required to describe the
rebound process is the rebound time constant $T$, which is easily estimated from the
measured recovery function. The rebound time constant was found to vary within a
small range: from 0.2 to 0.4 ms.

The suppress-and-rebound process affects the relationship between the conditional
mean function $E[\tau_{n+1} | \tau_n]$ and the shifting function $s(\tau_n)$. When no rebound occurs,
the shifting function equals the conditional mean function plus an additive constant.
Thus, measuring the conditional mean in this case is equivalent to measuring the
shifting function directly. When the suppress-and-rebound phenomenon occurs, the
conditional mean function depends nonlinearly on the shifting function. Hence, the
interaction of a linear shifting function with the deadtime in the suppress-and-rebound
process results in a nonlinear conditional mean function. This nonlinear effect is more
evident at conditioning intervals that cause large negative shifts (shifts to the left).
As a consequence, the conditional mean functions of bimodal units and high-rate fast
choppers are more likely to be nonlinear. The effect is subtle and not clearly evident
unless the conditional mean is compared directly with a linear fit.

2.4.2 Noise model

The sharp increase in the post spike discharge rate observed in some recovery func-
tions motivated the postulation and description of the suppress-and-rebound process.
However, although very sharp, the step-like change in the post spike discharge rate
does not occur instantly—not within a single binwidth. In contrast, simulated discharges generated by the intensity function defined in Equation 2.10, under conditions that trigger the suppress-and-rebound process, are characterized by recovery functions with an instant increase in the discharge probability at the end of the absolute deadtime.

The instant change in the post-spike discharge rate is traced back to the lack of variability in the duration of the absolute deadtime. The transition from zero post spike discharge rate to the ‘rebounded’ post spike discharge rate occurs within a single binwidth, across the bin occurring at the end of the absolute deadtime. It is thereby evident that some noise has to be introduced to simulate the exact shape of the leading edge of the rebound in the post-spike discharge rate. Two possible noise models were considered:

1. The absolute deadtime as a random variable. The specific version that was implemented is based on a uniformly distributed random variable having a value of $d \pm \Delta d$, with $\Delta d$ of 100$\mu$s. Such a noise model may reflect fluctuations in the absolute deadtime process.

2. Additive noise. A white Gaussian noise (with standard deviation $\sigma$ of 60—100$\mu$s) is added to the simulated interspike intervals. Such a model may reflect possible measurement noise [38] or temporal fluctuations in spike generation [77].

Simulations based on either noise model result in the desired smoothing of the step-like change in the post-spike discharge rate at the end of the absolute deadtime. The recovery functions derived from simulated discharges augmented by either noise model agree well with the recovery functions derived from measured discharges. As will be discussed later, in the context of the transient response (Section 3.4.2), the second noise model has the advantage of describing and properly modeling the shape of the first peak in PST histograms, as well. Simulation results will be shown in
the next chapter, after the effects of the ipsilateral stimulus level are analyzed and incorporated into the model.
Chapter 3

Excitatory effects

LSO neurons recover from a spike discharge in a characteristic way, modeled by an intrinsic recovery function that is history invariant up to a shift. The shifting process secondarily interacts with the absolute deadtime according to the suppress-and-rebound process and results in non-linear serial dependency. The analysis of LSO unit discharges presented in this chapter reveals that the major effect of changing the excitatory stimulus level is to amplify and shift the intrinsic recovery function. The more complicated effects on the shape of the recovery function are traced to the interaction of the shifting process with the absolute deadtime.

3.1 Monaural sustained response – Analysis

3.1.1 Excitatory effects - apparent variability between units

Recent studies of the effects of excitatory stimulus level on the discharge patterns of LSO units [73] indicate that the relationships between stimulus level and response measures depend on the unit type. Figures 3.1 and 3.2 illustrate this observation. The mean sustained discharge rates of slow choppers and of fast choppers increase with excitatory stimulus level, as indicated in the series of PST histograms in these figures. Superficially, the effects of the excitatory stimulus level on the interval histograms and recovery functions derived from the sustained discharges do not appear to be consistent from unit to unit. The slow choppers interval histograms are mostly symmetric at all stimulus levels (e.g., Figure 3.1, top right). In contrast, those of fast choppers (e.g., Figure 3.2, top right) become more skewed as level increases.
Consequently, the shapes of the recovery functions produced by slow choppers remain fairly constant, almost independent of stimulus level (e.g., Figure 3.1, middle right), while those produced by fast choppers vary with level. In particular, a step-like change in the discharge probability appears immediately after the deadtime in the recovery functions derived from the sustained responses to high ipsilateral stimulus levels (e.g., Figure 3.2, middle right).

Examination of the recovery functions produced by slow choppers (e.g., Figure 3.1) reveals that the interval at which the likelihood of a discharge first departs from zero (the apparent deadtime) shifts to shorter intervals as stimulus level increases. In contrast, the apparent deadtime exhibited by the fast chopper recovery functions do not depend strongly on the stimulus level (e.g. Figure 3.2, note the recovery function time scale differs from that in Figure 3.1). The above examples are typical and illustrate the general observation drawn from a monaural population study [73]: As a function of the mean discharge rate, the duration of the apparent deadtime measured from different units decreases at low discharge rates, reaches a limiting value at mid discharge rates, and exhibits little change at higher discharge rates. Thus, units that can generate a very high sustained (or initial) discharge rates cannot produce interspike intervals that are shorter than some limit. This observation further supports our previous postulate [82] of an absolute deadtime during which the unit cannot discharge. Based on this population study, the duration of the absolute deadtime is expected to vary within a narrow range under different excitatory stimulus levels and across different units.

When a unit is driven fast enough to produce intervals as short as the absolute deadtime, any potential discharge is suppressed during the absolute deadtime and a rebound in the post spike discharge rate occurs immediately after the absolute deadtime as described in Section 2.2. This ‘suppress-and-rebound’ process distorts the shape of the measured recovery function immediately after the deadtime and may obscure the effect of the stimulus level. Hence, the effect of the excitatory
Figure 3.1  Excitatory effects - slow chopper

Effects of excitatory stimulus level on statistical measures of the responses of a slow-chopper. The PST histograms (binwidth 500 μs) elicited under three different excitatory stimulus levels are shown on the left. The monaural excitatory stimulus level expressed in dB above unit threshold is indicated at the top of each graph and is assigned a letter for further reference. The interval histograms (top row), recovery functions (middle row), and conditional mean functions (bottom row) elicited by the same three excitatory stimulus levels (referred to by the assigned letters) were computed from the sustained discharges of the unit’s responses, specifically from the PST interval (50 – 100 ms) with binwidth 100 μs. The conditional mean function elicited by the highest stimulus level is shifted upward and superimposed (thin lines) on each of the conditional mean functions elicited by the lower stimulus levels to demonstrate the constancy of shape of the conditional mean functions.
Figure 3.2  Excitatory effects - fast chopper
Effects of excitatory stimulus level on statistical measures of the responses of a fast-chopper. The PST histograms (binwidth 500 μs) elicited under three different excitatory stimulus levels are shown on the left. The interval histograms (top row), recovery functions (middle row), and conditional mean functions (bottom row) elicited by the same three stimulus conditions are compared in the panels on the right (binwidth 50 μs). The stimulus conditions and statistical measures are marked as in Figure 3.1.
stimulus level on the conditional recovery function can be best determined by studying monaural response series of slow choppers or slowly driven fast choppers in which the apparent deadtime is longer than the absolute deadtime. Once the excitatory process is thereby defined, it can be combined with the suppress-and-rebound process to produce the observed excitatory effect for the monaural response series of fast choppers.

3.1.2 Shifting and amplifying effects

The effect of the excitatory stimulus level on the recovery functions of two slow choppers is demonstrated in Figure 3.3. As the stimulus level increases down each column, the likelihood of a discharge first becomes nonzero at shorter intervals (shorter apparent deadtime) and increases thereafter at a higher rate. Most importantly, however, the shape of the recovery function appears to be invariant to the ipsilateral stimulus level for each LSO unit: only its scale and origin vary. To demonstrate this observation, the recovery function at the lowest discharge rate (Figure 3.3, top row of graphs) is shifted to the left, amplified, and then superimposed (thin line) on the recovery functions at the higher discharge rates (thick line, lower two rows).

The magnitude of the shift was determined by comparing the durations of the apparent deadtime, in those cases when the apparent deadtime exceeded the absolute deadtime, or by visual inspection. The scaling factor was determined by an homogeneous linear regression technique. The recovery function measured from the discharges elicited by the higher excitatory stimulus level, which corresponds to a relatively narrower interval distribution, was assumed exact. The interval histogram of the discharges elicited by the lower excitatory stimulus level was used to estimate the uncertainty in the corresponding recovery function. The regression analysis was limited to those intervals where both recovery functions are nonzero and distortion effects, due to the suppress-and-rebound phenomenon [82], are not apparent. The
magnitude of the shift $\Delta \tau$ and the amplification factor $A$ are indicated above each graph.

When shifted and amplified, the recovery functions produced by the sustained discharges to different ipsilateral stimulus levels match well. Analysis of the responses of other slow choppers and slowly driven fast choppers support the postulates that a stimulus independent intrinsic recovery function defines the recovery process of a given unit and that the main effect of increasing the excitatory stimulus level is to shift-to-the-left and to scale-up the intrinsic recovery function. Note that these conclusions are apparent even when studying the overall recovery function; because no distortion occurs, we can conclude that a similar effect occurs in the conditional recovery function.

3.1.3 Interaction with the rebound process

The effect of the excitatory stimulus level on the recovery functions of a fast chopper and a bimodal unit are shown in Figure 3.4. As the excitatory stimulus level increases down each column, the shape of the recovery function appears to change. Consequently, when the recovery function at the lowest discharge rate is shifted and amplified (as suggested by the conclusion drawn from the analysis of slow choppers), it does not match well the recovery functions at higher rates (thin vs. thick lines, two lower rows of Figure 3.4). The observed discrepancies can be attributed to the interaction of the shifting recovery function with the absolute deadtime according to the suppress-and-rebound process. Note that the discrepancies between the shifted and amplified recovery functions at the lowest discharge rate and those at higher discharge rates occur mainly at short intervals immediately before and after the deadtime; the match at longer intervals is adequate. As the recovery function is shifted toward shorter intervals, it eventually reaches the absolute deadtime. Discharge probability is reduced to zero in that portion of the recovery function shifted into the absolute deadtime. When this suppression occurs, the recovery function after the deadtime
Figure 3.3 Shifting and amplifying effects - slow choppers
The shifting and amplifying effects of the ipsilateral excitatory stimulus level on the
recovery functions of two slow-choppers are illustrated (binwidth 100 μs). The stim-
ulus level increases down each column and is indicated, in dB above unit threshold,
within the parentheses at the upper left of each graph. For each unit, the recovery
function generated by the sustained discharges elicited under the lowest stimulus level
(top row) is shifted toward shorter intervals and amplified before being superimposed
(thin line) on each of the recovery functions produced by the higher stimulus levels
(thick lines). The magnitude of the shift Δτ (in ms) and the amplification factor A
are indicated at the top middle and top right of each graph, respectively. A good
match is demonstrated.
increases beyond the level expected by a pure shift. This “rebound” in the probability of a discharge following the absolute deadtime is approximately equal to that suppressed as noted also in Section 2.4.1. The excitatory process and its interaction with the suppress-and-rebound process are modeled in the next section followed by simulation results for verification.

The suppress-and-rebound process is commonly activated in the discharges of fast choppers and bimodal units. The conditional recovery functions of fast choppers are often shifted into the absolute deadtime because of the high discharge rates, while the conditional recovery functions of bimodal units are often shifted into the absolute deadtime because of a combination of slowly increasing intrinsic recovery functions and large values of negative serial dependency. Consequently, as the excitatory stimulus level increases and the intrinsic recovery function shifts toward shorter intervals, the shapes of the recovery functions characterizing the sustained discharges elicited by fast choppers and by bimodal neurons seem to change. In contrast, the suppress-and-rebound process is rarely activated in the discharges of slow choppers because they respond at low rates, and the recovery function shapes are maintained independent of the stimulus level.

3.2 Monaural sustained response — Modeling

3.2.1 Excitatory effects

Point process models for the sustained discharges are defined by an intensity function, which describes the probability of an immediate occurrence of a spike given the relevant history of the spike train. The point process model presented in the previous chapter describes the serial dependency exhibited in the discharges of LSO neurons and highlights the following three characteristics:

- The effect of the history of the spike train on the recovery process is mainly attributed to a first-order serial dependence. Thus, a point process description
Figure 3.4 Shifting and amplifying effects - rebound effect

The shifting and amplifying effects of the ipsilateral excitatory stimulus level on the recovery functions of a fast chopper (binwidth 50 μs) and a bimodal unit (binwidth 75 μs) are illustrated. The stimulus level increases down each column and is indicated in dB above unit threshold within the parentheses at the upper left of each graph. For each unit, the recovery function generated by the sustained discharges elicited under the lowest stimulus level (top row) is shifted toward shorter intervals and amplified before being superimposed (thin line) on each of the recovery functions produced by the higher stimulus level (thick lines). The magnitude of the shift Δτ (in ms) and the amplification factor A are indicated at the top middle and top right of each graph, respectively. The match is good at long intervals, but fails at short intervals.
of LSO unit discharges necessitates the specification of the conditional intensity functions, which depend on the duration of the preceding interspike interval $\tau_n$ as well as the time elapsed since the last discharge $\tau_{n+1}$ [41].

- The effect of the serial dependence can be described by conditional intensity functions that are shifted versions of a single intrinsic recovery function [41, 82].

- Shifting the intrinsic recovery function into the absolute deadtime results in activation of a suppress-and-rebound process. This phenomenon reflects the fact that no spike is generated during the absolute deadtime and describes the rebound in firing rate immediately after the absolute deadtime [82].

The results presented in this chapter suggest that the effect of the excitatory stimulus level can also be described by applying simple operations, shifting and amplifying, to the intrinsic recovery function. Thus, the intrinsic recovery function is history and stimulus independent. For clarity, let's focus for now on modeling the conditional intensity function when the magnitude of the shift is positive: The shift is away from the absolute deadtime and the conditional intensity function does not interact with the absolute deadtime. In this case, the shifting and amplifying operations can be formulated as

$$\tilde{\mu}(\tau_{n+1}; \tau_n) = \mu_0(E)r[\tau_{n+1} - d - s(\tau_n; E)]u(\tau_{n+1} - d)$$  \hspace{1cm} (3.1)$$

where $\mu_0(E)$ is the amplitude of the intensity, $E$ is the excitatory stimulus level, $r(\cdot)$ is the intrinsic recovery function, $d$ is the absolute deadtime, $s(\cdot; E)$ is the shifting function, and the unit step $u(\cdot)$ assures that the intensity function is zero during the absolute deadtime.

This formulation clearly restricts the effect of the excitatory stimulus level to shifting and amplifying the intrinsic recovery function. Furthermore, the effect of the excitatory stimulus level on the shifting operation can be easily characterized.
It has been shown [41] that the shifting function equals, up to an additive constant, the conditional mean function (for positive shifts). Because the shape of the conditional mean function is independent of the excitatory stimulus level (Figures 3.1-3.2, also [41]), it must be concluded that the effect of the excitatory stimulus level on the shifting function is to change only the baseline shift. For linear shifting functions (equation 2.11), which describe well the measured conditional mean functions (Figure 3.1), the stimulus dependent shifting function is

\[ s(\tau_n; E) = a(E) - b\tau_n \]  

(3.2)

The effect of the excitatory stimulus level \( E \) is explicitly restricted to the baseline shift \( a(\cdot) \) and is linearly separable from the effect of the preceding interval \( \tau_n \) on the magnitude of the shift.

This expression for the shifting function permits negative shifts, which correspond to shifts into the absolute deadtime. Such negative shifts trigger the interaction between the conditional intensity function and the absolute deadtime according to the suppress-and-rebound process described in Section 2.4.1. It is only when this interaction is triggered that the effect of the absolute deadtime is observable; otherwise its effect cannot be distinguished from the effect of the baseline shift \( a \). Detailed modeling work indicates that the duration of the absolute deadtime may vary slightly (by less than 10 \%) as the excitatory stimulus level is varied. Thus, the complete model for the conditional intensity function, which explicitly describes the effects of both the excitatory stimulus level and the absolute deadtime, is

\[ \tilde{\mu}(\tau_{n+1}; \tau_n) = \mu_0(E)\{\tau[\tau_{n+1} - d(E) - s(\tau_n; E)] + g(\tau_{n+1}; \tau_n; E)\}u(\tau_{n+1} - d(E)) \]  

(3.3)

where \( g(\cdot; \tau_n; E) \) is the rebound function, and the absolute deadtime \( d(E) \) may depend on the excitatory stimulus level. An exponential function has been shown in Section 2.4.1 to well approximate the rebound function [82], and equation 2.12 is rewritten here with explicit note of the excitatory effects:

\[ g(\tau_{n+1}; \tau_n; E) = \frac{1}{T}g_0(\tau_n; E)\exp[-(\tau_{n+1} - d(E))/T], \quad \tau_{n+1} > d(E) \]  

(3.4)
where $T$ is the time constant of the rebound process. As in section 2.4.1, Equation 2.13, the area $g_0(\cdot; E)$ of the rebound is set equal to the suppressed probability of firing due to the absolute deadtime process:

$$g_0(\tau_n; E) = \int_{r_{\max}(\tau_n)+d(E),0}^{d(E)} r[\tau_{n+1} - d(E) - s(\tau_n; E)]d\tau_{n+1}, \quad s(\tau_n) < 0. \quad (3.5)$$

The last four equations (Equations 3.2–3.5) completely describe the conditional intensity function of LSO units discharges under different excitatory stimulus levels in terms of the shifting function, the intrinsic recovery function, the rebound function, and the rebound area, respectively.

As before, the intrinsic recovery function is restricted to be a non-decreasing function of the time elapsed since last discharge [41]. Furthermore, the intrinsic recovery function is restricted to be a saturating linear function of the form given by Equation 2.7, and is thereby defined by a single parameter $R$, the interval at which saturation is reached.

These equations are used to generate streams of 'noise-free' intervals. A Gaussian white noise (with standard deviation $\sigma$ of 60–120 $\mu$s) is then added to each of these intervals according to the noise model described in Section 2.4.2.

3.2.2 Simulation results

Computer simulations of the responses of various neurons to monaural stimulation at different excitatory stimulus levels were performed to confirm that the effect of varying the excitatory stimulus level is restricted to scaling and shifting the intrinsic recovery function.

The invariant parameters of the conditional intensity function—the interval $R$ at which the linear intrinsic recovery function reaches the saturation level (Equation 2.7), the strength of the serial dependency $b$, and the rebound time constant $T$—were determined by inspecting the shape of the measured recovery function, the slope of the measured conditional mean, and the shape of the rebound, respectively. The
stimulus dependent parameters—the intensity amplitude $\mu_0(E)$, the baseline shift $a(E)$, and the absolute deadtime $d(E)$ were then adjusted to simulate the responses of the same neuron to different excitatory stimulus levels. The ability of the model to generate spike trains with statistics similar to those generated by LSO neurons is demonstrated in Figure 3.5 for a slow chopper, in Figure 3.6 for a fast chopper, and in Figure 3.7 for a bimodal unit. The values of the parameters defining the conditional intensity functions—including the stimulus dependent parameters used to simulate the response to the lowest stimulus level—are summarized in the table 3.1. Changes in the stimulus dependent parameters, i.e. the change in the absolute deadtime $\Delta d$, the change in the baseline shift $\Delta a$, and the amplification applied to the amplitude of the intensity, denoted by $\alpha$, are indicated above the corresponding graphs in Figures 3.5-3.7.

The measured and simulated statistics of the slow-chopper discharges, shown in Figure 3.5, demonstrate the excitatory effects—shifting and scaling—with no interference from interactions with the absolute deadtime. The simulation of the fast chopper discharges (Figure 3.6) demonstrates that the excitatory effects and their interactions with the absolute deadtime process do indeed produce the complex effects of the excitatory stimulus level on the recovery function (compare to Figure 3.4, left column, where shifting and scaling do not seem to account for the complex excitatory effects). The simulation of the bimodal unit discharges (Figure 3.7) further demonstrate that a negatively sloped section in the recovery function can be produced by the suppress-and-rebound process even when the underlying intrinsic recovery function is a non-decreasing function (specifically, a saturating linear function). Here again, the observed complex excitatory effects are fully accounted by the model (compare to Figure 3.4, right column). The added variations in the duration of the simulated intervals introduces variations in the observed absolute deadtime that smooth the step-like increase in the post-spike discharge rate in agreement with the measurement, as demonstrated in Figure 3.6 and 3.7.
Figure 3.5  Simulation vs. measurements - slow chopper

The recovery functions (left column) and conditional mean functions (right column) derived from discharges of a slow-chopper unit (thick lines) compared with those derived from simulations (thin lines). The binwidth is 100 μs. Three of the parameters defining the intensity function used to generate the simulation for the lowest stimulus level—the baseline shift, the amplitude of the intensity function, and the absolute deadtime—have been varied to generate the simulations for the higher stimulus levels. The excitatory stimulus level above threshold (in dB), the change in the duration of the absolute deadtime Δd (in ms), the change in the baseline shift Δα (in ms), and the amplification of the amplitude $\alpha = \mu_0(\text{higher level})/\mu_0(\text{lowest level})$ are indicated above each graph.
Figure 3.6 Simulation vs. measurements - fast chopper

The recovery functions (left column) and conditional mean functions (right column) derived from discharges of a fast-chopper unit (thick lines) compared with those derived from simulations (thin lines). The binwidth is 50 μs. Three of the parameters defining the intensity function used to generate the simulation for the lowest stimulus level—the baseline shift, the amplitude of the intensity function, and the absolute deadtime—have been varied to generate the simulations for the higher stimulus levels. The excitatory stimulus level above threshold (in dB), the change in the duration of the absolute deadtime Δd (in ms), the change in the baseline shift Δa (in sec), and the amplification of the amplitude $\alpha = \mu_0(\text{higher level})/\mu_0(\text{lowest level})$ are indicated above each graph.
Figure 3.7 Simulation vs. measurements - bimodal neuron

The recovery functions (left column) and conditional mean functions (right column) derived from discharges of a bimodal unit (thick lines) compared with those derived from simulations (thin lines). The binwidth is 50 μs. Three of the parameters defining the intensity function used to generate the simulation for the lowest stimulus level—the baseline shift, the amplitude of the intensity function, and the absolute deadtime—have been varied to generate the simulations for the higher stimulus levels. The excitatory stimulus level above threshold (in dB), the change in the duration of the absolute deadtime Δd (in ms), the change in the baseline shift Δa (in sec), and the amplification of the amplitude α = μ₀(higher level)/μ₀(lowest level) are indicated above each graph.
Table 3.1 Parameters used in simulations of the sustained monaural response

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Slow choppers</th>
<th>Fast choppers</th>
<th>Bimodal Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stimulus (dB)</td>
<td>+20</td>
<td>+22</td>
<td>+20</td>
</tr>
<tr>
<td>Intensity amplitude $\mu_0$ (Spikes/s)</td>
<td>1750</td>
<td>1650</td>
<td>2745</td>
</tr>
<tr>
<td>Absolute deadtime $d$ (ms)</td>
<td>1.4</td>
<td>1.4</td>
<td>1.7</td>
</tr>
<tr>
<td>Shifting function:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>baseline shift $a$ (ms)</td>
<td>7.4</td>
<td>3.6</td>
<td>0.7</td>
</tr>
<tr>
<td>slope $b$</td>
<td>0.2</td>
<td>0.285</td>
<td>0.22</td>
</tr>
<tr>
<td>Rebound function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time constant $T$ (ms)</td>
<td>0.4</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td>Intrinsic recovery:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturation interval $R$ (ms)</td>
<td>14.0</td>
<td>14.0</td>
<td>18.0</td>
</tr>
<tr>
<td>Additive noise:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Gaussian) Standard</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>deviation $\sigma$ (ms)</td>
<td>0.06</td>
<td>0.06</td>
<td>0.1</td>
</tr>
</tbody>
</table>

The values of the parameters used to simulate the discharges of two slow choppers, two fast choppers and two bimodal units under the indicated stimulus levels are specified. The intrinsic recovery functions are restricted to the space of saturating linear functions specified by the parameter $R$. The saturation interval $R$, the slope of the shifting function $b$, and the rebound time-constant $T$ were held fixed while modeling the responses of any one neuron to any other stimulus conditions. The intensity amplitude $\mu_0$, the baseline shift $a$, and the duration of the absolute deadtime $d$ were modified when modeling the responses of any one neuron to different ipsilateral stimulus levels. The standard deviation $\sigma$ of the additive white Gaussian noise is specified in the lower row.
The general trend is for the baseline shift $a$ to decrease, and for the intensity amplitude $\mu_0$ to increase as the excitatory stimulus level is increased (Figures 3.5-3.7). An exception has occurred in the simulation shown in Figure 3.7 of the response of the bimodal unit to the intermediate stimulus level: the baseline shift had to be increased. Also, the standard deviation of the white Gaussian noise added to the simulated intervals had to be increased to 160 $\mu$s to generate good agreement with the measured recovery function without changing the time constant of the rebound process. The intermediate stimulus level was presented toward the end of the experiment with this bimodal unit—after the lowest and the highest stimulus levels among others were presented. Hence, the above anomaly may reflect some change in the neuron or its environment that obscured the effect of the stimulus level.

To summarize, the sustained discharges of a LSO neuron under different excitatory stimulus conditions are described by a single point process model wherein the underlying intensity process is related to ipsilateral stimulus levels. The excitatory stimulus effects are described by a baseline shift and by an amplification factor. The model provides a unifying point process representation of the discharges produced by all three LSO unit types. Variations observed in the response patterns of the different LSO unit types are attributed to the interaction of the unit's post-spike recovery process with the absolute deadtime process.

Description of LSO units response patterns to time-varying stimuli is thereby simplified to specifying the temporal variations in the baseline shift, in the amplitude of the intensity process, and in the absolute deadtime. Other parameters of the model, including the strength of the serial dependency and the shape of the intrinsic recovery function, are independent of the ipsilateral stimulus level. These parameters may be postulated to remain constant during the response and can be estimated from stationary portions of the response.
3.3 Monaural transient response - Analysis

3.3.1 Chopping response

One of the most prominent features of the discharges of LSO neurons to repeated presentations of the same stimulus is the chopping pattern produced by the initial discharges. The chopping pattern is clearly evident in the post-stimulus-time histograms of the response of LSO neurons to tone bursts and reflects the synchronization of the initial spikes to the stimulus onset time. The tightly distributed time-of-occurrence of the first spike in each response indicates that variations in the latency period—the period between stimulus onset and the first spike—are very small (less than 100 μs). Following the first spike, the neuron needs to 'recover' before it is ready to generate another spike. The effect of this refractory period has been shown to introduce transients in the PST histograms [40]. To gain insight into this phenomenon, consider a neuron that recovers completely after an absolute deadtime period \( d \). In this case the expected duration of the interspike intervals is \( d + \frac{1}{\mu_0} \), with a standard deviation \( \frac{1}{\mu_0} \), where \( \mu_0 \) is the constant amplitude of the intensity after the deadtime. Hence, if the amplitude of the intensity is large, the interspike intervals will be tightly distributed. The time-of-occurrence of the \( n \)th spike is the summation of all the preceding intervals and its distribution is given by the \( n \)th convolution of the distribution of a single interval. Consequently, the distribution of the time-of-occurrence of the \( n \)th spike will be tight for small \( n \) and will become increasingly wider as \( n \) increases and more ISIs occur, giving rise to a transient chopping response.

Thus, the response of LSO neurons to a step-like change in the stimulus level is expected to exhibit an initial transient. The nature of this transient response is investigated using the point process model that has been developed in Section 3.2 to describe the sustained discharges [83]. In particular, the response of the model to a step-like change in the intensity amplitude \( \mu_0 \) are compared in Figure 3.8 with the measured transient responses of a slow chopper, a fast chopper and a bimodal
neuron. As expected, the step response of the underlying point process model does produce a chopping pattern. However, the extent of the transient step response of the point process model is too small to account for the transient response observed in the recorded discharges of LSO neurons. Thus, the transient chopping response of LSO neurons cannot be attributed solely to the nature of the step response of the corresponding point process model. It is concluded that a step-like change in the stimulus results in a transient change in the parameters of the point process model, reflecting possibly transients in the inputs to the LSO or transient variations in the biophysical variables that affect spike generation.

The point process model of the sustained discharges of LSO neurons, developed in Section 3.2, Equations 3.2—3.5, describes the conditional intensity function using the following parameters [82]:

1. The amplitude of the intensity $\mu_0(E)$.
2. The absolute deadtime $d(E)$.
3. The baseline shift $a(E)$.
4. The strength of the serial dependency $b$.
5. The functional shape of the intrinsic recovery function $r(\cdot)$. To the extent that intrinsic recovery functions can be restricted to the space of saturating linear functions, the intrinsic recovery function can be described by a single parameter: the interval at which saturation is reached.
6. The time constant of the decay of the rebound process $T$.

As indicated, the first three parameters may change with the excitatory stimulus level—these parameters are stimulus dependent. In contrast, the last three parameters do not change with the excitatory stimulus level—these parameters are stimulus independent. The observation that some of the parameters of the point process model are independent of the ipsilateral (and as will be see later, of the contralateral) stim-
Figure 3.8  Step response of the sustained model

The response to a step change in the intensity amplitude is simulated using the point process model for LSO neurons sustained discharges (Equation 3.3). The PST histograms (binwidth 100 µs) derived from the simulated step-responses are compared with PST histograms derived from the measured monaural discharges of a slow chopper (upper left) a fast chopper (upper right) and a bimodal neuron (lower row). The transient step response does not capture the extent of the observed transient response.
ulus level, motivates the assumption that the stimulus independent parameters do not vary during the transient response. The following issues are therefore posed:

- Can the chopping transient response be attributed to transient changes in the values of the stimulus dependent parameters?

- How do the stimulus dependent parameters have to vary with the post stimulus time to simulate the observed chopping response?

- What is the effect of the assumption that the stimulus independent parameters—particularly the strength of the serial dependency—are constant during the transient response?

### 3.3.2 Estimation technique

Modeling the transient response of LSO neurons proceeds by assuming that the values of the stimulus independent parameters are known and remain constant during the transient response. The values of these parameters are derived from the sustained response and are assumed to hold during the transient response. Three effects are carefully considered in developing the technique for estimating the time courses of the stimulus dependent parameters from the discharges:

1. The discharges of LSO neurons are characterized by negative serial dependence.

2. The effect of the absolute deadtime cannot be distinguished from the effect of the baseline shift, unless the suppress-and-rebound process is triggered.

3. The functional form of the time course of each stimulus dependent parameter is unknown (non parametric estimation problem).

These issues are examined below to help in formulating the relevant estimation problem:
1. The serial dependence has been modeled as a shift in the recovery function which depends on the duration of the preceding interval. When the shift is negative, the interaction with the absolute deadtime give rise to a more complicated and nonlinear dependence modeled by the rebound process. When the shift is positive, the serial dependence is captured by the shift model (Equation 2.8) and can be removed in a model-specific fashion using a 'whitening filter' [41]. In this case, the derived sequence

$$\tau_{n+1}' = \tau_{n+1} - s(\tau_n)$$

(3.6)

is statistically independent. The shift function is modeled as a linear (affine) function of the previous interval, Equation 3.2. It is noted that during the transient response the baseline shift $a$ is unknown and may vary with the post-stimulus time. However, the strength of the serial dependence $b$ is assumed known, and the linear term in the equation for the shift function, which is the critical term for removing serial dependence, can be evaluated. Hence, the sequence of intervals:

$$x_{n+1} = \tau_{n+1} + b\tau_n$$

(3.7)

is derived from the measured sequence of ISIs instead of the sequence defined by Equation 3.6. The interaction with the absolute deadtime complicates the dependence structure as modeled by the suppress-and-rebound process. When this interaction is triggered, the above filter reduces but does not eliminate serial dependence.

2. The effect of the absolute deadtime can be distinguished from the effect of the baseline shift only when the recovery process interacts with the absolute deadtime. The absolute deadtime limits the minimum duration of an interval, but this limit is observable only when the suppress-and-rebound process is triggered [83]. Recall that the baseline shift $a$ is defined relative to the absolute deadtime. Hence, it is more meaningful in this context to replace the baseline
shift parameter $a$ by a new parameter $a^*$ describing the total baseline shift—the sum of the baseline shift and the absolute deadtime: $a^* = a + d$. The total baseline shift $a^*$ is estimated below using the maximum likelihood estimation technique, while the absolute deadtime is estimated from the minimum duration of the observed intervals.

3. The stimulus dependent parameters are assumed to vary continuously with the post-stimulus time. However, only their accumulated effect on the duration of the intervals is observable. To estimate the time course of the parameters of interest, intervals from different responses to the different presentations of the same stimulus are grouped together according to the post-stimulus time of their occurrence, as described in the next paragraph. The value of each parameter is assumed to be approximately constant during the duration spanning all the intervals that are grouped together and a maximum likelihood estimate is derived with respect to that constant value. The estimation method is therefore most suitable for analyzing responses with high transient discharge rate (and short initial intervals). The derived estimates are assumed to sample the underlying transient function describing the time course of that parameter. Because the absolute deadtime constitutes a major part of each interval, especially during the initial discharges, the temporal assignment is based on the average time of occurrence of the spikes at the end of the considered intervals.

One method for picking the intervals that occur at about the same time during different responses to the same stimulus is to pick from each spike train the interval that straddles a given time. However, even for a stationary process where the probability density function does not vary with time, this method of picking intervals at a random incidence biases the probability of selecting intervals toward longer intervals [17]. The probability density function describing the duration of intervals selected at a random time is different from the proba-
probability density function describing the duration of intervals following any spike. An alternative method is to pick from each spike train the interval that follows the first spike that occurs after a given time \( t \). This method does not bias the probability density function of the statistically independent intervals \( x_{n+1} \).

In view of the above discussion, estimation of the time courses of the stimulus dependent parameters can be formulated as a parameter estimation problem with respect to the family of distribution functions [84]:

\[
p_L[X_{N+1} \mid W_{N+1} > t]
\]  

(3.8)

indexed by the parameter vector \( \theta \), composed of the total baseline shift \( a^* \) and the intensity amplitude \( \mu_0 \). The process \( X \) is derived from the measured intervals by removing the linear serial dependence according to equation 3.7 and by picking from each spike train the interval that follows the first spike after a given time \( t \).

The family of probability density functions is derived from the corresponding family of intensity functions according to Equation 2.5. The family of intensity functions describing the discharge rate following the first spike that occurred after time \( t \) is expressed in terms of the whitened sequence \( x_n \) and the total baseline shift \( a^* \):

\[
\tilde{\mu}_{\theta, t}(x_{N+1} \mid \tau_{N+1}) = \mu_{0, t}\{r[x_{N+1} - a^*] + g(x_{N+1} \mid \tau_{N+1})\}u(x_{N+1} - a^*)
\]  

(3.9)

Note that, when the rebound process is triggered and \( g(\cdot) \) is not identically zero, the intensity includes serial dependence.

A commonly used technique to estimate unknown parameters of the probability density function from observations of the random variable is the maximum likelihood technique [57]. To illustrate the application of the maximum likelihood technique for the above problem, a simple case—where the rebound process is never triggered and the intrinsic recovery function \( r(\cdot) \) is a deadtime modified linear recovery function—is considered first. The maximum likelihood estimate for the more general case—including the rebound process and a saturating linear recovery function—is described
in the appendix and is the one actually implemented in analyzing the data. For the simple case considered here, the intensity is given by:

\[ \bar{\mu}_g(x) = \mu_0 [x - a^*] u(x - a^*) \]  

and the probability density function of a single interval is:

\[ p_g(x) = \mu_0 [x - a^*] \exp(-\frac{\mu_0}{2} (x - a^*)^2) \]  

where the time-related indices are omitted for simplicity. The intervals, picked from different spike trains according to the method outlined above, are independent identically distributed random variables with constant parameters \( a^* \) and \( \mu_0 \). Hence, the joint probability density function is easily determined from the probability density function of a single interval:

\[ p_g(x_1, \ldots , x_M) = \prod_{i=1}^{M} p_g(x_i) \]  

where \( M \) is the number of spike trains indexed by \( i \).

The likelihood function is defined as the logarithm of the probability density function of the observed random variables conditioned on the unknown parameters.

\[ l(\theta) = \sum_{i=1}^{M} \log(p_g(x_i)) = M \log \mu_0 + \sum_{i=1}^{M} \log(x_i - a^*) - \frac{\mu_0}{2} \sum_{i=1}^{M} (x_i - a^*)^2 \]  

The maximum likelihood estimate of a parameter is the value that maximizes the likelihood function [76]. The value of the parameter \( \mu_0 \) that maximizes the likelihood function is easily evaluated by setting the derivative of the above likelihood function with respect to \( \mu_0 \) to zero. The resulting maximum likelihood estimate of the intensity amplitude \( \mu_{0,ML} \) is given by

\[ \hat{\mu}_{0,ML} = \frac{2M}{\sum_{i=1}^{M} (x_i - a^*)^2} \]  

Similar derivation of the value of the maximum likelihood estimate of \( a^* \) (i.e. from \( \frac{\partial l}{\partial a^*} = 0 \)), results in an expression that cannot be solved analytically. Instead, the
expression for $\mu_{0,ML}$ (Equation 3.14) is substituted in the expression for the likelihood function (equation 3.13) and the value of $a^*$ that maximizes the likelihood function

$$l(a^*) = \sum_{i=1}^{M} (x_i - a^*) - M \log(\sum_{i=1}^{M} (x_i - a^*)^2)$$  \hspace{1cm} (3.15)

is found by direct search. The maximum likelihood estimate of the intensity amplitude $\mu_{0,ML}$ is then computed by substituting $\hat{a}_{ML}^*$ for $a^*$ in equation 3.14.

The maximum likelihood estimates for the unknown parameters $a^*$ and $\mu_0$ are found in a similar way when the rebound process is effective (as detailed in the appendix) with two exceptions:

1. The expression for the likelihood function depends on the value of the shift function. The shift function is evaluated using the value of the preceding interval and the value of the total baseline shift that is considered at each step in the direct search for $\hat{a}_{ML}^*$.

2. The duration of the absolute deadtime is both observable and critical for the estimate of the intensity amplitude. During the sustained response an estimate of the absolute deadtime can be obtained from the initial rise of the rebound in the recovery function. This estimate will be referred to as the sustained absolute deadtime. An estimate of the absolute deadtime during the transient response is generated from the shortest interval observed at each post-stimulus time step, as long as it is shorter than the sustained absolute deadtime. When all the intervals at some post-stimulus time are longer than the sustained absolute time, it is indicative that the rebound process was not triggered. Due to possible noise sources (Section 2.4.2), the observed shortest interval at each post-stimulus time step provides only a lower bound on the duration of the absolute deadtime. This initial bound on the duration of the absolute deadtime is increased in two steps to provide a better bound. First, the time course of the observed shortest interval is filtered to enforce monotonicity. Second, the monotone bound is
increased by a constant to offset the effect of the additive noise and to achieve the best match between the simulated and measured chopping responses in the measured PST histograms.

3.3.3 The time courses of the parameters

The estimates of the intensity amplitude \( \hat{\mu}_{0,ML} \), the total baseline shift \( \hat{\delta}^*_{ML} \), and the absolute deadtime as a function of the post-stimulus time were derived from the measured discharges of LSO neurons using the above estimation technique. The estimates derived from the discharges of a slow chopper, a fast chopper and a bimodal neuron in response different ipsilateral stimulus levels are illustrated in bold lines in Figures 3.9–3.11. The estimated intensity amplitude \( \hat{\mu}_{0,ML} \) (upper row) is very high at the beginning of the response and decays sharply to the steady state level. Of particular interest is the large dynamic range (1:50 to 1:200) over which the estimated intensity amplitude varies during the transient response. Note however that the recorded level of the intensity amplitude corresponds to the saturated intensity level: The neuron would have produced such a high post-spike discharge rate if it would have not discharged for an interval \( R \)—the saturation interval (Equation 2.7). The high level of the intensity amplitude indicates that the rate at which the discharge probability increases with the time elapsed since the last spike is very large. It is the slope of the intensity function, rather than the saturating level that is meaningful, especially since the interval at which saturation is reached, and therefore the intensity amplitude, are not uniquely determined (see Section 2.3 for more details).

While the estimated intensity amplitude increases with the stimulus level, the decay profile is similar across different stimulus levels and looks exponential. An exponential curve fit is overlayed in thin lines over the estimated time course of the intensity amplitude. Specifically, the exponential fit is given by:

\[
\hat{\mu}_{0,ML} = \mu_{0,f} + \mu_{0,s} \exp(-t/\tau_{0})
\]  

(3.16)
Figure 3.9 Estimated transient variations - slow chopper
Estimated time course of the intensity amplitude (upper row) and total baseline shift (middle row) derived from the tone-bursts responses of a slow-chopper as a function of the post-stimulus time (bold lines) with exponential curve fits (overlaid thin lines). The two ipsilateral stimulus levels are indicated in dB above threshold in parenthesis. All the intervals are longer than the absolute deadtime derived from the sustained response so the time course of the absolute deadtime is not observable. The analysis was evaluated at every 1 ms.
Figure 3.10 Estimated transient variations - fast chopper
Estimated time course of the intensity amplitude (upper row), total baseline shift (middle row), and lower bound on the absolute deadtime (lower row) derived from the tone-bursts responses of a fast-chopper as a function of the post-stimulus time (bold lines) with exponential curve fits (overlayed thin lines). The two ipsilateral stimulus levels are indicated in dB above threshold in parenthesis. The estimates for the lower bound on the absolute deadtime are derived from the time course of shortest registered interval (lower row, regular line). The analysis was evaluated at every 1 ms.
Figure 3.11  Estimated transient variations - bimodal unit
Estimated time course of the intensity amplitude (upper row), total baseline shift (middle row), and lower bound on the absolute deadtime (lower row) derived from the tone-bursts responses of a bimodal unit as a function of the post-stimulus time (bold lines) with exponential curve fits (overlayed thin lines). The three ipsilateral stimulus levels are indicated in dB above threshold in parenthesis. The estimates for the lower bound on the absolute deadtime are derived from the time course of shortest registered interval (lower row, regular line). The analysis was evaluated at every 1 ms.
The general trend for the estimated total baseline shift $\hat{a}_{ML}^*$ (middle rows) is to increase gradually or to remain approximately constant with the post-stimulus time. The durations of the total baseline shift immediately after the latency period are approximately the same regardless of the monaural stimulus level. Thereafter, the duration of the total baseline shift increases with post-stimulus time during responses at low ipsilateral stimulus levels or remains approximately constant as the stimulus level is increased. While the total baseline shift decreases during the early phase of the responses elicited by the bimodal unit analyzed here, Figure 3.11, the overall trend is also exponential or constant. An exponentially saturating function (with a constant as a special case) matches well the time course of the total baseline shift as shown in Figures 3.9–3.11 (second rows) in thin lines. Specifically:

$$\hat{a}_{ML}^* = a_f^* - a_s^* \exp(-t/\tau_a)$$  \hspace{1cm} (3.17)

The shortest interval encountered at each time step registered and shown in regular lines in the lower row of Figures 3.10 and 3.11. The shortest interval observed during the response of the slow chopper analyzed here is longer than the absolute deadtime derived from the sustained response, indicating that the recovery functions are shifted away from the deadtime so the absolute deadtime is not observable. The overall trend is for the duration of the shortest interval to increase with the post-stimulus time. The duration of the shortest interval immediately after the latency period is approximately the same in responses to different stimulus levels. Thereafter, the duration of the shortest interval increases to a steady state level that decreases as the stimulus level increases. Applying the monotonicity constraint, a new lower bound on the duration of the absolute deadtime is obtained as shown in bold lines. This is the 'on-the-fly' estimate of the absolute deadtime that was used during the analysis to estimate the other two parameters—the intensity amplitude and the total baseline shift. An exponentially saturating curve fit, having the same form as the curve fit for the total baseline shift, equation 3.17, is superimposed on the resulting lower bound.
to the duration of the absolute deadtime. Note that the steady state level reached by the curve fit may be lower than the duration of the sustained absolute deadtime.

In summary, during the transient portion of the response, the intensity amplitude decays exponentially, with a very short time constant, while the total baseline shift and the absolute deadtime increase exponentially, with a longer time constant, or remain approximately constant. Section 3.4.4, simulation results, provides specific numerical equations for those transient parameters.

3.3.4 Effect of Assumed strength of serial dependency

The estimation results are conditioned on the assumed strength—and in general, the assumed time course—of the serial dependency. The strength of the serial dependence was assumed constant during the response and its value was determined from the sustained response. The estimates of the time course of the unknown parameters, shown in Figure 3.10, are conditioned on this assumption. It is critical to assess the sensitivity of these estimates to the underlying assumption about the strength of the serial dependency.

When a different value for the strength of the serial dependency $b$ is assumed, it is expected that the amplitude of the total baseline shift $a^*$ will change to compensate for the effect on the shift function $s(\tau_n)$, Equation 2.11. Specifically, assuming a smaller value for $b$ will result in a larger estimate for $a^*$. The estimates of the intensity amplitude $\hat{\mu}_{0,ML}$ and the total baseline shift $\hat{a}_{ML}^*$ are evaluated using different values for the strength of the serial dependency and compared in Figure 3.12. The comparison demonstrates that other than the expected effect on the total baseline shift, the assumption relative to the strength of the serial dependency has little effect. In particular, the large dynamic range over which the intensity amplitude varies is independent of this assumption.
**Figure 3.12** Effect of assumed serial dependence on estimated transients
The effects of the assumed strength of the serial dependence on the estimation of the intensity amplitude (left) and the total baseline shift (right) are assessed. The effect on the intensity amplitude is negligible. The strength of the serial dependence is indicated by $b$. 
3.4 Monaural transient response – Modeling

3.4.1 Transient point process model

The analysis of the transient response and the estimation results suggest that it may be possible to extend the point process model of the sustained responses of LSO neurons to describe the transient portions of the responses as well, by letting each stimulus dependent parameter be a function of the post-stimulus time. The point process model of LSO discharges, both transient and sustained, is formulated below using the new notation for the total baseline shift.

\[
\tilde{\mu}(\tau_{n+1}; \tau_n; t; E) = \mu_0(t; E)\{r[\tau_{n+1} - s^*(\tau_n; t; E)] + g(\tau_{n+1}; \tau_n; t; E)\}u(\tau_{n+1} - d(t; E))
\]

(3.18)

where:

- \( t \) is the post-stimulus time,
- \( E \) is the excitatory ipsilateral stimulus level
- \( \tau_{n+1} \) is the time elapsed since the last spike,
- \( \tau_n \) is the previous interval,
- \( \tilde{\mu}(\cdot; \tau_n; t; E) \) is the intensity of the point process,
- \( \mu_0(\cdot; E) \) is the amplitude of the intensity,
- \( r(\cdot) \) is the intrinsic recovery function,
- \( s^*(\cdot; t; E) \) is the total shift function, and
- \( g(\cdot; \tau_n; t; E) \) is the rebound function.

The dependency of the intensity amplitude \( \mu_0(t; E) \) on the post-stimulus time \( t \) is made explicit. The dependency of the total baseline shift \( a^* \) and the absolute deadtime \( d \) on the post-stimulus time are mirrored in the dependency of the shift function \( s^*(\cdot; t; E) \) and the rebound function \( g(\cdot; \tau_n; t; E) \) on the post-stimulus time.
Specifically, the shift function given in Equation 3.2, is restated here in terms of total baseline shift:

$$s^*(\tau_n; t; E) = a^*(t; E) - b\tau_{n-1} \tag{3.19}$$

where the total baseline shift depends on the post-stimulus time $t$ but the strength of the serial dependency $b$ does not.

The rebound function describes the rebound in the probability of firing immediately after the absolute deadtime as a result of suppression of the probability of firing during the absolute deadtime, Equation 3.4. The form of the rebound function is extended to include the transient response:

$$g(\tau_{n+1}; \tau_n; t; E) = \frac{1}{T} g_0(\tau_n; t; E) \exp[-(\tau_{n+1} - d(t; E))/T] u(\tau_{n+1} - d(t; E)) \tag{3.20}$$

where $T$ is the time constant of the rebound process, and the area $g_0(\cdot; t; E)$ equals the suppressed probability of firing during the absolute deadtime.

$$g_0(\tau_n; t; E) = \int_{\max(s^*(\tau_n; t; E), 0)}^{d(t; E)} r[\tau_{n+1} - s^*(\tau_n; t; E)] d\tau_{n+1}, \quad s(\tau_n; t; E) < 0 \tag{3.21}$$

The intrinsic recovery function is restricted to be a saturating linear function of the form of Equation 2.7.

The point process model described by the above four equations (Equation 3.18–Equation 3.21) has been motivated by analysis of LSO discharges to tone bursts. However, as stated so far, the model does not depend on the stimulus type—the functional dependency of the stimulus dependent parameters on the excitatory stimulus level $E$ and on the post-stimulus time $t$ are not specified. Thus, the point process model may apply to the discharges of LSO neurons to any type of stimulus.

The model of the transient response of LSO neurons to tone-bursts stimuli can be completed by specifying the functional dependency of the stimulus dependent parameters on the post-stimulus time, based on the transient analysis described in the previous section. The intensity amplitude was found to decay exponentially, thus motivating the following expression for $\mu_0(t; E)$

$$\mu_0(t; E) = \mu_{0, f}(E) + \mu_{0, s}(E) \exp(-t/\tau_{\mu_0}(E)) \tag{3.22}$$
where, $\mu_0, f(\cdot)$ is the final intensity amplitude reached during the sustained portion of the response, $\mu_{0,s}(E)$ is the scale of the transient decay, and $\tau_{\mu s}(E)$ is the time constant of the decay. While all the three parameters defining the time course of the intensity amplitude may depend on the excitatory stimulus level, the sensitivity to the time constant of the decay is expected to be weak as the decay profiles of the intensity amplitude in responses to different ipsilateral stimulus levels are similar.

The total baseline shift was found to increase as an exponentially saturating function

$$a^*(t; E) = a^*_s(E) - \alpha_s(E) \exp(-t/\tau_a(E))$$

(3.23)

where $a^*_s(\cdot)$ is the final duration of the total baseline shift, $a^*_s(\cdot)$ is the scale of the transient change, and $\tau_a(\cdot)$ is the time constant of the transient. The excitatory stimulus level affects the value of all the three parameters defining the time course of the total baseline shift.

The duration of the shortest interval was found to vary as an exponentially saturating function having the same functional expression as the one for the total baseline shift. The absolute deadtime is assumed to vary according to a similar function:

$$d(t; E) = d_f(E) - d_s(E) \exp(-t/\tau_d(E))$$

(3.24)

where $d_f(\cdot)$ is the final duration of the absolute deadtime reached during the sustained response, $d_s(\cdot)$ is the scale of the transient change, and $\tau_d(\cdot)$ is the time constant of the transient change. The excitatory stimulus level may affect the value of all the three parameters defining the time course of the absolute deadtime.

### 3.4.2 Noise Model

The point process model can be used to generate a sequence of intervals having the desired intensity, as described in Section 2.1. The simulated interspike intervals are derived from this sequence of intervals by adding a white Gaussian noise as described in Section 2.4.2. The additive noise model was postulated in the context of simulating
the sustained response of LSO neurons to describe the less-than-ininitely sharp edge of the rebound in the post-spike discharge rate immediately after the deadtime. In the context of the transient response, the additive noise is capable of describing the shape and height of the first peak in the PST histogram. The first spikes in the responses to repeated presentations of the same stimulus are very tightly locked to the stimulus onset but do not occur exactly at the same time. PST histograms derived from ‘noise free’ simulations are characterized by a first peak that is as narrow as the binwidth. In comparison, PST histograms derived from simulations that included additive noise are characterized by a wider first peak that is similar to the one observed in the PST histograms derived from measured discharges.

An alternative source of noise that may explain the shape of the first peak is associated with variations in the latency period from one presentation to another. Under this scenario, additive noise is significant only at long post-stimulus time when the discharge rate is low, while latency variability dominates the ‘jitter’ in the first peak. Thus, each of these two phenomena, the shape of the step-like change in the post-spike discharge rate and the shape of the first peak in the PST histogram, may be caused by different noise sources. However, the additive jitter model is elegant and powerful in its ability to generate discharges that are similar to the measured ones with respect to both of these subtle aspects, covering phenomena that are observable as early as the first peak as well as during the sustained portion of the response. While the additive noise was sufficient in most cases, it was still necessary to add latency noise in some simulations to achieve best results.

3.4.3 Simulations

The transient response of LSO neurons is simulated by using the same method used for simulating the sustained response except that the stimulus dependent parameters are varied with the post-stimulus time according to the functional expressions defined above (equations 3.22 – 3.24). A curve fit of the form of equation 3.16 is found for
the maximum likelihood estimate of the intensity amplitude and is used to specify the time course of the intensity amplitude in equation 3.22. Similarly, a curve fit of the form of equation 3.17 is found for the total baseline shift and is used to specify the time course of the total baseline shift in equation 3.23.

The time course of the absolute deadtime is derived from the time course of the shortest interval and from the estimate of the sustained absolute deadtime. The sustained absolute deadtime provide an upper limit on the value of the absolute deadtime during the transient response and should be attained during the sustained response. When the suppress-and-rebound is triggered, the shortest interval is equal to the absolute deadtime in a 'noise free' case; and provides a lower bound on the duration of the absolute deadtime when jitter does exits. These two bounds on the duration of the absolute deadtime, namely the sustained absolute deadtime and the time course of the shortest interval, do not define the time course of the absolute deadtime completely. The time course of the absolute deadtime is derived systematically in three steps. First, a curve fit of the form of Equation 3.17 is found for the lower bound on the absolute deadtime. Secondly, this curve fit is shifted vertically by a constant magnitude so that the final duration of the absolute deadtime is equal to the sustained absolute deadtime. Finally, in some cases it was necessary to further shift the curve fit of the absolute deadtime to achieve good fit between the simulated and measured PST histograms. In those cases, the curve fit was clipped at the level corresponding to the sustained absolute deadtime.

3.4.4 Simulation results

The PST histograms generated from simulated discharges are superimposed, for comparison, on PST histograms generated from the measured discharges for the slow chopper (Figure 3.13), the fast chopper (Figure 3.14) and the bimodal neuron (Figure 3.15) analyzed above. The transient portions of the PST histograms are compared in details in the right columns of these figures. The comparisons demonstrate the power
of the transient model in generating discharges characterized by a transient chopping response that is very similar to the measured one.

Equations 3.24–3.22, instantiated by the parameters specified in Table 3.4.4, and demonstrated in Figures 3.9–3.11, were used to simulate the time course of the stimulus dependent parameters. The time course of the absolute deadtime is a (vertically) shifted version of the curve fit shown in Figures 3.10—Figure 3.11. Note that the time constant of the transient in each parameter varies within a narrow range for the same neuron across different stimulus levels. Comparing the time constant of the transient in the different parameters, the time constant of the decay of the intensity amplitude is the smallest, corresponding to the sharp decay of the estimated intensity amplitude.

The analyze-simulate cycle—demonstrated for example in the pairs of figures (3.9,3.13), (3.10,3.14), (3.11,3.15), can be completed by estimating the time course of the stimulus dependent parameters from the simulated discharges. These estimated functions can be compared with the known functions that were used to drive the simulations or equivalently, with the respective estimated functions derived from the measured discharges. This exercise is demonstrated in Figure 3.16 for the fast chopper neuron analyzed in Figure 3.10 at two stimulus levels. The estimates derived from the simulated discharges agree well with the estimates derived from the measured data (and hence with the transient functions used to drive the simulations). The only subtle discrepancy is evident during the transient change in the duration of the shortest interval: The shortest interval observed in the simulated discharges is shorter than the one observed in the measured discharges (under the higher excitatory stimulus level only). This discrepancy suggests that either:

- The jitter model does not describe accurately the noise processes or their effects on the timing of spikes. As noted above, the shape of the first peak in the PST histogram and the shape of the leading edge of the rebound in the recovery
Figure 3.13  Simulation vs. measurements
of slow chopper transient response

The PST histograms (binwidth 100 μs) derived from recorded discharges of a slow chopper (thick lines) compared with those derived from simulations (thin lines). The details of the transient responses are compared in the right column. The parameters used in the simulations are specified in Table 3.4.4; The time course of the intensity amplitude and the total baseline shift are shown in Figure 3.9. The absolute deadtime is constant.
Figure 3.14  Simulation vs. measurements of fast chopper transient response

The PST histograms (binwidth 100 μs) derived from recorded discharges of a fast chopper (thick lines) compared with those derived from simulations (thin lines). The details of the transient responses are compared in the right column. The parameters used in the simulations are specified in Table 3.4.4. The time course of the intensity amplitude and the total baseline shift are shown in Figure 3.10. The time course of the absolute deadtime is a (vertically) shifted version of the curve fit shown in Figure 3.10.
Figure 3.15 Simulation vs. measurements of bimodal unit transient response

The PST histograms (binwidth 100 μs) derived from recorded discharges of a bimodal unit (thick lines) compared with those derived from simulations (thin lines). The details of the transient responses are compared in the right column. The parameters used in the simulations are specified in Table 3.4.4. The time course of the intensity amplitude and the total baseline shift are shown in Figure 3.11. The time course of the absolute deadtime is a (vertically) shifted version of the curve fit shown in Figure 3.11.
Table 3.2 Parameters for simulating complete—transient and sustained—monaural response

<table>
<thead>
<tr>
<th>Neuron type</th>
<th>Stimulus</th>
<th>Intensity amplitude $\mu$</th>
<th>Absolute deadtime $d$</th>
<th>Total baseline shift $a$</th>
<th>latency average $\sigma$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>final dB</td>
<td>transient amplitude Spikes/s</td>
<td>final ms</td>
<td>trans. amp. ms</td>
</tr>
<tr>
<td>Slow chopper-B</td>
<td>(+30/-)</td>
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<td>80100</td>
<td>7.40</td>
<td>1.4</td>
</tr>
<tr>
<td></td>
<td>(+22/-)</td>
<td>1650</td>
<td>30300</td>
<td>11.50</td>
<td>1.4</td>
</tr>
<tr>
<td>Fast chopper-A</td>
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<td>11700</td>
<td>12373400</td>
<td>3.84</td>
<td>1.6</td>
</tr>
<tr>
<td></td>
<td>(+20/-)</td>
<td>2750</td>
<td>18416800</td>
<td>2.64</td>
<td>1.9</td>
</tr>
<tr>
<td>Fast chopper-B</td>
<td>(+30/-)</td>
<td>22000</td>
<td>156468000</td>
<td>2.70</td>
<td>1.38</td>
</tr>
<tr>
<td>Bimodal-A</td>
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<td>17706660</td>
<td>5.52</td>
<td>1.5</td>
</tr>
<tr>
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<td>(+ 4/-)</td>
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<td>13700</td>
<td>23.70</td>
<td>1.55</td>
</tr>
</tbody>
</table>

The values of the stimulus dependent parameters during simulations of the monaurally induced discharges.

The values of the stimulus independent parameters were held constant during simulations and are specified in Table 3.1.

The excitatory latency is modeled as a Gaussian random variable with the specified average and standard deviation $\sigma$ (last columns).
function may result from the effects of different noise generating mechanisms that may not affect most of the transient response.

- The additive noise modeled here is appropriate but its effect on the estimation of the absolute deadtime may vary during the response. For example, the effect of the additive noise on the difference between the duration of the absolute deadtime and the duration of the shortest interval may depend on the percentage of intervals that are affected by the suppress-and-rebound process.

Similar conclusions are drawn from the comparison of the corresponding analysis results of other neurons. The transient response is successfully modeled, thereby supporting the postulate that the transient response arises from transients in the stimulus dependent parameters.
Figure 3.16  Estimated transient variations during simulated vs. measured responses

The time course of the intensity amplitude (upper row), total baseline shift (middle row), and shortest interval (lower row) are estimated from the simulated discharges and compared with the estimates derived from the measured discharges. The match is very good except for the shortest interval during the transient response at the higher ipsilateral stimulus level; the shortest interval produced by simulations are shorter than the observed ones.
Chapter 4

Binaural response - excitatory/inhibitory interaction

LSO neurons are excited by stimulation of the ipsilateral ear and inhibited by stimulation of the contralateral ear. Hence, a LSO neuron may discharge at the same mean rate in response to different combinations of ipsilateral and contralateral stimulus levels. However, while the discharge rate may be the same, the discharge patterns do depend on the specific input conditions, suggesting that the inhibitory effect is not symmetrically opposite to the excitatory effect. Indeed, once the complex effects of the suppress-and-rebound process, which depend on the intensity amplitude, are discounted, the inhibitory effect is revealed to only scale the intrinsic recovery function.

The effect of simultaneous stimulation of the contralateral ear on the initial chopping pattern are attributed to transients in the scaling factor interacting with the transients in the parameters that depend on the excitatory stimulus level. While this may not be the only possible model, it is capable of producing discharge patterns that are similar to the measured ones both in their statistical and in their temporal characteristics.

4.1 Binaural sustained response - Analysis

4.1.1 Inhibition not restricted to input or output interactions

Recent studies comparing LSO unit discharges to monaural and binaural stimulation [69, 70] questioned the hypothesis that the pattern of LSO unit discharges de-
pends only on the average discharge rate independent of the stimulus conditions [25]. Figures 4.1—4.3 summarize the results of these studies. The effects of contralateral stimulation on ipsilaterally elicited discharges are illustrated by comparing the binaural response elicited by simultaneous stimulation of the two ears to those elicited under two monaural stimulus conditions: The monaural control stimulus at the ipsilateral level used to elicit the binaural response and the monaural comparison stimulus reduced in level to elicit a mean discharge rate similar to that of the binaural response. Figure 4.1 is composed of PST histograms derived from the responses of a slow chopper and a fast chopper under these three stimulus conditions. Note that contralateral stimulation (middle histograms) eliminates the chopping pattern except for a brief poststimulus-onset interval where the chopping is similar to that elicited by the monaural control stimulus (top histograms). In comparison, reducing the ipsilateral stimulus level (bottom histograms) has the effect of reducing the overall chopping rate and does not eliminate the later chopping pattern.

The recovery functions of discharges under binaural stimulation and monaural comparison stimulation also differ despite similar average discharge rates (Figure 4.2). The recovery under binaural stimulation starts after a shorter deadtime (Figure 4.2, left) or at a higher discharge rate (Figure 4.2, right) and rises thereafter at a lower slope compared with the recovery under monaural comparison stimulation. Thus, the effects of inhibition on the studied statistical measures of LSO unit discharges are not symmetrically opposite to the effects of excitation. This observation questions statistical models of LSO E/I unit activity that assume that the effect of inhibition on the membrane potential is symmetrically opposite to the effect of excitation [12]. The results portrayed in Figures 4.1 and 4.2 were typical, leading to the conclusion that the inhibitory process in LSO units is not confined to linear interactions with the excitatory process at cell input.

Comparison of the conditional mean functions (Figure 4.3), which describe the dependency of the spike-generation mechanism on the duration of the previous interval,
Figure 4.1 PST histograms of binaurally and monaurally elicited responses

Examples of poststimulus-onset time (PST) histograms generated by a slow chopper (left column, binwidth 250 µs) and a fast chopper (right column, binwidth 500 µs) that illustrate the effects of simultaneous stimulation, with no interaural onset time delay, of the contralateral ear on the ipsilaterally elicited discharges. Indicated at the top of each histogram are, to the left the stimulus levels expressed in dB above unit threshold (ipsilateral level/contralateral level) and, to the right, r the mean sustained discharge rate in spikes per second. The PST histograms were generated from the monaural control responses (top row), the binaural responses (middle row), and monaural comparison responses (bottom row).
Figure 4.2  Recovery of binaurally and monaurally elicited responses
Comparison of the recovery functions of monaurally and binaurally elicited sustained discharges for a slow chopper (left, binwidth 100 µs) and a fast chopper (right, binwidth 50 µs) illustrates that the recovery under binaural stimulation (thick line) differs from that under monaural stimulation (thin lines). The recovery functions were computed from the interval histograms of the sustained discharges of the slow chopper (in PST interval 40 – 100 ms) and fast chopper (in PST interval 75 – 200 ms) illustrated in Figure 4.1. The stimulus levels are indicated in the parentheses (ipsilateral level/contralateral level) in dB above unit threshold.
indicates that contralateral inhibition does not affect serial dependence. The slope of the conditional mean function remains unchanged when the contralateral stimulus is presented, while the decreased mean rate has the effect of shifting the conditional mean function upward. Hence, models which manipulate the monaurally elicited spike trains to derive the binaurally elicited spike trains, by spike-canceling for example, are inappropriate [45].

4.1.2 Inhibition revealed to scale the unit recovery function

The nature of binaural interaction emerges when studying the recovery of LSO units under increasing contralateral stimulus levels (Figure 4.4). The major effect of increasing the contralateral inhibitory stimulus level, while holding the ipsilateral stimulus level constant, is to scale the recovery functions. More precisely, the shapes of the recovery functions appear to be inhibition-invariant: Only the scaling magnitude varies with the inhibitory stimulus level. To demonstrate this effect, the scaling factor between the recovery function characterizing the binaural response and the one characterizing the monaural control response was estimated using homogeneous linear regression. Noting that the monaural control response is characterized by higher discharge rates compared to the binaural response, and consequently by a narrower and 'smoother' interval histogram, the corresponding recovery function was assumed exact. The interval histogram of the binaural response was used as an estimate of the uncertainty associated with the measurement of the recovery function of the binaural response. Thus, the scaling factor was determined by computing the homogeneous linear regression of the binaural post-spike discharge rates against the monaural control post-spike discharge rates weighted by the binaural interval histogram. Intervals immediately after the absolute deadtime were omitted from the regression analysis in those cases when it was apparent that the 'suppress-and-recovery' process affected the shape of the recovery function. The estimated scaling factor $\gamma$ was used to scale the recovery function characterizing the monaural control response (top row of graphs).
Figure 4.3  Conditional mean of binaurally and monaurally elicited discharges

Comparison of the conditional mean functions of monaurally and binaurally elicited sustained discharges for a slow chopper (left, binwidth 100 μs) and a fast chopper (right, binwidth 50 μs) illustrates that inhibition does not affect the strength of serial dependency. The conditional mean functions were computed from the the sustained discharges of the slow chopper (in PST interval 40 – 100 ms) and fast chopper (in PST interval 75 – 200 ms) illustrated in Figure 4.1. The stimulus levels are indicated in the parentheses (ipsilateral level/contralateral level) in dB above unit threshold.
The scaled recovery functions are superimposed (thin lines) on the binaural recovery functions (thick lines) in the lower three rows of graphs in Figure 4.4, with the corresponding scaling factor $\gamma$ marked above each graph.

When scaled, the recovery function characterizing the monaural control response matches well the recovery functions characterizing the binaural responses at different ILDs, as demonstrated for the slow chopper (Figure 4.4, left) and for the bimodal unit (Figure 4.4, right). The match for the fast chopper (Figure 4.4, middle) is adequate at long intervals, but fails at short intervals immediately after the deadtime: The likelihood of firing at short intervals is disproportionately high under binaural stimulation.

Be that as it may, analysis of other LSO units’ discharges supports the conclusion that the main effect of contralateral inhibition is the scaling of the monaural recovery function. For some units, the likelihood of firing at short intervals immediately after the deadtime appears to be higher than expected from a uniform scaling of the monaural recovery function (Figure 4.4, middle). This apparent deviation from uniform scaling is traced in the next section to the effect of the suppress-and-rebound process. Thus, the scaling factor $\gamma$ summarizes the effect of contralateral inhibition on the discharges elicited by an ipsilateral excitatory input at a specific level and frequency.

For an array of LSO units (Figure 4.5), the scaling factor decreases with increasing contralateral (inhibitory) stimulus level or equivalently with decreasing ILD (interaural level difference — ipsilateral stimulus level minus contralateral stimulus level, expressed in decibels). The sensitivity of the scaling curves to the parameters of the excitatory stimulus, namely the ipsilateral level and frequency, has not been studied for lack of relevant experimental measurements. The scaling factor provides a fundamental measure of inhibitory effects: It changes monotonically with the ILD and gives rise to the reported monotonic relation between the mean rate and the ILD [39]. Because ILD can be related to azimuth, LSO units appear to be spatially
Figure 4.4  Binaural series - recovery function
The scaling effect of the contralateral inhibitory stimulus level on the recovery functions of a slow chopper (left column, binwidth 100 $\mu$s), a fast chopper (middle column, binwidth 50 $\mu$s) and a bimodal neuron (right column, binwidth 150 $\mu$s) are illustrated. The stimulus levels in dB above unit threshold are indicated within the parentheses at the upper left of each graph. Within each column the ipsilateral stimulus level was held constant while the contralateral stimulus level was increased. The recovery functions generated by the sustained discharges to the monaural control stimulus (top row) are scaled down by the factor $\gamma$ indicated at the top right of each graph in the bottom three rows and superimposed (thin line) on the recovery function produced by a binaural stimulus (thick line).
sensitive to the sound source's lateral position. Furthermore, fast choppers, which are characterized by a large dynamic range in discharge rate, seem to be sensitive over a significant part of the ipsilateral hemisphere close to midline. In contrast, slow choppers, which have a much smaller dynamic range in discharge rate, seem to be sensitive to sound sources located laterally and are completely inhibited by sounds emanating from locations close to midline. (The single slow chopping unit shown is representative of the ILD sensitivity of slow choppers.) Bimodal units, especially those that are characterized as slow chopping bimodal units, seem to be least sensitive to ILD changes and may respond over the widest range of azimuthal angles.

4.1.3 Interaction of the inhibitory process with the rebound process

Contralateral stimulation seems to scale the recovery function of the discharges generated by the ipsilateral stimulus, thereby reducing the discharge rate. As a consequence, the abundance of long interspike intervals in the binaural discharges increases. According to the shift model (Equation 2.8), the discharge probabilities following these long intervals are governed by conditional intensity functions that are shifted toward relatively short intervals. In the likely event that these conditional intensity functions "cross" into the absolute deadtime interval, the suppress-and-rebound process is triggered: The probability of firing during the absolute deadtime is reduced to zero and a proportional rebound in the probability of firing occurs immediately after the deadtime.

To summarize, the contralateral inhibitory input simply scales the conditional recovery function. The apparently complex effects of inhibition on the shape of the recovery functions immediately after the deadtime are a consequence of the interaction between three underlying processes: the deadtime process, the shifting process, and the scaling process. In contrast, the effect of reducing ipsilateral stimulus level on the recovery function is twofold: as ipsilateral stimulus level is decreased, the re-
Figure 4.5 Scaling curves

The estimated scaling factor $\gamma$ plotted as a function of interaural level difference ($ILD =$ ipsilateral stimulus level - contralateral stimulus level). The scaling factor required to match the scaled recovery function of the monaural control discharges to binaural discharges decreases with increasing contralateral inhibitory stimulus level, that is, it decreases as a sound source moves toward the midline.
covery function shifts toward longer intervals and increases with lower slopes. These complicated effects are quantified in the next section.

4.2 Binaural sustained response - modeling and simulations

4.2.1 Relation of the intensity to binaural stimulus conditions

The inhibitory contralateral stimulus scales down the conditional intensity function

\[ \tilde{\mu}(\tau_{n+1}; \tau_n) = \mu_0(E)S(E, I)\{\tau_0 [\tau_{n+1} - d(E) - s(\tau_n; E)] + g(\tau_{n+1}; \tau_n; E)\}u(\tau_{n+1} - d(E)) \]  

(4.1)

where the only new factor \( S(E, I) \) (compare with Equation 3.3) describes how the scaling factor decreases with increasing inhibitory stimulus level under a given excitatory stimulus level. A good initial estimate for the scaling \( S(E, I) \) is provided by computing the ratio \( \gamma \) between the corresponding monaural and binaural recovery functions as described in Section 4.1.2. The expression for the shifting function \( s(\cdot; E) \) and the rebound function \( g(\cdot; \tau_n; E) \) are the same as those given in the context of the monaural model in Section 3.2, Equations 3.2–3.4, respectively. The intrinsic recovery function is a saturated linearity of the form given in Section 2.3, Equation 2.7.

The model clearly distinguishes between excitatory and inhibitory mechanisms: Their effects are not symmetrically opposite. The excitatory and inhibitory effects—described as operators applied on the intrinsic recovery functions—are schematically illustrated and contrasted in Figure 4.6 (upper panels). Three-dimensional plots of the intensity as a function of the current interval \( \tau_{n+1} \) (time elapsed since last discharge), and the previous interval \( \tau_n \) are illustrated in the lower three panels of Figure 4.6 to contrast the effects of decreasing excitation and increasing inhibition on the intensity function. The minor effect of the excitatory stimulus level on the duration of the absolute deadtime is not included. Increasing inhibition affects only the scale of the intensity function (lower right and central panels); decreasing excitation produces more complicated effects, including a dramatic change in the form of the intensity
(rebound eliminated) and increased apparent deadtime (lower left and central panels). The overall effects on the recovery function computed from the regular (unconditional) interval histogram are further complicated in either case by the corresponding effects on the relative distribution of interval durations.

The dependence of the scaling factor on the ILD - the ratio between the excitatory and inhibitory level - corresponds to the unit's spatial sensitivity. Whether this dependence is affected by the absolute stimulus level as well was left unanswered due to a lack of data. However, regardless of the absolute stimulus level, the scaling factor approaches unity at large ILD (e.g., under monaural stimulation).

4.2.2 Simulation results

Computer simulation of the response of different neurons to both monaural control and binaural stimulations were performed to confirm that the effect of inhibition is simply to scale down the intrinsic recovery function. Simulations of the monaural responses were first obtained by adjusting the parameters defining the intensity function: the intensity amplitude \( \mu_0 \), the saturation interval \( R \) defining the intrinsic recovery function \( r(\cdot) \), the parameters of the shifting function \( a \) and \( b \), and the rebound time constant \( T \). The response to the binaural stimulus was then simulated by adjusting only the scaling factor \( S(E, I) \). To demonstrate the model's ability to generate spike trains with statistics similar to those generated by LSO units, the recovery and conditional mean functions derived from the sustained portion of the simulated spike trains (thin lines) are superimposed on those derived from the sustained portion of the measured spike trains (thick lines) for a slow chopper in Figure 4.7, a fast chopper in Figure 4.8, and a bimodal unit in Figure 4.9.

The measured and simulated statistics of the discharges elicited by a slow-chopper, shown in Figure 4.7, demonstrate the scaling effect of inhibition with no interference from the interaction with the deadtime, i.e. there is no rebound. The statistics of the simulated discharges of a fast-chopper (Figure 4.8) demonstrate the effect of the
Figure 4.6 Excitatory/Inhibitory effects
Illustration comparing the main effects of excitation and inhibition on the intrinsic recovery function (upper panels) and on the conditional intensity functions (central and lower panels). The three-dimensional plots describe the intensity as a function of the current interval $\tau_{n+1}$ and the previous interval $\tau_n$. The intensity describing the response to a monaural control stimulus (central panel) provides a baseline. The effect of decreasing excitation on the intensity description (lower left) is contrasted with the effect of increasing inhibition (lower right). To facilitate comparison, all the 3-dimensional illustrations are plotted on the same scales. Also, the minor effect on the duration of the absolute deadtime is not included.
Figure 4.7 Simulations - slow chopper binaural series
The recovery functions (left column) and conditional mean functions (right column) derived from discharges of a slow chopper (thick lines) compared with those derived from simulations (thin lines). The amplitude of the intensity function used to generate the simulation of the monaural response, \((40/-)\), has been scaled to generate the simulations for each of the binaural stimulus conditions. The scaling factor for each simulation, \(S\), is indicated at the top right of each graph.
Figure 4.8  Simulations - fast chopper binaural series

The recovery functions (left column) and conditional mean functions (right column) derived from discharges of a fast chopper (thick lines) compared with those derived from simulations (thin lines). The amplitude of the intensity function used to generate the simulation of the monaural response, \((30/-)\), has been scaled to generate the simulations for each of the binaural stimulus conditions. The scaling factor for each simulation, \(S\), is indicated at the top right of each graph.
Figure 4.9  Simulations - bimodal neuron binaural series
The recovery functions (left column) and conditional mean functions (right column) derived from discharges of a bimodal unit (thick lines) compared with those derived from simulations (thin lines). The amplitude of the intensity function used to generate the simulation of the monaural response, \((97/-)\), has been scaled to generate the simulations for each of the binaural stimulus conditions. The scaling factor for each simulation, \(S\), is indicated at the top right of each graph.
interaction of the shifting recovery function with the absolute deadtime. The complete model successfully generates the disproportionate increase in the likelihood of firing immediately after the deadtime when the inhibitory stimulus level is increased, (compare with Figure 4.4 middle column). Figure 4.9 demonstrates the ability of the model to simulate the statistics of the sustained discharges generated by a bimodal unit. In particular, negative aging—segments in the recovery functions where the probability of firing decreases (Figure 4.9)—are shown to result from the suppress-and-rebound phenomenon even when the intrinsic recovery function is monotonically increasing.

The values of the scaling factors $S(E, I)$ used in the above simulations are shown in Table 4.1 along with the corresponding estimates $\gamma$ based on regression analysis of the binaural recovery function on the monaural recovery function. The scaling factors used in the simulations and the ones computed by regression vary with inhibition in a similar way. However, their values differ and are usually higher when computed by regression. This discrepancy is attributed to the fact that the regression analysis is computed from the overall recovery functions whereas the scaling factors used in the simulation describe the inhibitory effect in a more precise way. To validate this hypothesis, the regression analysis has been applied to the recovery functions derived from simulated responses to binaural and monaural stimulations where the underlying scaling factor $S$ is known. The computed scaling factors overestimated the known underlying scaling factor $S$, thus supporting this conjecture.
Table 4.1  Scaling factors estimated from data analysis and scaling factors used in simulations

<table>
<thead>
<tr>
<th>Unit Type</th>
<th>Stimulus E/I (dB/dB)</th>
<th>ILD (dB)</th>
<th>Estimated Scaling factor ($\gamma$)</th>
<th>Scaling factor ($S$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slow Chopper-A</td>
<td>+40/+05</td>
<td>40</td>
<td>0.4</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>+40/+10</td>
<td>35</td>
<td>0.19</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td>+40/+15</td>
<td>30</td>
<td>0.08</td>
<td>0.033</td>
</tr>
<tr>
<td>Fast Chopper-B</td>
<td>+30/+05</td>
<td>27</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>+30/+10</td>
<td>22</td>
<td>0.3</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td>+30/+13</td>
<td>19</td>
<td>0.16</td>
<td>0.125</td>
</tr>
<tr>
<td>Bimodal-B</td>
<td>+37/+15</td>
<td>28</td>
<td>0.58</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>+37/+25</td>
<td>18</td>
<td>0.36</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td>+37/+35</td>
<td>8</td>
<td>0.14</td>
<td>0.08</td>
</tr>
</tbody>
</table>

E/I, Excitatory and Inhibitory stimulus level in dB above threshold; ILD, Interaural Level Difference (including excitatory and inhibitory threshold differences).
Scaling factor estimates $\gamma$, based on regression analysis of the binaural recovery function on the monaural recovery function, are compared with the values of the scaling factors used in the simulations $S(E, I)$. 
4.3 Binaural transient response - analysis

4.3.1 Chopping response

Simultaneous stimulation of the contralateral ear reduces the mean discharge rate and affects the temporal pattern of the initial chopping response, as demonstrated in Figure 4.1 (second vs. first row). The chopping pattern during a brief post-stimulus-onset interval is similar to that elicited by the monaural control stimulus (monaural stimulus at the ipsilateral level used to elicit the binaural response). Thus, the initial chopping response may be undisturbed by binaural tone bursts having an ILD that favors the ipsilateral ear, even when there is no interaural onset time delay. The later part of the ipsilaterally elicited chopping response is eliminated by the contraterally presented stimulus: The discharge rate is greatly reduced and may be completely suppressed. A transient gradual increase in the discharge rate follows until a sustained level is reached. Thus, two distinguished transient parts characterizes the binaural response: An initial transient response that reflects only the excitatory effect and a later transient response that results from the transient excitatory and inhibitory effects. As the contralateral stimulus level is increased, the abrupt transition between these two transient parts occurs at earlier post-stimulus times; at very large contralateral stimulus levels the first transient part may be completely eliminated.

During the second part of the transient binaural response the discharge rate is very low and is varying with time. Low discharge rates correspond to long interspike intervals during which the stimulus dependent parameters may vary significantly. Consequently, the assumption that the stimulus dependent parameters are constant during an interspike interval may not be appropriate for analyzing the transient binaural response. Note that in analyzing the transient monaural response, the assumption that the parameters are constant during an interval is more reasonable: The intervals are very short when the rate of change in the parameters is large while the rate of change is small when the intervals become long. The maximum likelihood estima-
tion technique that was developed for analyzing the monaurally elicited discharges is therefore not suitable for analyzing the transient binaural response.

The model of the sustained binaural response, presented above in Section 4.2.1, indicates that inhibition scales the intensity function. The absolute deadtime \(d\) and the baseline shift \(a\) are independent of the inhibitory (contralateral) stimulus level and depend only on the excitatory (ipsilateral) stimulus level. It is therefore reasonable to assume that the time courses of the absolute deadtime and baseline shift during the binaural response are the same as the respective time courses during the monaural control response. Thus, only the time course of the intensity amplitude has to be estimated from the binaurally elicited discharges.

### 4.3.2 Estimation technique - binaural case

Given the time courses of the absolute deadtime \(d(t; E)\) and the total baseline shift \(a^*(t; E)\) derived by analyzing the monaural control response, the recovery function can be evaluated at any time during the binaural response:

\[
r^*(\tau_{n+1}; \tau_n; t; E) = r[\tau_{n+1} - s^*(\tau_n; t; E)] + g(\tau_{n+1}; \tau_n; t; E)
\]  

(4.2)

where \(r^*(\cdot; \tau_n; t; E)\) is the conditional recovery function and \(r(\cdot)\) is the intrinsic recovery function. Thus, the intensity amplitude is the only unknown function in the expression for the intensity of the underlying point process description of the binaurally elicited discharges.

\[
\tilde{\mu}(\tau_{n+1}; \tau_n; t; E) = \mu_{BIN}(t; E; I)r^*(\tau_{n+1}; \tau_n; t; E)
\]  

(4.3)

where \(\mu_{BIN}(t; E; I)\) is the intensity amplitude of the binaurally elicited discharges and \(I\) is the inhibitory stimulus level.

A maximum likelihood estimate can be derived which maximizes the corresponding likelihood function with respect to variation in the intensity amplitude \(\mu_{BIN}(t; E; I)\)
at any post-stimulus time $t$ independent of its value at other times [40].

$$\hat{\mu}_{BIN,ML} = \frac{1}{r^*(\tau_{n+1}; \tau_n; t; E)} \frac{dN_t}{dt}$$  \hspace{1cm} (4.4)

where $\hat{\mu}_{BIN,ML}$ is the maximum likelihood estimate of the intensity amplitude $\mu_{BIN}$, and $N_t$ is the counting process. This estimate is nonzero only when a spike occurs (and the second term is non zero) and has the effect of changing the contribution of a spike in any further computation according to the inverse of the recovery function at the time of occurrence.

The corresponding maximum likelihood PST histogram can be computed from spike trains after the proper weighting described by Equation 4.4 is applied. When the intervals are long relative to the duration of the absolute deadtime, the expected value of the maximum likelihood PST histogram equals samples of $\mu_{BIN}(t; E; I)$.

$$\hat{p}_{ML}(n)|_{E,I} = \mu_{BIN}(n\delta; E; I)$$  \hspace{1cm} (4.5)

where $\delta$ is the binwidth used in computing the PST histogram and $\hat{p}_{ML}(n)$ is the expected value of the maximum likelihood PST histogram at the $n$th bin.

The intensity amplitude of the binaurally elicited discharges reflects the shunting interaction between the excitatory and inhibitory effects.

$$\mu_{BIN}(t; E; I) \equiv \mu_0(t; E)S(t; E; I)$$  \hspace{1cm} (4.6)

where $S(t; E; I)$ is the time course of the scaling factor—the inhibitory effect—which, as indicated, may depends on the excitatory stimulus level. For comparison with the time course of the intensity amplitude $\mu_0(t; E)$—the excitatory effect—it is more meaningful to look at the time course of the inverse of the scaling factor. Given samples of the intensity amplitude of the binaurally elicited discharges $\mu_{BIN}(t; E; I)$ and the time course of the intensity amplitude of the monaurally elicited discharges (at the same ipsilateral stimulus level) $\mu_0(t; E)$, the time course of the scaling factor, or its inverse, can be derived by a curve fit to the corresponding samples [84]:

$$S^{-1}(n\delta; E; I) = \frac{\mu_0(n\delta; E)}{\mu_{BIN}(n\delta; E; I)}, \quad \mu_{BIN}(n\delta; E; I) > 0.0$$  \hspace{1cm} (4.7)
4.3.3 The time course of the scaling factor

Maximum likelihood PST histograms, computed from binaural discharges produced by fast chopper-A, are compared in Figure 4.10 with the regular PST histograms (thick lines). The responses of the same unit to the monaural control stimuli (same ipsilateral stimulus levels) are analyzed in Section 3.3.3, Figure 3.10. The absolute deadtime and the total baseline shift were computed at the time of occurrence of each spike based on Equations 3.24 and 3.23 and the parameters specified in Table 3.4.4. The stimulus independent parameters were assumed constant, having the values given in Table 3.1. The recovery function, Equation 4.2, was evaluated at the time-of-occurrence of each spike and the appropriate correction, Equation 4.4, was applied before computing the maximum likelihood PST. To facilitate the comparison of the shapes of the PST histograms, the histograms are plotted on two different scales so that their sustained levels match. The shapes of the two PST histograms differ mainly during the second transient part of the binaural response: The maximum likelihood estimate is relatively lower during this period where the intervals are very long and the positively aging intensity makes it more likely for a spike to occur as the time elapsed since the last interval increases.

The time course of the inhibitory effect—the inverse scaling factor—is derived from the maximum likelihood PST histogram by factoring out the excitatory effect of the ipsilateral stimulus. The time course of the intensity amplitude during the ipsilaterally elicited response was estimated previously, Figure 3.10, and has the form of Equation 3.22 with the parameters specified in Table 3.4.4. The estimates of the inverse scaling factors $S^{-1}(t; E; I)$ derived from the responses of fast chopper-A under two stimulus conditions are shown in Figure 4.11 (upper right, bold line). Note that while the two stimulus conditions produce the same ILD, the scaling factors characterizing the inhibitory effects evolve differently with the post-stimulus time, and reach different steady state scaling levels (Table 4.2).
Examples of the time course of the inverse scaling factor derived by applying the above procedure to binaural responses of other neurons are illustrated for another fast chopper (fast chopper-B, upper left) and for a slow chopper (slow chopper-B, lower row) in Figure 4.11. The parameters defining the intensity function during the monaural response of the same ipsilateral stimulus level are specified in Table 3.1 and Table 3.4.4. Exponential curve fits, of the same form as the exponential fit to the intensity amplitude of the monaurally elicited discharges (Equation 3.16), are superimposed on the inverse scaling curves. The exponential functions that fit the inverse scaling curves are specified in Table 4.2.

4.4 Modeling - binaural response

4.4.1 Transient model of the binaural response

The point process model of transient and sustained monaural response is extended to describe the transient and sustained binaural response by scaling the intensity function. The point process model of the binaural response—transient and sustained—is

\[
\tilde{\mu}(\tau_{n+1}; \tau_n; t; E) = \mu_0(t; E)S(t; E; I)\{r[\tau_{n+1} - s^*(\tau_n; t; E)] +
g(\tau_{n+1}; \tau_n; t; E)\}u(\tau_{n+1} - d(t; E))
\] (4.8)

where the scaling factor \(S(t; E; I)\) depends explicitly on the post-stimulus time. The inverse of the scaling factor varies exponentially during the response to tone burst in the same manner as the intensity amplitude of the monaurally elicited discharges \(\mu_0(t; E)\).

\[
S^{-1}(t; E; I) = F_f(E; I) + F_s(E; I)\exp(-t/\tau_F(E; I)), \quad t > l_i
\] (4.9)

where, \(F_f(E; I)\) is the final inhibitory effect—the inverse of the scaling factor used to simulate the sustained portion of the binaural response, \(F_s(E; I)\) is the scale of the transient decay, \(F_r(E; I)\) is the rate of decay of the inhibitory effect, and \(l_i\) is the
Figure 4.10  Maximum likelihood PST - fast chopper
Maximum likelihood PST histograms (thin line, right scale, binwidth 500 μs) and regular PST histograms (bold lines, left scale, same binwidth) derived from the discharges of fast chopper-A at two binaural stimulus levels (indicated in parenthesis as ipsilateral/contralateral stimulus levels in dB above threshold) are compared. The scale of the maximum likelihood PST histogram was adjusted to match the levels of the histograms during the sustained portion of each response. When so adjusted, the shapes of the two types of PST histograms can be compared; the main difference is during the second part of the transient response (right column). See text for discussion.
Figure 4.11 Estimated transient inhibitory effect
Estimated time course of the inhibitory effect—the inverse scaling factor—derived from discharges of two fast choppers and one slow chopper. The binaural stimulus levels are indicated in parenthesis as ipsilateral/contralateral stimulus levels in dB above threshold. The parameters defining the intensity function during the respective monaural control responses are specified in Table 3.1 and Table 3.4.4. Exponential curve fits are overlayed in thin lines. The analysis was evaluated at every 1 ms.
inhibitory latency. The inhibitory latency is expected to be longer than the excitatory latency in those cases where the first ipsilaterally elicited spike is not suppressed by presentation of the inhibitory stimulus. Note that the ipsilateral and contralateral stimuli were presented simultaneously with no relative delay; while natural stimulus are expected to exhibit ITD that is correlated with ILD.

4.4.2 Simulation results

The PST histograms generated from simulated binaural discharges are superimposed in Figure 4.12 on the PST histograms generated from the measured binaural discharges analyzed above (Figure 4.11). The exponential functions that fit the inverse scaling curves are specified in Table 4.2. The other transient parameters—the excitatory intensity amplitude, the total baseline shift, and the absolute deadtime—vary with time in the same manner as during simulations of the corresponding monaural control response (Equations 3.22, 3.23 and 3.24, instantiated with the parameters specified in Table 3.4.4, respectively).

The inhibitory latency is slightly longer than the excitatory latency as indicated in Table 4.2. In some cases the contralateral stimulus affected the second peak in the PST histogram, or equivalently, "lengthened" the first interval [69]. In these cases, it was necessary to model the inhibitory latency as a random variable having a Gaussian distribution with a standard deviation \( \sigma \) as specified in Table 4.2. The subtle discrepancy between the PST histograms derived from simulated and measured binaural discharges of fast chopper-A at (+20/+10) is attributed to inaccuracies in modeling the inhibitory latency.

The response of fast chopper-B to two stimulus conditions with different ILDs is demonstrated on the PST histograms of the discharges of fast chopper-B in response to two stimulus conditions with different ILDs are shown on the right (top (+30/+13), bottom (+30/+05)). Recall that the excitatory and inhibitory stimuli were presented always simultaneously. It is therefore interesting to note that the different ILDs
are converted into different effective interaural time difference between the latencies of the excitatory and inhibitory inputs to the neuron. Hence different ILDs are converted into different effective ITDs that modulate the timing of the initial chopping discharges. The difference in the relative latency is around 2 ms (Table 4.2); much longer than natural ITD (with full scale of about 300 μs for cats).

The comparison between simulated and measured PST histograms demonstrates the power of the point process model to describe in details the timing of the discharges of LSO neurons to binaurally presented tone-bursts.
Figure 4.12 Simulation vs. measurements - transient binaural response
PST histograms (binwidth 500 μs) derived from recorded discharges (thick lines) are compared with those derived from simulations (thin lines). The initial 20 ms of the responses are compared in details in the insets. The parameters used in the simulations are specified in Table 3.4.4 and Table 4.2; with the time course of the stimulus dependent parameters shown in Figures 3.9–3.10 and Figure 4.11.
Table 4.2  Parameters used in simulations of the complete binaural response

<table>
<thead>
<tr>
<th>Neuron type</th>
<th>Stimulus</th>
<th>Scaling factor inverse $S^{-1}$</th>
<th>Inhibitory latency Average $\sigma$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(dB/dB)</td>
<td>Final amplitude</td>
<td>Transient time constant (ms)</td>
</tr>
<tr>
<td>Slow chopper-B</td>
<td>(+29/+12)</td>
<td>5.0</td>
<td>400</td>
</tr>
<tr>
<td>Fast chopper-A</td>
<td>(+20/+10)</td>
<td>4.0</td>
<td>48,360</td>
</tr>
<tr>
<td></td>
<td>(+30/+10)</td>
<td>15.0</td>
<td>332,000</td>
</tr>
<tr>
<td>Fast chopper-B</td>
<td>(+30/+13)</td>
<td>10.0</td>
<td>323,800</td>
</tr>
<tr>
<td></td>
<td>(+30/+05)</td>
<td>2.0</td>
<td>180</td>
</tr>
</tbody>
</table>

Numerical values for the parameters describing the time course of the inverse scaling factor during simulations. The values of all the other parameters are the same as during the corresponding simulation of the monaural control response and are specified in Table 3.4.4 and Table 3.1.
Chapter 5

Discussion

5.1 Point process modeling

The sustained discharges of LSO units under different stimulus conditions are described by a single point process model wherein the underlying intensity process is related to stimulus levels at the two ears. The model clearly factors the cell recovery characteristics from the effects of the stimulus conditions and the timing of previous spikes. Each unit is characterized by an intrinsic recovery function that is stimulus and history independent. The stimulus and history effects are described by shifting and scaling operators applied to the intrinsic recovery function: The serial dependency is described by a shift that is proportional to the length of the previous interval [41]. The excitatory stimulus effect is described by a baseline shift and by an amplification factor while the inhibitory stimulus effect is described by a scaling factor [82]. The model provides a unifying point process representation of the discharges produced by all three LSO unit types.

The simple nature of the stimulus effects is obscured by measurements of unconditional statistical quantities. Such measurements, as the usual interval histograms, often exhibit complex changes as a function of contralateral or ipsilateral stimulus levels. For example, as contralateral level increases, the interval histogram may convert from a unimodal form into a bimodal one. The conditional statistics of LSO unit activity reveal that the underlying structure of all activity is simple and based on unimodal interval histograms and monotonic recovery functions. Furthermore, the modeling work presented here suggests that LSO neurons may all have the same in-
**trinsic recovery function**—a saturating linear function. The model explains how the apparently complex behavior of LSO binaural responses results from the interaction of the unit’s shifting recovery function with its deadtime interval. Thus, the model based approach to data analysis has yielded a parsimonious model within which components of the point process intensity find simple interpretation. The experience gained in developing a point process model for LSO neuron discharge may encourage and enhance the ability to develop similar models for discharges of other neurons.

Within the context of the point process model, the differences in the response characteristics of the three LSO unit types are correlated (Table 3.1) with the strength of the serial dependence $b$, the baseline shift $a$, and the slope of the intensity function (the ratio between the intensity amplitude $\mu_0$ and the saturation interval $R$). The model developed here suggests that the later two parameters depend on the stimulus level, and indeed as the stimulus level changes so do the characteristics of the unit response. For example, a unit classified as a fast chopper based on its response to an ipsilateral stimulus at $+25$–$+35$ dB above unit threshold, may respond like a slow chopper at lower stimulus levels. Compared with fast choppers, slow choppers are characterized by a substantially longer baseline shift: the recovery of slow choppers starts after longer apparent deadtime. Other, less distinctive differences, include a slightly smaller slope of the intensity function and a relatively small serial dependence (Table 3.1). Bimodal neurons are characterized by either a small intensity slope $\frac{\mu}{R}$ or very strong serial dependence. While the differences in the baseline shift $a$ and in the intensity slope $\frac{\mu}{R}$ may reflect differences in the number of inputs (i.e. input rate) to the neuron, those differences may also be attributed to differences in the characteristics of the AHP channels as discussed below (Section 5.3.2).

Inhibitory and Excitatory effects are clearly distinguished. Decreasing the excitatory stimulus level reduces the discharge rate due to two mechanisms: The recovery function is both shifted toward longer intervals and scaled. In contrast, when the same reduction in discharge rate is achieved by increasing the inhibitory stimulus
level, only the scale of the intrinsic recovery function is affected. Consequently, the response to the second stimulus condition (increased inhibition) can be differentiated from the response to the first stimulus condition (decreased excitation) by comparing the number of relatively short intervals. Comparing a monaural discharge with a binaural discharge of similar mean rate, the binaural discharge should exhibit the relatively frequent occurrence of very short intervals accompanied by relatively frequent occurrence of long intervals. Thus, the discharge microstructure—the timing of the discharges in an individual spike train, or alternatively the shape of the interspike interval distribution—can be used to differentiate between responses elicited under different stimulus conditions producing the same mean sustained discharge rate. We pose the following question: To what extent is this information, rather than just the average rate, extracted by higher centers receiving inputs from the LSO? Are the differences in the characteristics of LSO unit responses to different stimulus conditions, which produce the same mean discharge rate, accidental or are they relevant for further information processing?

Description of LSO units response patterns to time-varying stimuli is simplified to specifying the temporal variations in the baseline shift, in the magnitude of the intensity process, and in the absolute deadtime. Other parameters of the model, including the strength of the serial dependency and the shape of the intrinsic recovery function, are invariant characteristics of the unit. These parameters do not vary with stimulus conditions and can be estimated from stationary portions of the response. The assumption that the transient response can be described in a similar way—with only the stimulus dependent parameters varying with the poststimulus time—result in a powerful technique for estimating the time course of these parameters and for modeling successfully the transient chopping response of LSO neurons to tone burst stimuli.
5.2 LSO Binaural processing

The E/I binaural response behavior of LSO units has been shown to be a characteristic of optimal level-based sound localization systems [39]. Theoretically, the optimum way of processing level cues is to produce a quantity that varies monotonically with ILD; that quantity is then used to estimate the source azimuth. According to our point process model, scaling of the recovery function summarizes the level-based binaural processing performed by the LSO units: The magnitude of the scaling factor $S(E, I)$ is determined by the ipsilateral (excitatory, $E$) and contralateral (inhibitory, $I$) stimulus levels. The functional dependency of the scaling factor on the inhibitory stimulus level, at a constant excitatory stimulus level, is monotone (Figure 4.5) as required for optimal level based sound localization. Most of the neurons analyzed here are sensitive to sound location over the same region of the ipsilateral hemisphere; with exceptions exhibiting sensitivity to regions either more lateral or mainly in the front.

For optimum estimation of sound source location, the scaling factor should not vary with the sound level but should be a function of ILD only (i.e., $S(E, I) = S(E/I)$). However, because of the nonlinear relation between the stimulus level and the discharge rate of the LSO inputs, it is expected that this optimum behavior does not exist over all stimulus conditions (e.g., Figure 4.11, fast chopper-A). More data recorded at different ILDs and stimulus levels are required to quantify the stimulus range over which the scaling factor depends only on the ILD irrespective of the stimulus level. Furthermore, since the relation between ILD and azimuthal angle is quite complicated and varies with tone frequency [37], LSO unit responses at different frequencies will also be required to completely specify the spatial sensitivity of the LSO. The resulting characterization of the scaling factor functional form will reveal the constraints imposed by the LSO on the processing that "higher centers" must perform to generate a good estimate of source location.

Encoding ILD in the average discharge rate of LSO neurons is enhanced by the negative serial inhibition exhibited by these neurons. Negative serial dependence
provides an error correction mechanism for estimating the average rate. Potential 
"higher centers" estimating ILD from the average mean rate of LSO neurons can 
obtain an accurate estimate after relatively short averaging time.

The highly structured transient chopping response of LSO neurons urges us to 
investigate possible utilisations of the timing of the initial discharges in the context 
of sound localization and discrimination. As noted in the analysis of the transient 
response, ILD affects the relative latency between the excitatory and inhibitory inputs; 
thereby resulting in an effective interaural time difference that modulates the 
response even in the absence of acoustic ITD [59]. This effective interaural time difference is larger than the ITD produced by the acoustic stimuli. Hence, it is possible 
that "higher center" sensitive to the timing of the discharges produced by individual 
neurons in the LSO, can extract the combined effect of the natural and effective ITDs. 
As long as the time evolution of the incoming discharges follows the "signature" of 
the monaurally elicited discharges, the estimate of the azimuth of the sound sources 
increases (more lateral). It is relevant to note in this context that there is a broad consenus that in many parts of the sensory nervous system, the identification of which nerve cells seems to be more important than the details of their activity [54, 60, 63]. However, the possibility of encoding information in the timing of individual spikes is not new. It has been postulated, for example, that the movement-sensitive neuron in the fly visual system encodes angular velocity in the timing of its discharges [3].

The error produced by an optimal leading edge ITD detector depends strongly 
on the assumed initial input rate [15]. When the onset input rate is higher than 
20,000 spikes per sec, time cues can be estimated more accurately than level cues. 
The extremely high intensity amplitude describing the discharges of LSO neurons— 
reflecting the extreme accuracy of the timing of the initial spikes—suggests that the 
LSO output may be used in computing the leading edge ITD, either directly or in comparison with discharges from units in a contralateral center [15].
5.3 Physiological Implications

5.3.1 Serial dependence and absolute deadtime

The negative serial dependence exhibited by LSO unit discharges may be attributed to a cumulative after-hyperpolarization (CAHP) mechanism as demonstrated by a stochastic spike generation model [23, 61]: The after-hyperpolarization arises from an increase in membrane conductance for potassium, which decays slowly (time constants of 2 – 7 ms were used in simulating responses of vestibular afferents [61]). Membrane channels with these characteristics have been identified as calcium-dependent, voltage-independent, potassium channels [32, 80]. The cumulation of the potassium conductance is critical for generating serial dependence. According to the cumulative after-hyperpolarization model, a spike is followed by a constant increase in the potassium conductance in addition to the potassium conductance left over from preceding activity. Hence, a short interspike interval contributes a large residual potassium conductance that inversely affects the probability of a subsequent spike, leading to a longer following interval. During a long interspike interval, the potassium conductance decays substantially, making it more likely for a short interspike interval to follow.

The absolute deadtime – a neuron's absolute refractory period – is commonly attributed to the voltage-dependent sodium and potassium channels involved in the spike generation process. These channels recover faster than the calcium-dependent voltage-independent potassium channels involved in the CAHP described above. The rebound phenomenon observed in LSO unit discharges indicates that excitatory synaptic events may continue to accumulate during the deadtime almost undisturbed by the spike generation process. As a consequence, when the average rate of excitatory synaptic events is high, there is some probability that the accumulated EPSPs could have produced a spike if the sodium channels were not inactive following spike initiation. If the summed EPSPs decay slowly, a spike is likely to be generated as soon as
the sodium channels recover from inactivation. Thus, the likelihood of firing at the end of the deadtime increases, reflecting the suppressed probability of firings during the deadtime and producing the rebound phenomenon.

The time constant of sodium inactivation is voltage dependent, ranging from less than .5 ms at positive membrane potentials to 5 ms at resting potential (based on measurements in a node of Ranvier of frog myelinated nerve fiber at 22 deg C [32]). Given the high discharge rates observed in LSO neurons (sustained discharges of up to 600 spikes/sec, and first interspike intervals as short as 1 ms), the time constant of recovery from inactivation is expected to be much smaller in LSO neurons (as supported by initial results from compartmental model of LSO neurons). The effect of spike initiation on the excitability of a neuron can be summarized by a time-varying threshold function [22, 31]. The threshold function is infinite during an absolute refractory period and decays to a steady state during a relative refractory period. The rebound process and the sharp increase in probability of firing at the end of the absolute deadtime implies that the decay of the threshold function (and possibly the recovery from sodium inactivation) are very quick. This conclusion is supported by fire-at-threshold simulations; simulating the interval histogram of high discharge rates neurons required a quickly decaying threshold function [23].

Recovery from sodium inactivation may also explain the time course of the duration of the absolute deadtime at the beginning of the response. As observed in Section 3.2 Figures 3.10–3.11, the absolute deadtime increases during the first 20 to 80 ms of the tone burst response. The steady-state inactivation level depends on the membrane potential: The percentage of inactive channels increases relatively sharply with depolarization above the resting potential. During the beginning of the response, the average membrane potential may increase (may depolarize) to a new average level, resulting in a higher percentage of inactive channels. Under this scenario, the effective threshold, and consequently the absolute deadtime, increase during the initial transient phase of the response.
According to a simplified spike initiation model, the cell produces a spike when the effect of the accumulated EPSPs on the membrane potential at the spike generator crosses a threshold voltage level. Due to the slow decay of the conductance of the AHP potassium channels, the effect of the accumulated EPSPs on the membrane potential depends on the level of the afterhyperpolarization potential. When the conductance of the AHP potassium channels is large, immediately after spike initiation, the accumulated EPSPs produce a relatively small depolarization, which is superimposed on the large AHP potential. As the conductance of the potassium channels decays, the same EPSPs produce a larger depolarization which, superimposed on the decaying hyperpolarization potential may lead to a new discharge. Accordingly, the probability of a discharge increases with the time elapsed since the last spike in a characteristic way that mirrors the decay of the conductance of the AHP potassium channels. This phenomenon along with the recovery from sodium inactivation may be the underlying mechanisms captured by the intrinsic recovery function and its non-decreasing nature.

5.3.2 Excitatory and transient effects

Physiological considerations support the observed shifting and scaling effects of the ipsilateral input on the intrinsic recovery function of LSO units. Excitatory terminals, containing round synaptic vesicles, are located on the distal dendrites [11, 24]. Presumably, within the LSO unit's dendrites the ipsilateral stimulus has the ultimate effect of producing excitatory post synaptic potentials (EPSPs) that sum and spread passively toward the cell body. As the excitatory stimulus level increases, the effect of the accumulated EPSPs on the membrane potential increases and may result in a new discharge even when superimposed on increasingly larger AHP potentials. Hence, increasing the excitatory stimulus level results in a nonzero probability of firing at shorter intervals, which corresponds to the shifting operation. Since the AHP potassium channels are located near the spike generation site, they have also
a divisive (shunting) effect on the EPSPs. Hence, as the conductance of the AHP potassium channels decay, a constant increase in the magnitude of the EPSPs will produce an increased effect on the membrane potential, which corresponds to the amplifying operation.

Two parameters determines the properties of the AHP potassium channels: The change in potassium conductance in response to an isolated spike $g_{k0}$ and the time constant of the decay of the potassium conductance $\tau_k$ [61]. The classification of LSO neurons into three groups may reflect variations in these parameters or in differences in the input rates. The large baseline shift characterizing the response of slow choppers may reflect either large initial potassium conductance $g_{k0}$, longer time constants $\tau_k$, or lower input rates. Changes in the potassium conductance are expected to affect only the baseline shift while longer decay time constants or lower input rates are expected to also reduce the slope of the intensity. Bimodal units are characterized by intensity functions that increase slowly (after the rebound effect) and by very small baseline shifts. These characteristics require a very small initial potassium conductance coupled with either large decay time constants $\tau_k$ or low input rates.

The point process modeling work attributes the transient chopping response to transients in the stimulus dependent parameters. These transients may reflect either transient variations in the inputs to the LSO, or adaptation mechanisms in the spike generation process. Although some stellate cells in the AVCN, producing chopper-type response patterns, may project to the LSO [8], the major ipsilateral excitatory projections arises apparently from the small spherical cells in the anteroventral cochlea nucleus (AVCN) producing primary-like responses [24, 52]. The primary-like response to tone bursts is characterized by PST histograms having a peak at stimulus onset followed by a gradual decline to a steady state level [43, 56]. The dynamic range, from the initial peak in the instantaneous discharge rate to the steady mean discharge rate, is in the order of 1:5 to 1:2. While the initial peak is relatively narrow, the gradual decline in discharge rate occur over 10-20 ms. Thus, the transients of the primary-like
inputs to the LSO do not correspond well with the characteristics of the transient response of LSO neurons; specifically the large dynamic range over which the intensity amplitude varies, and the short time constant of its decay. Thus, it is suggested that the transient response reflects more than just transient variations in the inputs; the spike generation process itself varies in the initial phase of the response.

One possible transient mechanism of spike generation is related to the calcium-dependent AHP channels postulated above in the context of mechanisms producing serial dependence. The concentration of free intracellular calcium increases in the process of spike generation due to the voltage dependent inward calcium current. Free calcium diffuses toward the center of the cell where it can bind with various calcium buffers. The dynamic of calcium buffering is controlled by the forward $f$ and backward $b$ rates of the binding reaction and by the concentrations of the free buffer $[B]$ and the calcium bounded buffer $[(Ca \cdot B)]$.

$$ \frac{\partial [Ca^{2+}]}{\partial t} = b[Ca \cdot B] - f[Ca^{2+}][B] $$

Prior to any discharge, the concentrations of the free calcium, the buffer and the calcium bounded buffer are at some steady state. During the early phase of a response, calcium concentration and the rate of the forward reaction increase. The time constant for achieving a new steady state is governed in the beginning of the response by the forward rate ($10^8 Molar^{-1} sec^{-1}$) and by the free buffer concentration. Assuming that the concentration of the free buffer is 3 to 30 $\mu Molar$ (based on estimation of calcium buffering in the bullfrog sympathetic type “B” ganglion cell immediately below the membrane ($30 \mu Molar$) and everywhere else (3 $\mu Molar$) [80]), the initial time constant of the change in free calcium concentration is:

$$ \tau_{[Ca]} = \frac{1}{f[\cdot]} = .33 to 3.3 \text{ msec} $$

The initial time constant of the calcium change provide a lower bound on the actual time constant of the change. Changes in calcium concentration affect the time course
of the AHP potential and thus the rate of increase in the post spike discharge rate. As a lower bound the above time constant of .33 to 3.3 msec compares favorably with the estimates for the time constant of the intensity amplitude (Table 3.4.4).

5.3.3 Inhibitory effect

The observed scaling effect of the contralateral input on the intrinsic recovery function of LSO units has important physiological implications. According to the current view, the contralateral input may inhibit LSO unit discharges by hyperpolarizing the membrane potential or by increasing membrane conductance, thereby shunting the excitatory postsynaptic potentials (EPSPs) [16, 42]. A simple mathematical model of a neuron as a leaky cable demonstrates that the type of inhibitory operation performed depends on the relative locations and magnitudes of the excitatory and inhibitory conductance changes [4]. The case that best describes the connectivity of LSO units, as detailed later, is the one in which the excitatory synapses are located on the distal dendrites and the inhibitory synapses on the soma. In this case, the above model demonstrates that the graded response of LSO units — increased firing rate with increased excitatory stimulus level — can be produced only if the excitatory conductance change is small. Under these conditions, shunting inhibition — scaling of the EPSPs — dominates when the inhibitory synapses produce large conductance changes. In contrast, linearly subtractive inhibition — a graded hyperpolarizing shift in the membrane potential without scaling EPSPs — dominates when the inhibitory synapses produce small conductance changes. “Pure” shunting inhibition, with no hyperpolarization, occurs only when the inhibitory reversal potential is similar to the membrane resting potential. When the inhibitory reversal potential is lower than the membrane resting potential, hyperpolarization occurs — but can never be greater than the inhibitory reversal potential. Consequently, when the inhibitory reversal potential is only slightly different from the resting membrane potential and the inhibitory
conductance change is large, hyperpolarization may occur but shunting inhibition dominates the interaction with the EPSPs.

In the case of somatic inhibition involving large conductance changes, i.e., shunting inhibition, each inhibitory event would completely suppress firing for the duration of each discrete inhibitory event. In contrast, inhibition involving small conductance changes, i.e., linearly subtractive inhibition, would produce a graded reduction in membrane potential that is temporally summed as long as the inhibitory events are occurring. The net effect of shunting inhibition, the punctate suppression of activity produced by each discrete inhibitory event, would be a scaling of the recovery function. This scaling corresponds well with the point process based analysis of the data. In contrast, the net effect of linearly subtractive inhibition, the graded continuous reduction in membrane potential, would be a shift in the recovery function toward longer intervals – which corresponds to the effect of decreased monaural (i.e., ipsilateral) stimulus level [73] as described above. The demonstrated scaling effect of the contralateral inhibitory stimulus on the monaural recovery function thereby indicates that a nonlinear shunting inhibitory process dominates the LSO's binaural processing mechanism.

The shunting mechanism is restricted in time to the active conductance phase of each IPSP. Intracellular measurements from LSO neurons in chinchilla [20], gerbil [59], mouse [79] indicate that the IPSPs rise rapidly over about 2 ms, decay slowly, and last up to 7 to 8 ms. Given the discrete nature of shunting inhibition, convergence of inhibitory inputs to a single LSO neuron may be required. Such convergence has been suggested based on comparison of the discharge characteristics of MNTB and LSO neurons in the cat [71], and electrophysical measurements in the Gerbil LSO (estimating approximately 8 inhibitory afferents per LSO neuron) [59].

The shunting inhibition produced by the contralateral input acts on the subthreshold membrane potential, and have no effect on the voltage-independent potassium channels involved in the CAHP mechanism. Hence, the serial dependence (i.e., slope
of the shifting function) is unaffected by inhibitory stimulation. These effects explain the measured invariance of the slope of the conditional mean to contralateral stimulus level and provide further support for the dominance of shunting inhibition in LSO binaural interaction.

The morphology, connectivity, and chemistry of the LSO cells support the notion of the shunting nature of the LSO inhibitory process. The typical LSO principal neuron possesses a spindle-shaped soma and polar dendrites that radiate to form a disc-like field. The distribution of synaptic terminals on the LSO neuron is optimal for shunting inhibition: Inhibitory terminals (i.e., those containing flat synaptic vesicles) are located on the soma and proximal dendrites while excitatory terminals (i.e., those containing round synaptic vesicles) are located on the distal dendrites [11, 24]. Terminals containing polymorphic synaptic vesicles are also located on the distal dendrites and may be inhibitory in action [30]. The source of this third type of terminal is unknown. Growing evidence indicates that the inhibitory neurotransmitter glycine, which produces membrane conductance changes by activating ligand-gated chloride channels [5], mediates the contralateral input from the medial nucleus of the trapezoid body (MNTB) to the LSO cell soma [51, 78]. In neurons, the reversal potential of chloride ions is relatively close to the membrane resting potential compared to the reversal potential of potassium ions [32]. Consequently, the hyperpolarization produced by activating chloride channels is small relative to that produced by activating potassium channels. Whether the activation of somatically located chloride channels dominates in the MNTB-to-LSO contralateral inhibitory operations is still unclear. Electrical stimulation in the MNTB and the trapezoid body produces conductance changes [20] and graded hyperpolarizing potentials in LSO neurons [20, 59, 79]. However, electrical stimulation in the MNTB or trapezoid body may antidromically activate inhibitory input at the LSO distal dendrites that would result in LSO hyperpolarization. More detailed measures of LSO inhibitory conductance changes are critical for assessing the shunting hypothesis.
In summary, point process analyses and modeling of LSO unit discharges has revealed the biophysical characteristics of the channels operating in the LSO cell membrane during excitatory and inhibitory interaction. Within the LSO unit’s dendrites, the ipsilateral stimulus produces EPSPs that sum and spread passively toward the cell body while on the LSO cell soma the contralateral stimulus activates inhibitory synapses that shunt the accumulated EPSPs by producing large conductance changes. This work, combined with others, suggests that the LSO unit’s membrane is characterized by: dendritic excitatory synapses producing small conductance changes; somatic inhibitory synapses producing large conductance changes; slowly-decaying calcium-dependent, voltage-independent, potassium channels producing cumulative after-hyperpolarization; and membrane capacitance that is significant enough to affect the post deadtime discharge based on the EPSPs accumulated during the deadtime. These suppositions motivate the construction of a compartmental model of LSO neurons to further test and refine these hypotheses.
Bibliography


Appendix A

Maximum Likelihood Estimate—General case

The maximum likelihood estimate of the constant parameters $\theta = (\mu_0, a^*)$ of the family of intensity functions specified in Equation 3.9 is derived here assuming a saturating linear intrinsic recovery function 2.7.

For simplicity, the following notation is used:

- $Z$ is the random variable of the considered intervals, $z_i$ is one interval. e.g. $z_i = \tau_{N_i+1,i}$.

- $Y$ is the random variable of the corresponding previous intervals, $y_i$ is the interval preceding $z_i$. e.g. $y_i = \tau_{N_i,i}$.

- $s^*$ is the total shift from the origin. e.g. $s^*(y_i) \equiv s(y_i) + d$.

The form of the intensity function specified in Equation 3.9 depends on the value of the shift function. Three cases are distinguished:

1. positive shifts, $s(y_i) \geq 0$,

2. small negative shifts, $-d \leq s(y_i) \leq 0$, and

3. large negative shifts, $s(y_i) \leq -d$.

The forms of the intensity function, the probability density function and the likelihood function are derived for each of these regions. The overall likelihood function is then derived and maximized to determine the unknown parameters.

1. Positive shifts, $s(y_i) \geq 0$

\[
\mu(z_i; y_i) = \begin{cases} 
0, & z_i \leq s^* \\
\frac{\mu_0}{R}[z_i - s^*], & s^* \leq z_i \leq (R + s^*) \\
\mu_0, & (R + s^*) \leq z_i 
\end{cases}
\]  
(A.1)
The probability density function is derived from the above intensity function according to Equation 2.5.

\[ p_\theta(z_i; y_i) = \begin{cases} 
0, & z_i \leq s^* \\
\frac{\mu_0}{R} [z_i - s^*] \exp\left(-\frac{\mu_0 (z_i - s^*)^2}{2}\right), & s^* \leq z_i \leq (R + s^*) \\
\mu_0 \exp\left(-\mu_0 [z_i - s^* - \frac{R}{2}]\right), & (R + s^*) \leq z_i 
\end{cases} \quad (A.2) \]

The likelihood function is the logarithm of the density function:

\[ l_\theta(z_i; y_i) = \begin{cases} 
0, & z_i \leq s^* \\
\log\left(\frac{\mu_0}{R}\right) + \log(z_i - s^*) - \frac{\mu_0 (z_i - s^*)^2}{2}, & s^* \leq z_i \leq (R + s^*) \\
\log(\mu_0) - \mu_0 (z_i - s^* - \frac{R}{2}), & (R + s^*) \leq z_i 
\end{cases} \quad (A.3) \]

2. Small negative shifts, \(-d \leq s(y_i) \leq 0\):

\[ \mu(z_i; y_i) = \begin{cases} 
0, & z_i \leq d \\
\frac{\mu_0}{R} [z_i - s^* + \frac{s^2}{2T} \exp(-\frac{z_i - d}{T})], & d \leq z_i \leq (R + s^*) \\
\mu_0 [1 + \frac{s^2}{2RT} \exp(-\frac{z_i - d}{T})], & (R + s^*) \leq z_i 
\end{cases} \quad (A.4) \]

where the rebound area \(g_0\), computed according to Equation 2.13:

\[ g_0(y_i) = \int_{s^*}^{d} \frac{1}{R} (y_i - s^*) dy_i = \frac{s^2}{2R} \quad (A.5) \]

and divided by the rebound time constant \(T\), determines the amplitude of the rebound function, as in Equation 2.12.

The probability density function is derived from the above intensity function according to Equation 2.5.

\[ p_\theta(z_i; y_i) = \begin{cases} 
0, & z_i \leq d \\
\frac{\mu_0}{R} [z_i - s^* + \frac{s^2}{2T} \exp(-\frac{z_i - d}{T})] \\
\exp\left(-\frac{\mu_0 [(z_i - s^*)^2 - \frac{s^2}{2} \exp(-\frac{z_i - d}{T})]}{2}\right), & d \leq z_i \leq (R + s^*) \\
\mu_0 [1 + \frac{s^2}{2RT} \exp(-\frac{z_i - d}{T})] \\
\exp\left(-\mu_0 [z_i - s^* - \frac{R}{2} - \frac{s^2}{2R} \exp(-\frac{z_i - d}{T})]\right), & (R + s^*) \leq z_i 
\end{cases} \quad (A.6) \]
The likelihood function is the logarithm of the density function:

\[ l_0(z_i; y_i) = \begin{cases} 
0, & z_i \leq d \\
\log\left(\frac{\mu_0}{R}\right) + \log(z_i - s^* + \frac{s^2}{2T} \exp\left(-\frac{z_i - d}{T}\right)) - \\
\frac{\mu_0}{R} \left[\frac{(z_i - s^*)^2}{2} - \frac{s^2}{4} \exp\left(-\frac{z_i - d}{T}\right)\right], & d \leq x \leq (R + s^*) \\
\log(\mu_0) + \log(1 + \frac{s^2}{2RT} \exp\left(-\frac{z_i - d}{T}\right)) - \\
\mu_0 [z_i - s^* - \frac{R}{2} - \frac{s^2}{2R} \exp\left(-\frac{z_i - d}{T}\right)], & (R + s^*) \leq z_i 
\end{cases} \]  
(A.7)

3. Large negative shifts, \( s(y_i) \leq -d \):

\[ \mu(z_i; y_i) = \begin{cases} 
0, & z_i \leq d \\
\frac{\mu_0}{R} [z_i - s^* + \frac{d}{2T} (d - 2s^*) \exp\left(-\frac{z_i - d}{T}\right)], & d \leq z_i \leq (R + s^*) \\
\mu_0 \left[1 + \frac{d^2}{2R^2T} (d - 2s^*) \exp\left(-\frac{z_i - d}{T}\right)\right], & (R + s^*) \leq z_i 
\end{cases} \]  
(A.8)

where the rebound area \( g_0 \), computed according to Equation 2.13:

\[ g_0(y_i) = \int_0^d \frac{1}{R} (y_i - s^*) dy_i = \frac{d}{2R} (d - 2s^*) \]  
(A.9)

and divided by the rebound time constant \( T \), determines the amplitude of the rebound function, as in Equation 2.12.

The probability density function is derived from the above intensity function according to Equation 2.5.

\[ p_0(z_i; y_i) = \begin{cases} 
0, & z_i \leq d \\
\frac{\mu_0}{R} \left[z_i - s^* + \frac{d}{2T} (d - 2s^*) \exp\left(-\frac{z_i - d}{T}\right)\right] - \\
\exp\left(-\frac{\mu_0}{R} \left[z_i - s^* - \frac{R}{2} - \frac{(s^*)^2}{2R} \exp\left(-\frac{z_i - d}{T}\right)\right]\right), & d \leq z_i \leq (R + s^*) \\
\frac{d}{2} (d - 2s^*) \exp\left(-\frac{z_i - d}{T}\right)), & (R + s^*) \leq z_i 
\end{cases} \]  
(A.10)
The likelihood function is the logarithm of the density function:

\[
l_\theta(z_i; y_i) = \begin{cases} 
  0, & z_i \leq d \\
  \log\left(\frac{\mu_0}{R}\right) + \\
  \log(z_i - s^* + \frac{d}{2R}(d - 2s^*) \exp(-\frac{z_i - d}{T})) - \\
  \frac{\mu_0}{R} \left(\frac{z_i - 2s^*}{2}\right) - \frac{d}{2R}(d - 2s^*) \exp(-\frac{z_i - d}{T})\right)], & d \leq x \leq (R + s^*) \\
  \log(\mu_0) + \log\left(1 + \frac{d}{2R}(d - 2s^*) \exp(-\frac{z_i - d}{T})\right) - \\
  \mu_0[z_i - s^* - \frac{R}{2} - \frac{(s^*)^2}{2R} - \\
  \frac{d}{2R}(d - 2s^*) \exp(-\frac{z_i - d}{T})], & (R + s^*) \leq z_i 
\end{cases}
\] (A.11)

The set of considered intervals may be regrouped as follows:

1. The subset of intervals \( \{z_{i_1}^{N_1}\} \) such that: \( s \geq 0 \) and \( s^* \leq z_{i_1} \leq (R + s^*) \).

2. The subset of intervals \( \{z_{i_2}^{N_2}\} \) such that: \( s \geq 0 \) and \( (R + s^*) \leq z_{i_2} \).

3. The subset of intervals \( \{z_{j_1}^{M_1}\} \) such that: \( -d \leq s \leq 0 \) and \( s^* \leq z_{j_1} \leq (R + s^*) \).

4. The subset of intervals \( \{z_{j_2}^{M_2}\} \) such that: \( -d \leq s \leq 0 \) and \( (R + s^*) \leq z_{j_2} \).

5. The subset of intervals \( \{z_{k_1}^{L_1}\} \) such that: \( s \leq -d \) and \( s^* \leq z_{k_1} \leq (R + s^*) \).

6. The subset of intervals \( \{z_{k_2}^{L_2}\} \) such that: \( s \leq -d \) and \( (R + s^*) \leq z_{k_2} \).

The probability density function of the set of intervals is:

\[
p(Z; Y) = \prod_{i=1}^{N_1+N_2} p_{\theta, s>0}(z_i; y_i) \prod_{j=1}^{M_1+M_2} p_{\theta, -d<s<0}(z_j; y_j) \prod_{k=1}^{L_1+L_2} p_{\theta, s<-d}(z_k; y_k) \quad \text{(A.12)}
\]

The likelihood function of the sequence of observed intervals is:

\[
l(Z; Y) = \sum_{i=1}^{N_1+N_2} l_{\theta, s>0}(z_i; y_i) + \sum_{j=1}^{M_1+M_2} l_{\theta, -d<s<0}(z_j; y_j) + \sum_{k=1}^{L_1+L_2} l_{\theta, s<-d}(z_k; y_k) \quad \text{(A.13)}
\]
Given the likelihood functions for a single interval, Equations A.3–A.11, the likelihood function of the set of intervals is:

\[
\ell(\mathbf{Z}; \mathbf{Y}) = (N_1 + M_1 + L_1) \log\left(\frac{\mu_0}{R}\right) + (N_2 + M_2 + L_2) \log(\mu_0) + \\
\sum_{i=1}^{N_1} \log(z_{i1} - s^*) + \sum_{j=1}^{M_1} \log(z_{j1} - s^* + \frac{s^2}{2T} \exp\left(-\frac{z_{j1} - d}{T}\right)) + \\
\sum_{k=1}^{L_1} \log(z_{k1} - s^* + \frac{d}{2T} (d - 2s^*) \exp\left(-\frac{z_{k1} - d}{T}\right)) - \\
\frac{\mu_0}{2R} \sum_{i=1}^{N_1} (z_{i1} - s^*)^2 - \frac{\mu_0}{2R} \sum_{j=1}^{M_1} (z_{j1} - s^*)^2 - \frac{\mu_0}{2R} \sum_{k=1}^{L_1} z_{k1} (z_{k1} - 2s^*) + \\
\frac{\mu_0}{2R} \sum_{j=1}^{M_1} s^2 \exp\left(-\frac{z_{j1} - d}{T}\right) + \frac{\mu_0 d}{2R} \sum_{k=1}^{L_1} (d - 2s^*) \exp\left(-\frac{z_{k1} - d}{T}\right) - \\
\mu_0 \sum_{i=2}^{N_2} (z_{i2} - s^* - \frac{R}{2}) - \mu_0 \sum_{j=2}^{M_2} (z_{j2} - s^* - \frac{R}{2}) - \\
\mu_0 \sum_{k=2}^{L_2} (z_{k2} - s^* - \frac{R}{2}) + \\
\sum_{j=2}^{M_2} \log(1 + \frac{s^2}{2RT} \exp\left(-\frac{z_{j2} - d}{T}\right)) + \\
\sum_{k=2}^{L_2} \log(1 + \frac{d}{2RT} (d - 2s^*) \exp\left(-\frac{z_{k2} - d}{T}\right)) + \\
\frac{\mu_0}{2R} \sum_{j=2}^{M_2} s^2 \exp\left(-\frac{z_{j2} - d}{T}\right) + \frac{\mu_0}{2R} \sum_{k=2}^{L_2} ((s^*)^2 - d(d - 2s^*) \exp\left(-\frac{z_{k2} - d}{T}\right))
\]  

(A.14)

where similar sums were grouped together.

Differentiating the likelihood function, Equation A.14, with respect to \(\mu_0\) and setting the resulting derivative to zero results in the following equation for \(\mu_0\):

\[
0 = (N_1 + M_1 + L_1 + N_2 + M_2 + L_2) \frac{1}{\mu_0} - \\
\frac{1}{2R} \sum_{i=1}^{N_1} (z_{i1} - s^*)^2 - \frac{1}{2R} \sum_{j=1}^{M_1} (z_{j1} - s^*)^2 - \frac{1}{2R} \sum_{k=1}^{L_1} z_{k1} (z_{k1} - 2s^*) + \\
\frac{1}{2R} \sum_{j=1}^{M_1} s^2 \exp\left(-\frac{z_{j1} - d}{T}\right) + \frac{d}{2R} \sum_{k=1}^{L_1} (d - 2s^*) \exp\left(-\frac{z_{k1} - d}{T}\right) -
\]
\[
\begin{align*}
&\sum_{i=1}^{N_1} (z_{i1} - s^* - \frac{R}{2}) - \sum_{j=1}^{M_1} (x_{j2} - s^* - \frac{R}{2}) - \sum_{k=1}^{L_2} (z_{k2} - s^* - \frac{R}{2}) + \\
&\frac{1}{2R} \sum_{j=1}^{M_1} s^2 \exp\left(-\frac{z_{j2} - d}{T}\right) + \frac{1}{2R} \sum_{k=1}^{L_2} ((s^*)^2 - d(d - 2s^*) \exp\left(-\frac{z_{k2} - d}{T}\right))
\end{align*}
\]

which can be solved for the maximum likelihood of \(\mu_0\) given the value of the total baseline shift \(a^*\):

\[
\frac{1}{\mu_{0ML[a^*]}} = \frac{1}{N_1 + M_1 + L_1 + N_2 + M_2 + K_2} \left\{ \right.
\]
\[
\frac{1}{2R} \sum_{i=1}^{N_1} (z_{i1} - s^* - \frac{R}{2}) + \frac{1}{2R} \sum_{j=1}^{M_1} (z_{j1} - s^*)^2 + \frac{1}{2R} \sum_{k=1}^{L_1} z_{k1} (z_{k1} - 2s^*) - \\
\frac{1}{2R} \sum_{j=1}^{M_1} s^2 \exp\left(-\frac{z_{j1} - d}{T}\right) - \frac{d}{2R} \sum_{k=1}^{L_1} (d - 2s^*) \exp\left(-\frac{z_{k1} - d}{T}\right) + \\
\sum_{i=1}^{N_2} (z_{i2} - s^* - \frac{R}{2}) + \sum_{j=2}^{M_1} (x_{j2} - s^* - \frac{R}{2}) + \sum_{k=2}^{L_2} (z_{k2} - s^* - \frac{R}{2}) - \\
\frac{1}{2R} \sum_{j=1}^{M_1} s^2 \exp\left(-\frac{z_{j2} - d}{T}\right) - \frac{1}{2R} \sum_{k=2}^{L_2} ((s^*)^2 - d(d - 2s^*) \exp\left(-\frac{z_{k2} - d}{T}\right)) \}
\]

\[
(A.16)
\]

Given the above equations, Equation A.14 and Equation A.16, the maximum likelihood algorithm is evaluated as follow:

1. For each time \(t\), the set of intervals that are the first to occur after time \(t\), \(\{z_{i1}\}\), is stored along with the corresponding set of previous intervals, \(\{y_{i1}\}\). The sets include one interval from each of the \(M\) responses to the repeated representations of the same stimulus.

2. The average time-of-occurrence of the spikes ending these intervals is computed.

3. The shortest interval for each time step is stored. The array of shortest intervals is filtered to assure monotonicity and the result is used as on-the-fly estimate of the absolute deadline.
4. For each value of $a^*$, the shift function $s(y_i)$ and the total shift function $s^*(y_i) \equiv s(y_i) + d$ are evaluated for each interval in the set, given the duration of the corresponding previous interval.

5. Each interval is classified according to the value of the shift function and its duration into one of the six classes listed above.

6. The proper contributions to the likelihood function, Equation A.14, and to the maximum likelihood of $\mu_0$ given $a^* - \mu_{0ML|a^*}$—Equation A.16 are made. The values of the likelihood function and $\mu_{0ML|a^*}$ are stored as a function of $a^*$.

7. The maximum value of the likelihood function is found and the corresponding total baseline shift $a^*$ is registered as the maximum likelihood estimate of $a^*$, $a_{ML}^*$.

8. The corresponding value of $\mu_{0ML|a^*}$, is registered as the maximum likelihood estimate of $\mu_0, \mu_{0ML}$.

9. The value of the parameters at the time corresponding to the average time-of-occurrence of the spikes ending these intervals are assigned the above estimates. (In cases when the intervals are long during the transient response, the temporal assignment is based on the average time of the mid-point of the considered intervals).

10. The procedure is repeated for different post-stimulus times to obtain the time course of the total baseline shift and the time course of the intensity amplitude.