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Summary of the Dissertation

Statistical models of information processing in neuronal systems

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Abstract

Understanding the mechanisms by which the brain processes and transmits information is a major goal of computational neuroscience. Neurons transform stimuli into sequences of action potentials, but the efficiency of this “neuronal code” is not fully understood. While spike count or temporal patterns alone may partially explain stimuli encoding, combining both features provides a more comprehensive representation.

In my thesis, I investigated information transmission in neuronal systems from the rate coding perspective by focusing on the instantaneous firing rate, which integrates rate coding and temporal coding features. Using classical statistical models of neural activity, I found that dispersion measures of the inter-spike intervals can differ significantly from the instantaneous rate dispersion measures in a model-dependent manner. Applying our findings to experimental data revealed that this approach offers deeper insights into the information-encoding mechanisms of neurons. Building on this foundation, I investigated the influence of biophysical properties on rate coding. Basic integrate-and-fire models lack firing rate and membrane voltage saturation, which is inconsistent with observed neural activity. Incorporating reversal potentials increased the slope of the “firing rate vs. input” curve, but did not achieve saturation. Extending the model to include two nodes (dendritic and somatic) effectively limited both voltage and firing rate, aligning the model more closely with biological observations.

In order to understand the rate coding principles that govern information transmission in neuronal systems, I studied how the olfactory receptor neurons (ORNs) of the male moth *Agrotis ipsilon* optimize information transmission under challenging sensory conditions. Analyzing responses to pheromones amid varying concentrations of volatile plant

compounds (VPCs) showed that these backgrounds can suppress neural responses in pheromone-responsive ORNs but also increase the information transmitted per spike. This study highlights ORNs' optimization mechanisms for navigating complex olfactory landscapes, enabling insects to detect crucial pheromonal cues despite environmental interference. Extending my research from neuron populations to neural networks, I investigated the effect of spike frequency adaptation (SFA) on neural variability quenching in cortical networks. Using a model with excitatory and inhibitory subpopulations, I demonstrated that SFA mechanisms significantly influence trial-to-trial variability, crucial for efficient information transmission.

Overall, my work provides a comprehensive analysis of information transmission from the perspective of rate coding, progressing from single neuron to complex neural networks. These findings enhance our understanding of the underlying mechanisms of neural coding, offering refined models that better reflect biological realities.

1 Background and objectives

Neurons, the fundamental units of the nervous system, are specialized for transmitting information throughout the body. Each neuron comprises a cell body (soma), dendrites, and an axon. The soma houses the nucleus and the metabolic machinery essential for the neuron's function and survival. Dendrites extend from the soma, receiving signals from other neurons and directing them toward the cell body. The axon, a long projection, carries electrical impulses away from the soma to other neurons, muscles, or glands. At the axon terminals, neurotransmitters are released to communicate with target cells across synapses. Action potentials, or spikes, are the primary method neurons use to send signals. These are sudden changes in the electrical charge of the neuron's membrane, triggered by the influx of sodium ions when the membrane potential reaches a threshold. This rapid depolarization is followed by repolarization as potassium ions exit the cell, restoring the resting membrane potential. This process propagates along the axon, enabling neurons to transmit information quickly and efficiently over long distances. Action potentials are all-or-none events, ensuring consistent signal transmission once the threshold is crossed.

Action potentials generally have a consistent shape and short duration [Dayan and Abbott, 2005]. Thus, to analyze the information being sent, it is often sufficient to consider the timing of action potentials, known as a spike train. Spike trains can be recorded by placing an electrode near the soma [Safronov et al., 2000]. Research continues into how specific and varied information is encoded within these sequences of spikes. Neural encoding schemes are usually categorized into two types: temporal codes, which rely on the precise timing of spikes, and rate codes, which depend on the frequency of spikes [Perkel, 1968, Victor and Purpura, 1997, Buracas and

Albright, 1999, Nemenman et al., 2004].

The classic rate coding paradigm suggests that neurons encode information by the number of spikes in a given time window [Dayan and Abbott, 2005]. This method is relatively straightforward and has shown that neurons can vary their firing rate in response to sensory inputs. Studies have demonstrated that the firing rate of sensory neurons increases with stimulus intensity, although this relationship is often non-linear [Adrian and Zotterman, 1926, Kandel et al., 1991]. In the visual cortex, neurons encode various stimulus features, such as orientation and direction, through firing rate change [Hubel and Wiesel, 1962]. Additionally, motor cortex neuron firing rates have been shown to vary with arm movement direction [Georgopoulos et al., 1986]. These findings support the rate coding hypothesis, suggesting neurons encode different stimuli aspects through firing rate variations.

Other studies show that neurons can encode information without changing the mean firing rate in response to a stimulus, prompting exploration of temporal coding schemes [Perkel, 1968, Gerstner and Kistler, 2002, Rigotti et al., 2013, Dettner et al., 2016]. The temporal coding hypothesis posits that the precise timing of spikes relative to each other and external events encodes information [Theunissen and Miller, 1995]. Examples include phase locking in the auditory system, where neurons fire at a specific phase of a sound wave to encode its frequency [Köppl, 1997], and spike timing-dependent plasticity (STDP), where the exact timing of spikes between neurons strengthens or weakens synapses, encoding information through synaptic strength changes rather than firing rate [Dan and Poo, 2006]. Temporal pairwise spike correlation has also been shown to capture information transmission in single neurons [Dettner et al., 2016].

Significant advances have been made in understanding and estimating firing rates in non-stationary processes, where neural firing patterns change over time. However, stationary processes, where firing rate properties are assumed constant over time, also present challenges. Despite their apparent simplicity, accurately estimating the firing rate in stationary processes requires careful consideration of factors such as time window selection for spike counting and temporal binning resolution, which can influence perceived firing rates [Shimazaki and Shinomoto, 2007]. Additionally, inherent variability in neuronal firing—even within stationary activity—necessitates robust statistical methods for distinguishing signals from noise [Stein, 1965, Kostal et al., 2007, Nawrot, 2010]. The concept of instantaneous firing rate has gained popularity as an alternative to the classical firing rate. Defined as the reciprocal of the interval between two spikes, it offers a more dynamic account of neural activity [Kostal et al., 2018]. Although the mean instantaneous firing rate is typically higher than the mean firing rate, under specific conditions, they can be equivalent. Our research explores the stochastic characteristics of the instantaneous firing rate, revealing insights that may not be evident from inter-spike interval (ISI) analysis alone. It also helps bridge the gap between rate coding and temporal coding paradigms, providing a more comprehensive understanding of neural information processing.

While rate coding has significantly advanced our understanding of neural communication, it's crucial to address the complexity and limitations of current models. Early models like the Hodgkin-Huxley model did not account for the stochastic nature of ion channels or the anatomical structure of neurons [Hodgkin and Huxley, 1952]. Subsequent models, such as the FitzHugh-Nagumo model and the Rall model, have focused on different aspects of neuronal dynamics [Fitzhugh, 1961, Rall, 1962]. The integrate-and-fire model and its variants include considerations for synaptic inputs and stochastic activity[Lapicque, 2007, Gerstein and Mandelbrot, 1964, Stein, 1965, 1967, Tuckwell, 1978]. However, many models assume infinitely high firing rates in response to increasing stimulus intensity, which does not align with biological constraints like the absolute refractory period. Our research addresses these limitations by introducing an analysis of models that incorporate mechanisms for firing frequency saturation, reflecting more accurately the physiological constraints observed in real neuronal systems.

Neuronal coding principles also apply to specialized contexts, such as olfactory receptor neurons (ORNs) in insects. ORNs process odor signals, with their diverse sensitivities and response properties forming the basis of odor coding [Yao et al., 2005]. Insects rely on these cues for locating food, mates, and habitats, making ORNs crucial for understanding insect behavior and ecology. Volatile plant compounds (VPCs) in the environment can significantly influence ORN firing patterns, affecting the detection and response to olfactory signals. Studies show that VPC backgrounds can alter ORN responses to pheromones, increasing response variability and affecting coding efficiency [Dupuy et al., 2017]. Our work investigates how different VPC concentrations affect the coding efficiency of pheromone-responsive ORNs in male moths of the *Agrotis ipsilon* species, demonstrating that higher VPC concentrations can enhance the encoding efficiency of pheromone signals.

Variability is a key aspect of rate coding, categorized into stimulus-evoked variability and ongoing variability. Prestimulus neural variability is higher compared to post-stimulus variability, suggesting sensory input reduces ongoing variability, known as variability quenching [Monier et al., 2003, Churchland et al., 2006, 2010]. Our research investigates the mechanisms underlying neural variability quenching, focusing on spike frequency adaptation (SFA). Using a cortical model, we show that SFA implemented through dynamic firing thresholds decreases trial-to-trial variability, while SFA through after-hyperpolarization currents increases variability.

These studies collectively advance our understanding of information processing in neural systems, particularly through rate coding. The thesis is based on five manuscripts, three published and two unpublished. In the following sections, the methodologies used for our work and then the results are summarized.

2 Material and methodology

2.1 Neural coding and firing rate estimation

Neurons transmit information through action potentials or spikes, primarily via their timing. Neural encoding schemes are broadly classified into rate coding and temporal coding. Rate coding suggests neurons encode information through the average number of spikes in a given time window. Temporal coding, in contrast, emphasizes the precise timing of spikes relative to each other and external events.

Determining firing rates from spike data poses challenges, especially in dynamic environments. The instantaneous firing rate (IFR) R, calculated as the inverse of the inter-spike interval (ISI) T, offers a detailed view of neural activity:

$$R = \frac{1}{T}. \tag{1}$$

Traditional methods like frequencygrams, time histograms, and kernel smoothing estimate the classical firing rate for non-stationary processes. For stationary processes, the mean firing rate λ is

$$\lambda = \frac{1}{\mathbb{E}(T)} = \lim_{w\to\infty} \frac{\mathbb{E}(N(w))}{w}, \tag{2}$$

where $N(w)$ is the number of spikes in the time window $[0, w]$. In general, the mean instantaneous rate is always higher than or equal to the mean classical firing rate [Lánský et al., 2004], however in the specialized case of equilibrium renewal processes, this inequality disappears.

2.2 Variability and randomness in neural activity

Variability in neural activity is crucial for understanding neural coding and brain function. Measures such as the standard deviation (σ) and coefficient of variation (C_V) quantify the variability of ISIs and firing rate:

$$\sigma(T) = \sqrt{\mathbb{E}([T - \mathbb{E}(T)]^2)}, \tag{3}$$

$$C_V(T) = \frac{\sigma(T)}{\mathbb{E}(T)} = \lambda\sigma(T), \tag{4}$$

$$\sigma(R) = \sqrt{\lambda\mathbb{E}(1/T) - \lambda^2}, \tag{5}$$

$$C_V(R) = \sqrt{\frac{\mathbb{E}(1/T)}{\lambda} - 1}. \tag{6}$$

The Fano factor measures trial-to-trial variability, indicating the consistency of spike counts:

$$\mathrm{FF} = \frac{\mathrm{Var}[N(w)]}{\mathrm{E}[N(w)]}. \tag{7}$$

Entropy-based measures, including differential entropy and relative entropy-based dispersion coefficients, quantify the randomness in spike trains, providing a normalized perspective on neural variability:

$$h(f_X) = -\int f_X(x)\ln f_X(x)\mathrm{d}x, \tag{8}$$

$$\sigma_h = \exp(h(f_X) - 1), \tag{9}$$

$$C_h = \lambda\sigma_h. \tag{10}$$

2.3 Modeling Neural Activity

Renewal point processes model the stochastic nature of spike trains, describing them through either spike times or ISIs. Common models include the gamma, lognormal, inverse Gaussian, and shifted exponential distributions. These models capture different aspects of neural variability and firing dynamics.

For instance, the gamma distribution has the firing rate (λ) and coefficient of variation of ISIs (C_V):

$$\lambda = \frac{b}{a}, \quad C_V(T) = \frac{1}{\sqrt{a}}, \tag{11}$$

where $a > 0, b > 0$ are the shape and rate parameters. The lognormal distribution provides:

$$\lambda = \frac{1}{me^{\sigma^2/2}}, \quad C_V(T) = \sqrt{e^{\sigma^2} - 1}, \tag{12}$$

where $m, \sigma > 0$ are the scale and shape parameters. The inverse Gaussian distribution is characterized by:

$$\lambda = \frac{1}{a}, \quad C_V(T) = \sqrt{b}, \tag{13}$$

where $a > 0, b > 0$ are the mean and scale parameters. The shifted exponential distribution accounts for a refractory period $\tau \geq 0$:

$$\lambda = \frac{a}{1 + a\tau}, \quad C_V(T) = \frac{1}{1 + a\tau}, \tag{14}$$

where $a > 0$ is the rate parameter.

Biophysical models integrate factors like ion channels and membrane properties to simulate neuronal activity. The leaky integrate-and-fire (LIF) model, with its variants incorporating reversal potentials and dual-compartment structures, represents fundamental neuronal behaviors. These models describe how neurons integrate inputs, generate spikes, and adapt to different stimulation patterns.

The LIF model is described by:

$$d\mathrm{V}(t) = \big(- \frac{V(t)}{\tau} + \mu \big) d\mathrm{t}, \tag{15}$$

where $V(t)$ is the membrane potential, τ is the membrane time constant, and μ is the input current. The two-point LIF model includes dendritic and somatic compartments:

$$\mathrm{d}V_1(t) = \left(-\frac{V_1(t)}{\tau} + \frac{V_2(t) - V_1(t)}{\tau_r} + \mu \right), \mathrm{d}t \tag{16}$$

$$\mathrm{d}V_2(t) = \left(-\frac{V_2(t)}{\tau} + \frac{V_1(t) - V_2(t)}{\tau_r} \right) \mathrm{d}t, \tag{17}$$

where $V_1(t)$ and $V_2(t)$ are the membrane potentials of the dendritic and somatic compartments, respectively, and τ_r is the junctional time constant. The LIF model and the two-point LIF model can be extended to include reversal potentials, adding more biologically realistic features. These extensions incorporate the effects of excitatory and inhibitory inputs more accurately. For example, incorporating reversal potentials into the LIF model involves modifying the input current term to account for these potentials. Similarly, the two-point LIF model can be adjusted to include reversal potentials, providing a more comprehensive view of the neuron's response to synaptic inputs.

Spiking neuron models, including the exponential integrate-and-fire model and those incorporating spike frequency adaptation (SFA), offer more detailed representations of neuronal dynamics. These models account for mechanisms like adaptation currents and dynamic thresholds, providing a closer approximation to biological neurons.

The exponential integrate-and-fire model is formulated as:

$$C\frac{\mathrm{d}V}{\mathrm{d}t} = -g_L(V - E_L) + g_L k_a \exp\left(\frac{V - S}{k_a}\right) + w + I, \tag{18}$$

where C is the membrane capacitance, g_L is the leak conductance, E_L is the resting potential, k_a is the slope factor, S

is the threshold potential, w is the adaptation current, and I is the input current. The adaptation current follows:

$$\tau_w \frac{\mathrm{d}w}{\mathrm{d}t} = a(V - E_L) - w, \tag{19}$$

where τ_w is the time constant of adaptation and a is the sub-threshold adaptation. Spiking neural networks (SNNs) extend these models to network-level simulations, capturing the connectivity and interactions among neurons.

2.4 Information transmission in insect olfactory system

The study focuses on the olfactory receptor neurons (ORNs) in male moths, particularly their response to pheromones and volatile plant compounds (VPCs). The aim was to investigate how VPCs affect the ORNs' ability to detect and process pheromone signals.

Experimental design

To mimic natural conditions, the ORNs were subjected to intermittent puffs of pheromones against different concentrations of VPC backgrounds. The experiment consisted of recording the ORNs' responses during an 8-minute sequence, which included two distinct 40-second stimulations separated by a 2-minute gap.

1. **Control Stimuli:** The first 40-second stimulation involved only pheromones.
2. **VPC Background:** The second 40-second stimulation included a continuous VPC background, either (Z)-3-hexenyl acetate or linalool.

The VPC background was designed to start 2 milliseconds before the pheromone stimulation to assess its impact on pheromone detection.

Data collection

- **Neurons:** The analysis included 186 ORNs recorded across the different experimental conditions.
- **Stimulations:** Each ORN was exposed to both the control (pheromone only) and the VPC background condition.

Firing rate estimation

The firing rate was estimated using kernel density estimation [Tomar, 2019]:

$$\lambda_t = \sum_{i=1}^{N} K_w(t - t_i), \tag{20}$$

where t_i is the spike time and $K_w(s)$ is the Gaussian kernel with bandwidth $w = 20ms$.

2.4.1 Neural response modelling

Two logistic regression models were formulated to assess the impact of VPCs on pheromone detection:

1. **Pheromone Only Model:** This model quantified the neuronal response to pheromones without VPC background.
2. **Pheromone + VPC Model:** This model incorporated the VPC background to evaluate its modulatory effects.

The probability of detecting a pheromone at a specific time bin j was modeled using the logistic function:

$$\text{prob}_j = \frac{e^{\beta_0 + \beta_1 * \lambda_j + \beta_2 * w_j}}{1 + e^{\beta_0 + \beta_1 * \lambda_j + \beta_2 * w_j}}, \tag{21}$$

where λ_j represents the firing rate at time bin j, w_j denotes the weighted history at time bin j, and β_0, β_1 and β_2 are regression coefficients derived from the model.

Prediction accuracy

The model was trained on three trials and then used to predict pheromone presence across 16 subsequent trials under each background condition. Prediction accuracy was measured as the proportion of correct predictions:

$$p_k = \frac{1}{m} \sum_{i=1}^{m} p_{k,i}, \tag{22}$$

where $p_{k,i}$ represents the accuracy for neuron i in trial k, and m is the number of neurons. To determine the efficiency of prediction relative to the neuron's spiking activity, the average prediction accuracy per spike p_k^* was calculated:

$$p_k^* = \frac{1}{m} \sum_{i=1}^{m} \frac{p_{k,i}}{,} a_{k,i}, \tag{23}$$

where $a_{k,i}$ is the number of spikes fired by neuron i in trial k.

Information-theoretic analysis

Mutual information was used to quantify the efficiency of information transfer under different sensory conditions:

$$I(R, S) = H(S) - H(S|R), \tag{24}$$

where $I(R, S)$ is the mutual information between the response R and stimulus S, $H(S)$ is the entropy of the stimulus, and $H(S|R)$ is the conditional entropy given the response. The mutual information per spike for each trial was calculated to assess the efficiency of information transfer:

$$I_k(R_k, S_k) = \frac{I_{k,d}(R_{k,d}, S_{k,d})}{a_{k,d}}, \tag{25}$$

where $I_{k,d}(R_{k,d}, S_{k,d})$ is the mutual information for trial k under VPC condition d, and $a_{k,d}$ is the number of spikes in trial k.

3 Results

3.1 Comprehensive overview of firing rate estimation methods

Attachment I

Neuronal firing rate estimation is crucial for interpreting neural activity and understanding the mechanisms of information processing in the brain. The firing rate, generally defined as the number of action potentials per unit of time, is a fundamental metric for quantifying neuronal output. This study provides a comprehensive review of various firing rate estimation methods, examining their theoretical foundations, application contexts, and implications for neural data analysis.

- **Simple Time Window Averaging:** Early methods relied on counting spikes within predefined intervals and normalizing by the duration of those intervals. While straightforward, this approach introduced variability related to the choice of window size, often requiring a balance between temporal resolution and statistical reliability.

- **Kernel-Based Methods:** Advances in computational techniques led to kernel-based methods, which offered a more sophisticated approach to firing rate estimation. By convolving spike trains with a predefined kernel function (e.g., Gaussian, exponential), these methods produced continuous estimates of the firing rate over time. The choice of kernel influenced the smoothness and responsiveness of the rate estimate. Kernel width played a critical role in capturing the dynamics of neuronal firing patterns.

- **Bayesian Frameworks:** Further refinement introduced Bayesian frameworks, which incorporated prior knowledge and probabilistic models to infer firing rates. These approaches allowed for the estimation of firing rates as probabilistic distributions, providing a means to quantify uncertainty in the rate estimates. Adaptive methods emerged, capable of adjusting estimation parameters in real-time based on spike train characteristics, thus enhancing the accuracy of firing rate reconstructions in varying neural activity regimes.

Overall, the evolution from simple averages to complex computational models reflects a deeper understanding of neural coding, with each method offering unique insights into neuronal activity across different temporal and spatial scales. These methods not only advanced our fundamental knowledge but were also useful for many of the subsequent analyses and models presented in this thesis. For instance, some of the firing rate estimation methods were applied in our studies on neuronal variability and the coding efficiency of olfactory receptor neurons, showcasing their broad applicability and critical role in neural data analysis. This review was published in the journal *Biosystems* [Tomar, 2019].

3.2 Variability and Randomness in Instantaneous Rate Analysis

Attachment II

This section focuses on analyzing the instantaneous firing rate within stationary renewal point processes and comparing dispersion coefficients for interspike intervals (ISIs) and instantaneous rates. Renewal processes are often used to model the activity of spontaneously active cells.

1. **Gamma distribution** The gamma distribution's dispersion measures for $C_V(T)$ and $C_V(R)$ are linked by

$$C_V(R) = \frac{C_V(T)}{\sqrt{1 - C_V(T)^2}}. \tag{26}$$

This relationship shows that the variability of the instantaneous firing rate can significantly diverge from ISI variability, revealing different neuronal dynamics (Fig. 1A).

2. **Lognormal and inverse Gaussian distribution** For the lognormal distribution, a symmetric relationship exists between $f_T(t)$ and $f_R(r)$:

   $$f_R(r; \lambda) = f_T(r; 1/\lambda). \tag{27}$$

   Both $C_V(T)$ and $C_V(R)$ follow an identity relationship, indicating statistical properties of neuronal firing are invariant to temporal or rate-based perspectives. This consistency is also seen in the inverse Gaussian distribution (Fig. 1A).

3. **Shifted exponential distribution** In this distribution, $C_V(T)$ depends on the firing rate and refractory period:

   $$C_V(T) = 1 - \lambda\tau. \tag{28}$$

   We analyzed the relationship between $C_V(T)$ and $C_V(R)$ by varying these parameters (Fig. 1A).

4. **Mixed exponential distribution** For the mixed exponential distribution, we used various parameter sets to analyze dispersion coefficients. Applying our analysis to experimental data from zebrafish afferent neurons, we showed that instantaneous rate dispersion measures offer a distinct perspective from ISI measures (Fig. 1C, D).

Our findings illustrate that the variability and randomness of the instantaneous firing rate provide additional insights beyond traditional ISI analysis (Fig. 1). These insights enhance our understanding of how information is encoded and processed in neural circuits, contributing to the broader theme of rate

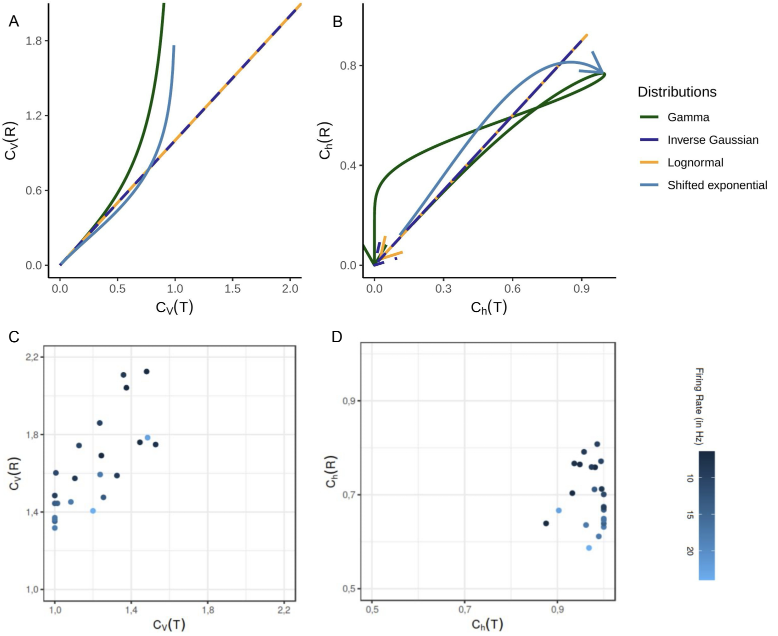

Figure 1: Exploring the relationship between statistical dispersion in interspike intervals (ISIs) and instantaneous rate across distributions and experimental data. A and **B**: Relationship between C_V and C_h of ISI and instantaneous rate. **C**: $C_V(T)$ and $C_V(R)$ reveal separate aspects of datasets. **D**: $C_h(R)$ differentiates datasets with equal $C_h(T)$.

coding in neural data analysis. This study was published in Frontiers in Computational Neuroscience [Tomar and Kostal, 2021].

3.3 Intrinsic Firing Rate Saturation in Neuronal Models

Attachment III

In our exploration of intrinsic firing rate saturation, we investigated four neural models: the basic leaky integrate-and-fire (LIF) model, the LIF model with reversal potentials, a two-point LIF model, and a two-point LIF model incorporating reversal potentials. These models were selected to assess how different structural complexities and biophysical properties influence neuronal firing rate responses to input currents. Understanding these mechanisms is crucial for accurately modeling neuronal behavior and information processing in neural circuits.

Basic LIF Model The basic LIF model demonstrated a linear relationship between input current and firing rate, without any intrinsic saturation. This model's simplicity fails to capture the realistic limitations observed in biological neurons, where firing rates typically saturate at high input levels due to biophysical constraints.

LIF Model with Reversal Potentials Introducing reversal potentials to the LIF model significantly altered its behavior. Reversal potentials, which account for the equilibrium potentials of ions, increased the slope of the firing rate versus input current curve by reducing the effective membrane time constant. However, this adjustment did not lead to intrinsic firing rate saturation, indicating that additional mechanisms are required to replicate the natural limitations of neuronal firing.

Two-Point LIF Model The two-point LIF model, which considers two nodes representing dendritic and somatic compartments, provided a more detailed simulation of neuronal behavior. Despite this added complexity, the model without reversal potentials still did not exhibit intrinsic firing rate saturation. This finding suggests that the model's structural

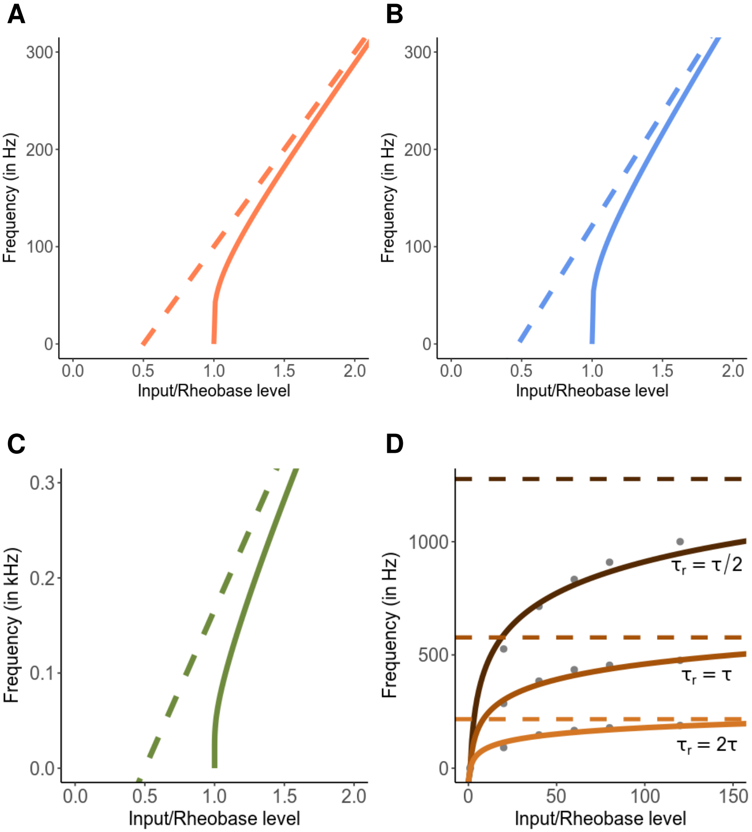

Figure 2: Transfer function plots for different leaky integrate-and-fire (LIF) neuron models with input normalized to rheobase. A Transfer function of a standard LIF neuron model. **B** LIF model with incorporation of a reversal potential with μ_I set to 0. **C** Two-point LIF model with parameter values set at $\tau = 5$ ms, $\tau_r = 2.5$ ms, and $S = 15$ mV. **D** Two-point LIF model with reversal potential, with parameter values set at $\tau = 5$ ms, $S = 15$ mV, $V_E = 60$ mV, $V_I = -10$ mV, and τ_r is 2.5 ms, 5 ms, and 10 ms for the different cases.

complexity alone is insufficient to impose realistic firing rate limits.

Two-Point LIF Model with Reversal Potentials The two-point LIF model with reversal potentials revealed a significant departure from the previous models. This configuration not only limited the maximum attainable voltage but also exhibited a clear saturation in firing rate. The presence of reversal potentials in this model imposed a ceiling on the firing rate, reflecting a built-in saturation frequency. The maximum firing frequency $f_{\max}$ can be described by the following equation:

$$f_{\max} = \frac{\tau + \tau_r}{\tau\tau_r \ln\left(\frac{V_E\tau}{V_E\tau - S(\tau+\tau_r)}\right)}, \tag{29}$$

where τ is the membrane time constant, τ_r is the junctional time constant and S is the firing threshold and V_E is the reversal potential for excitatory inputs. We compared the transfer functions across these models, as shown in Fig. 2, highlighting distinct behaviors in how each model approaches its firing rate limit. The two-point model with reversal potentials demonstrated the most realistic saturation effect, aligning more closely with observed neuronal behavior compared to the simpler models. These findings were published in the journal *Biosystems* [Tomar et al., 2022].

3.4 Efficient Information Transmission in Moth Olfactory Receptor Neurons

In our study of moth pheromone receptor neurons (Phe-ORNs), we investigated how volatile plant compounds (VPCs) influence the coding efficiency of these neurons. The olfactory system of male *Agrotis ipsilon* moths was used as a model to simulate naturalistic olfactory environments. We exposed the ORNs to intermittent puffs of pheromone amidst varying concentrations

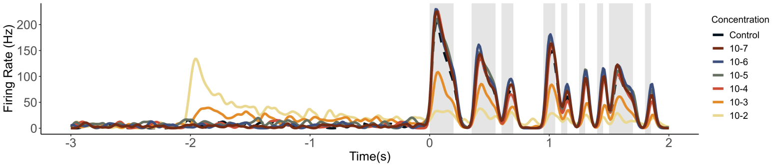

Figure 3: The inhibiting effect of various concentrations of (Z)-3-hexenyl acetate on the neural response in moth ORNs. Average firing rate of ORNs when exposed to (Z)-3-hexenyl acetate at -2s and pheromone introduced at 0s (indicated by the grey shaded area). The control is represented by the black dashed line.

of VPCs, specifically linalool and (Z)-3-hexenyl acetate, to understand how environmental odors affect sensory processing.

The results showed that high concentrations of VPCs, such as (Z)-3-hexenyl acetate and linalool, activated neuronal firing and suppressed the response to pheromones (Fig. 3). This suppression was most pronounced at the highest tested concentrations, suggesting that beyond a certain threshold, VPCs significantly interfere with pheromone detection.

To quantify the coding efficiency of ORNs, we used logistic regression models to predict the presence of pheromones under different VPC backgrounds. Despite the overall suppression of neuronal firing rates at high VPC concentrations, the coding efficiency of ORNs, measured by prediction accuracy per spike, increased. This was further supported by the increase in mutual information per spike, indicating that each spike conveyed more information about the pheromone presence under high VPC conditions (Fig. 4).

To ensure that the improvement in coding efficiency was not due to neural adaptation to repetitive stimuli, we compared neurons with similar firing rates exposed to different VPC concentrations. Neurons exposed to higher concentrations of

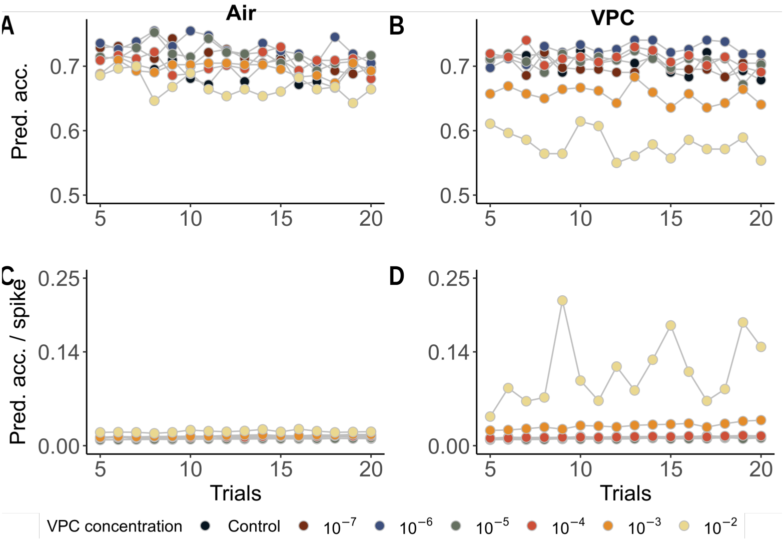

Figure 4: Stimulus prediction model has a high efficiency per spike under high concentrations of (Z)-3-hexenyl acetate. Predictive accuracies as well as predictive accuracies per spike in Phe-ORNs exposed to intermittent pheromones amidst variable (Z)-3-hexenyl acetate concentrations. The x-axis represents the trial number, indicating repeated exposure, while the y-axis measures predictive accuracy in **A** and **B**, displaying a decrease in accuracy at higher concentrations. In contrast, the y-axis measures predictive accuracies per spike in **C** and **D**, displaying an increase in efficiency per spike at higher concentrations of (Z)-3-hexenyl acetate. Each line corresponds to a different concentration of VPC, with the control group depicted as black dots.

VPCs showed better prediction accuracy per spike, even when their firing rates were comparable to those exposed to lower VPC concentrations. This suggests that the enhancement in coding efficiency is an effect of the VPC concentration itself rather than an adaptation to repeated stimuli.

Our study highlights a fascinating ecological interaction where environmental odors can enhance the coding efficiency of Phe-ORNs. This adaptive response suggests an evolutionary advantage in complex olfactory environments, allowing moths to discern mating signals amidst various plant odors. These findings provide significant insights into the mechanisms of olfactory perception in moths and contribute to our understanding of sensory processing in dynamic chemical landscapes. The manuscript for this study is attached (Attachment IV).

3.5 Neural Variability Quenching in Networks

Our investigation into the phenomenon of stimulus-evoked quenching of trial-to-trial variability in neural activity revealed significant insights into how different spike frequency adaptation (SFA) mechanisms contribute to variability reduction in neural networks. Using a recurrent neural network model, we aimed to replicate and analyze the observed decrease in neural variability upon stimulus presentation, a widely documented effect across various brain areas.

We constructed a recurrent neural network consisting of 10,000 neurons, with 7,500 excitatory and 2,500 inhibitory neurons. Each neuron was modeled as an exponential leaky integrate-and-fire (LIF) neuron. The probability of connection between neurons was set to 5%, and we also explored proximity-based connection matrices where neurons with similar stimulus preferences had a higher probability of connection. This setup mimicked the organization observed in cortical neurons.

We compared two types of networks characterized by different SFA mechanisms:

- SFA through after-hyperpolarization (AHP) currents
- SFA through dynamic firing thresholds

Each neuron received a background input until the stimulus was presented. In networks with a fixed connection matrix, neurons receiving strong input exhibited increased firing activity, while those with weak input showed decreased activity due to enhanced inhibitory input from the network. This behavior was observed regardless of the SFA mechanism.

In contrast, networks with proximity-based connectivity showed that neurons at the periphery of the network exhibited lower activity due to fewer connections, whereas clusters of neurons with strong stimuli and high connectivity displayed increased activity. This difference in network behavior highlights the impact of connectivity patterns on neural activity and variability.

To quantify the trial-to-trial variability, we ran $3,600$ simulation repetitions for each network configuration. We plotted the variance of each neuron's response against its mean response before and after the stimulus. Neurons with AHP-mediated SFA showed increased trial-to-trial variability following stimulus onset, while those with dynamic threshold-mediated SFA demonstrated a reduction in variability (see Fig. 5). This model proposes a mechanism for the reduction in trial-to-trial variability upon stimulus presentation, emphasizing the role of SFA mechanisms. Future work will explore the impact of varying connection probabilities for excitatory-excitatory (EE), excitatory-inhibitory (EI), inhibitory-excitatory (IE), and inhibitory-inhibitory (II) connections on neural variability. Additionally, we aim to investigate the functional role of excitatory and inhibitory neuron clusters within these diverse connectivity frameworks.

This study explores how different SFA mechanisms influence neural variability and highlights the importance of network connectivity in shaping neural responses. Our findings contribute to a deeper understanding of how neural networks process information and adapt to stimuli, offering insights into the

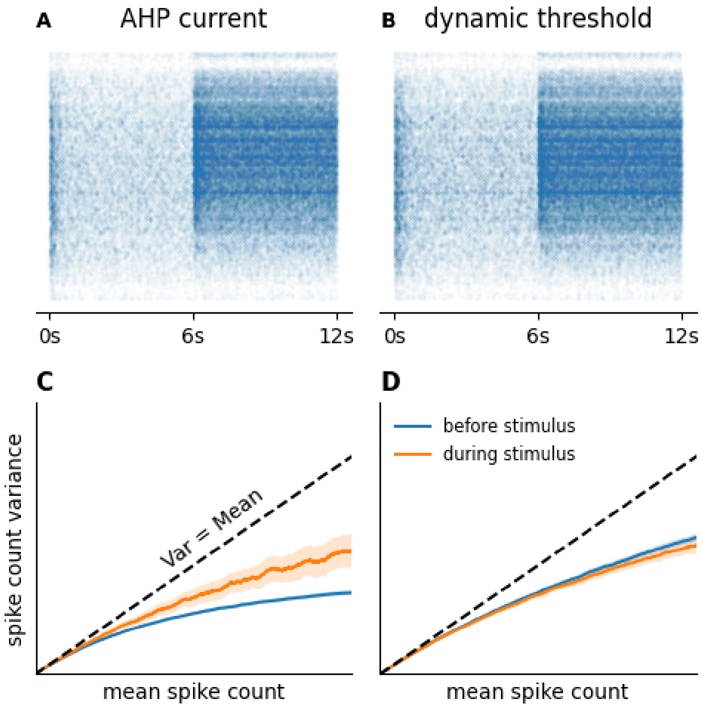

Figure 5: Neural variability quenching in recurrent neural networks with proximity-based connectivity. **A-B:** Simulation of excitatory neurons with consistent background input and additional input at 6s, varying by stimulus preference. Raster plots show activity under different spike frequency adaptation (SFA) mechanisms: after-hyperpolarization (AHP) current (**A**) and dynamic threshold (**B**). **C-D:** Variance vs. mean response for 3,600 trials. Neurons with AHP SFA (**C**) show increased variability post-stimulus, while those with dynamic threshold SFA (**D**) show reduced variability.

underlying mechanisms of variability quenching in the brain.

Conclusion

In this thesis, I examined the information transmission mechanisms in neuronal systems from the rate coding perspective. By incorporating measures such as the instantaneous firing rate, I provided a more nuanced understanding of neural encoding. Through detailed analysis and comparison of existing models, I evaluated how biophysical properties influence the dynamics of firing rate. My research demonstrated the significant impact of environmental stimuli on information transmission and highlighted the crucial role of adaptation mechanisms in maintaining efficient neural communication.

The neural coding problem is a key research area in neuroscience. To make further advances in this area, it is important to understand how neurons encode information and what principles they use to optimize this information transmission. Several studies have been done to determine which features of the spike train contain relevant information about the stimuli. Some of the candidates for these features over the year have been the average number of spikes per observation time window [Gerstner et al., 1997] or the occurrence frequency of a pair or trio of spikes [Oram et al., 1999] or the pairwise autocorrelation function along with the pairwise cross-correlation across noisy trials [Dettner et al., 2016]. Fukushima et al. [2015] found that temporal coding carries more information than spike counts when discriminating between different versions of the bird's own song in the zebra finch auditory system. Foffani et al. [2009] showed that spike timing is more critical for discriminating between tactile stimuli when stimulus discriminability is low, while spike count becomes increasingly important as discriminability improves. These findings underscore that rate coding alone cannot capture the complexity of neuronal coding, highlighting the need to integrate metrics like the instantaneous firing rate that encapsulate both spike count and temporal properties of neural data. This approach allows for a more accurate representation of neural activity compared to averaging over longer time windows [Ostojic and Brunel, 2011]. Furthermore, the instantaneous firing rate is directly proportional to input variance, highlighting its sensitivity to changes in stimulus statistics which makes it a valuable metric for understanding how neural populations encode information and respond to varying inputs [Fourcaud-Trocmé and Brunel, 2005].

Despite the advancements provided by metrics like the instantaneous firing rate, another significant obstacle in understanding information transmission mechanisms lies in the limitations of biophysical models. Brette [2015] argued that single-compartment integrate-and-fire (IF) models are more realistic than single-compartment Hodgkin-Huxley models. However, single-compartment IF models fail to capture several crucial features of neuronal behavior, like the effects of dendritic spikes [Górski et al., 2018] or the impact of multiplicative dendritic integration [An et al., 2019] and neither do they have an intrinsic saturation of the firing rate. More detailed models can address these limitations, sometimes at the cost of computational efficiency. The two-compartment IF models with reversal potentials have an intrinsic saturation of the firing rate. Additionally, a two-dimensional integrate-and-fire model incorporating an exponential spike mechanism with an adaptation equation has been proposed to effectively describe neuronal activity [Brette and Gerstner, 2005]. This model called the adaptive exponential IF (AdEx) model, can replicate various firing patterns observed in neurons [Naud et al., 2008, Górski et al., 2021]. A spiking neural network, where single neuron dynamics is based on the AdEx model and the network dynamics consist of excitatory and inhibitory subpopulation with recurrent architecture and excitatory feedforward input captures the trial-to-trial variability typically observed in cortical neurons. This trial-to-trial variability of spiking activity in cortical neurons has been recognized as a source of information about the state of neurons and their involvement in behavioral tasks [Hussar and Pasternak, 2010]. Using the SNN model, our research demonstrated that stimulus onset can lead to a quenching of neural variability, dependent on the spike frequency adaptation (SFA) mechanisms employed. These findings emphasize the importance of SFA mechanisms in shaping neural response dynamics and their critical role in accurately modeling neural variability in cortical networks.

Empirical research into the influence of environmental stimuli on olfactory receptor neurons (ORNs) provides new insights into how external factors modulate neural coding strategies. The study on volatile plant compounds (VPCs) and their effect on ORNs demonstrated that high concentrations of VPCs enhance information per spike despite reducing overall firing rates, suggesting an adaptive mechanism that optimizes information transmission in complex sensory environments.

The research presented offers a detailed exploration of information transmission in neuronal systems from the rate coding perspective. By integrating advanced models and empirical studies, and focusing on biophysical properties and adaptation mechanisms, new insights are provided into how neurons encode and adapt to varying inputs, enhancing our understanding of neural dynamics and information processing.

Summary

This dissertation focuses on understanding information processing in neuronal systems from a rate coding perspective. It aims to uncover how neurons encode and transmit information, integrating both statistical and biophysical models.

The study begins by examining traditional rate coding theories, emphasizing the need to combine spike count and temporal coding to fully capture neuronal information processing. Through classical statistical models, we demonstrate that dispersion measures of the inter-spike intervals can differ significantly from the instantaneous rate dispersion measures in a model-dependent manner, thus providing a more nuanced understanding of the neuronal code's efficiency. The research extends traditional integrate-and-fire models to include biophysical properties such as reversal potentials and dual-node structures, representing dendritic and somatic compartments. These extensions align model predictions more closely with observed neural activities, addressing limitations like firing rate and membrane voltage saturation. A significant part of the dissertation explores the olfactory receptor neurons (ORNs) in male moths of the species *Agrotis ipsilon*. It investigates how these neurons optimize information transmission in the presence of volatile plant compounds (VPCs), which can suppress neural responses to pheromones but increase the information transmitted per spike. This finding highlights the ORNs' ability to navigate complex olfactory landscapes, crucial for detecting pheromonal cues despite environmental noise. Additionally, the dissertation delves into the effects of spike frequency adaptation (SFA) on neural variability within cortical networks. It reveals that SFA mechanisms play a vital role in modulating trial-to-trial variability, which is essential for effective information transmission in neural circuits.

Overall, this work provides a detailed analysis of information processing from single neuron to complex neural networks, enhancing our understanding of neural coding mechanisms. It offers refined models that better reflect biological realities, significantly contributing to the field of computational neuroscience by advancing theoretical frameworks and practical methodologies for studying neuronal information processing.

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List of attachments

Attachment I Manuscript on comprehensive review of firing rate estimation methods published in *Biosystems*, **IF: 1.6** [Tomar, 2019]

Attachment II Manuscript on the variability and randomness of instantaneous rate published in *Frontiers in Computational Neuroscience*, **IF:4.8** [Tomar and Kostal, 2021]

Attachment III Manuscript on intrinsic firing rate saturation in neuronal models published in *Biosystems*, **IF:1.6** [Tomar et al., 2022]

Attachment IV Manuscript on efficient information transmission by moth olfactory receptor neurons

Attachment V Manuscript on trial-to-trial variability quenching in neural networks

Conferences and talks

Invited Talks

Association for Women in Mathematics Student Seminar Series, 2022 Department of Mathematics, University of Pittsburgh, “The Neural Coding Problem and the Role of Instantaneous Firing Rate”
International Conference on Mathematical Neuroscience (ICMNS), 2022 Invited as a young speaker in the mini-symposium “Stochastic Models for neuronal activity”

International conferences

2023 Society for Neuroscience (SfN2023), Washington, D.C., USA
2023 32nd Annual Computational Neuroscience Meeting (CNS23), Leipzig, Germany
2022 31st Annual Computational Neuroscience Meeting (CNS22), Melbourne, Australia
2022 Federation of European Neuroscience Society (FENS22), Paris, France
2022 International Conference on Mathematical Neuroscience (ICMNS), Online
2021 Neural Coding Conference, Online
2021 Biannual PhD Conference of the Institute of Physiology, CAS
2021 European Neuroscience Conference for Doctoral Students (ENCODS), Online
2020 Neuromatch 2.0, Online
2020 Federation of European Neuroscience Society (FENS), Online
2019 Biannual PhD Conference of the Institute of Physiology, CAS, Prague, CZ