Doctoral Thesis

Dynamic neuronal representations of static sensory stimuli

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DYNAMIC NEURONAL REPRESENTATIONS OF STATIC SENSORY STIMULI

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for the degree of
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presented by
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Zusammenfassung


In einer theoretischen Untersuchung wird zunächst die Dekodierung von zeitlich kodierter Information erörtert. Dabei verwenden wir ein kürzlich publiziertes Kodierverfahren um statisch-sensorische Reize in ein zeitliches Aktivitätsmuster zu konvertieren. Für die Dekodierung benutzen wir ein Modell, das auf der Struktur und Dynamik von Mikronetzwerken der Hirnrinde basiert, und welches für eine kontinuierliche Verarbeitung von zeitlich kodierter Information vorgeschlagen wurde. Wir zeigen, dass eine kontinuierliche


Eine bislang offene Frage ist, wie diese spezifische Art von räumlich-zeitlicher Kodierung generiert werden kann. Wir untersuchen in einem anatomisch plausiblen Modell des Antennenlappens die Hy-
Abstract

The strategies the brain can use to represent sensory information are intensely debated. Usually, a distinction is made between rate and temporal codes, and between single cell and population codes. In the context of the representation of static sensory stimuli, the contribution of the temporal dimension to the representation of these stimuli is not fully resolved. In this thesis, we investigate the role of time in the neuronal processing of static sensory stimuli with respect to three interconnected questions: how are dynamic neuronal representations of static sensory stimuli generated, what is the information content of these representations, and how are they read out by a neuronal decoder. We address these questions in reverse order because this allows us to establish constraints on the neuronal code and the encoding process imposed by the decoder. As a central hypothesis of this thesis, we speculate that a densely laterally coupled neuronal network can generate dynamic responses to static stimuli. Because the establishment of a neuronal coding strategy requires their validation in experimental approaches, we employ here a combined experimental and theoretical approach. The experimental system we investigate is the antennal lobe of the moth olfactory system. It ideally satisfies both the condition of static sensory stimuli as well as that of a dense lateral coupling.

We theoretically investigate the decoding of temporally encoded information. Using a recently proposed encoding scheme called "temporal population code", static sensory stimuli are transformed into temporal patterns of activity. For the decoding of these patterns we evaluate a model based on the structure and dynamics of cortical microcircuits that is proposed for computations on continuous temporal streams: the liquid state machine. We demonstrate that the presentation of the temporal patterns in a continuous stream induces a mixing of information across stimuli into a joint spatial representation, which compromises the success of a linear classifier that reads out these spatial representations. We investigate two complementary strategies to improve the decoding process. First,
we show that initializing the decoder upon presentation of a new stimulus leads to an almost doubled performance of the classifier, suggesting that the decoding network is in principle able to process these stimuli. Second, we discuss that a further optimization of this encoding-decoding system requires the specific adaption of the decoding stage to the information carrying properties of the temporal patterns. Hence, the question raises of how the temporal dimension contributes to the encoding of static stimuli.

The temporal dimension can play two distinct roles in the processing of static sensory stimuli; spatial response patterns across a population of neurons may display stimulus-dependent dynamics, or the temporal structure of these responses may itself contain stimulus-specific information. Using optical imaging of antennal lobe output neurons, we show that spatial response patterns are dynamic in a way that the spatial representation between odors decorrelates with time. Moreover, we also show that the temporal change of neuronal activity of antennal lobe output neurons is stimulus specific and boosts the accuracy of the encoding by 60% compared to purely spatial encoding. Hence, the encoding of odor stimuli is complementary in the sense that both spatial and temporal properties of the neuronal response contain distinct information about these stimuli. These data thus indicate that both spatial and temporal dynamics contribute to the encoding of static sensory stimuli.

A question that remained unanswered so far is how this specific type of spatio-temporal encoding can be generated. We investigate in an anatomically constrained model of the antennal lobe the hypothesis that a tight lateral coupling, mediated by inhibitory connections, can generate such an encoding. Our results show that a slow lateral inhibition suffices to obtain dynamic spatial response patterns which decorrelate over time for different odor stimuli. At the same time, this slow inhibition causes the temporal change of antennal lobe output neuron firing rate to convey complementary information about odor stimuli in way that its combination with the instantaneous firing rate improves the accuracy of the encoding by up to 150%. These theoretical results closely match with our ex-
perimental data and confirm our hypothesis that lateral connectivity is crucial for dynamic neuronal representations of static sensory stimuli. The generality and abstractness of our model allows us to predict that decorrelation and complementary encoding are generic properties of densely laterally connected neuronal structures.
Chapter 1

Introduction

It was at the beginning of the last century, when the cellular nature of the body was discovered. These efforts culminated in Ramón y Cajal’s observation, that the brain itself was composed of cells [112]. Ever since then, the question arose how the activity of the cells of the brain relates to perceptions. According to an early hypothesis that arose at this time, a sensory stimulus activates only certain, but not other, nerve fibers, which therefore represent the identity of that stimulus [18]. This view was supported by an analysis of the inner ear which suggested that different cells along the cochlear spiral are sensitive to different sound frequencies [145]. Hence, the idea of a spatial map of activity representing features of sensory stimuli was born. Until this day, this view of spatial feature maps has been a dominating component in our current thinking about the nervous system [22, 35, 71, 77].

An experimental procedure to test these early ideas, however, was facilitated only later with the advent of vacuum tubes in the first decade of the last century. For the first time was it possible to amplify small signals with very low noise – a prerequisite for recording from single sensory nerve cells. E. D. Adrian was among the first ones to make crucial discoveries about the properties of single neu-
1.1. The neuronal code

rons. His discoveries are still influential in the way we think about the problem of neuronal coding. Two of Adrian's discoveries are of particular importance [2–4]. The first discovery is that sensory neurons produce stereotyped signals of action potentials, so-called spikes. A stimulus either evokes spikes which travel along the axon of the nerve cell, or it does not. Indeed, spikes provide the substrate for most of the communication between nerve cells in the brain. The second discovery of Adrian was that the number of spikes elicited by a sensory neuron in a fixed time window, i.e. its firing rate, is informative about some parameter of the stimulus applied. This discovery actually represents the birthday of what is now called a rate code, that is, a code where the firing rate of a neuron contains information about a stimulus. Adrian's discoveries of spikes and of rate coding triggered one central key question about the brain that is until this day controversially discussed: how is information coded in the brain?

### 1.1 The neuronal code

The rate coding hypothesis is very influential in the way we think nowadays about the neuronal code. Many examples exist where the mean firing rate of single neurons changes gradually as a function of a stimulus parameter. The firing rate of retinal ganglion cells, for instance, responds selectively to the size of a spot of light [12, 13]. An important property of the rate coding hypothesis is that it greatly simplifies the question of neuronal coding by condensing the complex spiking pattern of a neuron into a single scaler value, its firing rate. Encoding and decoding of this scalar value is straightforward, i.e. a single feature of a stimulus is transformed into a certain firing rate, and a decoder counts the number of spikes to identify the stimulus feature.

A rate code is determined by counting the number of spikes over some time interval. The duration of this interval is often adapted to the timescale relevant to the particular experiment, such as how quickly a stimulus changes. The smaller this interval is, however,
the less spikes are counted until effectively only zero or one spike are counted for each time bin. In this case, the timing of individual spikes becomes important. Because of that, the code is in this case called a *temporal code*.

The distinction between rate and temporal codes, based on the duration of the time interval selected for counting spikes, is actually arbitrary. It is a priori unclear, what a short or a long interval, correspondingly, what a temporal or a rate code would be. In order to disambiguate this situation, two definitions are commonly used to determine what a rate and a temporal code is [31]. The first definition uses the response itself to define a temporal code. In this case, a temporal code is identified if peaks in the firing rate occur with roughly the same frequency as the spikes themselves. Hence, fast fluctuations of the firing rate are called a temporal code independently of whether or not they are informative about a stimulus. This definition, however, is problematic because the existence of particular features of a neuronal code is not sufficient for establishing this code. In fact, it is essential to show that a significant amount of information is carried by these particular features. The second definition, which we will use throughout this thesis, solves this issue by using the stimulus itself to define a temporal code, instead of using the response as before. In the second definition, a temporal code is identified if information about a stimulus is carried by variations in the spike timing occurring on a faster time scale than the stimulus itself [31, 138]. Thus, fast fluctuations of the firing rate are only called a temporal code if they contain information about a stimulus. In terms of frequencies, this definition implies that information about a stimulus is carried by Fourier components of the firing rate at frequencies higher than those inherent in the stimulus. In the extreme case of a temporally static stimulus, this thus means that any fluctuations in the firing rate containing information about a stimulus are considered a temporal code.

To what extent the temporal structure of a neuronal response carries information about a stimulus is one of the most disputed questions in neuroscience. It is generally accepted that the tem-
The neuronal code

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temporal structure of a spike train can carry information about the temporal structure of a stimulus [11, 19, 24, 100]. However, a much more controversially discussed claim is that the temporal structure of a neuronal response conveys information about a static stimulus, i.e. a stimulus that has no inherent temporal structure. What is important in this discussion is that temporal patterns should carry more information than spike counts – i.e. a rate code – alone. A temporal code is effectively only significant if this condition is satisfied. Following this consideration, it has for instance been suggested that temporal components other than the mean firing rate carry information about visual stimuli to higher cortical areas [70, 99, 113, 114]. However, later results suggested that most of this information contained in the temporal profile of firing rate was due to the increase of the spike rate following the onset of the stimulus [141]. On the other hand, it was found that spike patterns carry more information about the location of a sound source than spike counts alone [102]. In summary, there is thus evidence of the importance of temporal codes, yet, the question whether the temporal pattern of spiking reflects static features of stimuli remains not fully resolved.

The view that a single neuron represents a separate feature of a stimulus that we discussed so far can be extended to populations of neurons [31, 32]. Two schemes are usually distinguished when one talks about neuronal populations. In the first encoding scheme, which is often referred to as independent coding, each neuron is considered as representing an independent signal. There may be some redundancy in that several neurons represent the same signal, but key property of independent coding is that every feature can be extracted from evaluating the response of this population of neurons individually, without reference to any other neuron.

The population vector method used in the analysis of movement directions is a well-studied example of independent coding [47, 122, 123]. In this method, many neurons are recorded independently, and each individual neuron’s response is interpreted as an independent “vote” for its own preferred movement direction. Similar as in an election, by counting all those votes, one obtains a prediction of the
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actual movement direction.

But why should actually all neurons be considered independently? In a population of neurons, many relationships between their signals are possible. Eventually, the information content obtained from evaluating such a population response would be higher if relationships between responses of different neurons were taken into account, instead of evaluating each neuron's response individually and independently.

These considerations lead us to the second population coding scheme, the coordinated coding hypothesis. In its general form, the coordinated coding hypothesis posits that information exists, at least partially, in the many possible relationships among signals from multiple neurons in a large population [31, 32]. As opposed to the independent coding hypothesis, the information contents of a neuronal signal can only be obtained if it is compared with other signals. Hence, in order to decode the response of a single neuron, it must be compared with the response of other neurons.

The coordinated coding hypothesis was very much instigated by a theoretical concept proposed by Milner and others about thirty years ago [103]. We saw above that single neurons can represent features about a stimulus with e.g. their firing rate, and different neurons can represent different features of the same stimulus. In this context, the question thus raises of how information about the same stimulus which is represented across different neurons is grouped together to form a single percept. According to the coordinated coding hypothesis, synchronous firing between neurons could provide a substrate to functionally link information that is encoded in such spatially distributed patterns of activity [103, 128, 144], and thus solve this issue. Milner’s theory, which is also called binding by synchrony, would therefore allow to dynamically label cells that represent information about the same stimulus: while the firing rate of a neuron would represent a feature about a stimulus, the synchronous firing between neurons would allow to identify those neurons that represent features about the same stimulus. However, whether binding by synchrony is effectively employed by neurons is
The neuronal code

1.1. The neuronal code

still heavily disputed [117, 125–127].

The advent of computer technology initiated a novel approach in the examination of neuronal coding strategies which was complementary to purely theoretical considerations and analysis of neuronal data. For the first time was it now possible to simulate artificial neural networks, and to generate predictions about the brain’s coding strategies. A very prominent and influential example of artificial neural networks was proposed by Hopfield in the early 1980’s with his associative networks, also known as Hopfield networks [62, 63]. These networks emphasized two crucial and closely interconnected concepts: recurrency and complex network dynamics. In contrast to the classical neuronal networks which were organized into layers connected by purely feed-forward connections, these networks possessed recurrent connections. These recurrent connections provide the substrate for non-trivial network dynamics. As a result, information distributed over both space and time can be processed. At that time, however, the temporal dimension was of less interest, and hence, temporal coding of information was generally not considered.

The importance of the temporal dimension became only apparent later in the context of artificial neural networks [21, 23, 64]. Both, the encoding and decoding of information represented in temporal patterns has been investigated. For instance, Buonomano and Merzenich, 1999, [23] proposed a model for position-invariant pattern recognition which uses temporal coding. In this model, feed-forward inhibition modulates the spike-timing such that stimuli are represented by the response latencies of the neurons in the network. It is hypothesized in this study that one function of local connections in neuronal circuits may be to generate temporal codes. Indeed, there is recent theoretical evidence supporting the notion that dense lateral connectivity is crucial to transform spatial patterns into temporal patterns [151]. Also the opposite transformation, from time back to space has received attention [21, 91]. In a model inspired by the connectivity of cortical microcircuits, Buonomano and Merzenich, 1995, [21] showed that temporal patterns of
activity can be discriminated by a neuronal network by virtue of their transformation into a spatial representation. Also this study suggests that local connectivity within a network is a crucial aspect to process temporal patterns of activity. In conclusion, these simulations studies suggest that a dense lateral connectivity is a key ingredient of networks encoding information into or decoding information from a temporal code.

1.2 The olfactory system of insects

The previous considerations showed that different coding strategies are distinguished, i.e. rate coding vs. temporal coding on the level of single cells, and independent vs. coordinated coding on the level of neuronal populations. If temporal dynamics are to play a role in the representation of static sensory stimuli, theoretical evidence suggests that a dense lateral connectivity of the substrate generating these dynamic responses is required.

A structure which is ideally suited to investigate the various aspects of neuronal coding from an experimental point of view is the olfactory system. As we will see below, the first relay of this system, the antennal lobe of insects and the olfactory bulb of vertebrates, exhibits a dense lateral connectivity and was suggested to employ temporal dynamics in the encoding of odor stimuli. Since antennal lobe and olfactory bulb are similar in terms of their anatomy and physiology, we restrict our investigations to the olfactory system of insects, i.e. the antennal lobe.

The insect antennal lobe, which is similar across species in terms of both its anatomy and physiology, is composed of spheroidal shaped structures separated by glia, the so-called glomeruli [9, 52]. The organization of these glomeruli is sexually dimorphic [9]. Whereas both, males and females, possess a large number of sexually isomorphic glomeruli (the so-called ordinary glomeruli), males have an additional subcompartment which, in moths, is called macroglomerular complex and is composed of a small number of enlarged glomeruli. Here, we exclusively deal with the "ordinary" part of the insect an-
1.2. The olfactory system of insects

The antennal lobe, i.e. the sexually isomorphic glomeruli. The number of these glomeruli differs from species to species. Usually, it is between 50 and 160. The antennal lobe of the moth *Manduca sexta*, for instance, is composed of 60 ordinary glomeruli [118]. In contrast to most insects, however, the locust antennal lobe contains around 1000 but smaller glomeruli [86]. Since the position as well as the size of the glomeruli is species-specific [9], they can be identified and mapped as has for instance been done in *Manduca sexta* [118].

Input to the glomeruli is provided by olfactory receptor neurons [9, 52, 118]. Receptor neurons expressing the same receptor gene converge onto the same glomerulus [46, 146]. Within a glomerulus, the receptor neurons synapse with projection neurons, the output neurons of the antennal lobe [9, 28, 58]. In addition, several morphological types of local interneurons [9] connect receptor neurons with projection neurons and also make reciprocal synapses with projection neurons and feedback connections with receptor neurons. A major part of the local interneurons are immunoreactive to GABA [140] and may thus act in an inhibitory fashion on target cells. Local neurons are called heterogeneous and homogeneous, dependent on whether they arborize only partly or throughout the entire antennal lobe, respectively [9, 36, 121]. Projection neurons arborize usually in single glomeruli, and transmit olfactory information to higher brain regions via up to five output tracts [9, 61]. In short, thus, the insect antennal lobe is a densely laterally connected structure that receives direct input from receptor neurons and sends its output to higher brain regions via projection neurons.

The projection neurons of the insect antennal lobe send their information to the mushroom bodies and other regions of the protocerebrum [9]. The mushroom bodies are neural structures involved in the processing of multimodal information [56]. Apart from olfactory input, they also receive multimodal input from the protocerebrum, and visual input from the optic lobes [108, 135–137]. They send output fibers to surrounding brain regions and recurrent feedback neurons to their main input region.

The mushroom bodies are essentially composed of a large num-
ber of densely packed intrinsic neurons called Kenyon cells. In the posterior dorsal part of the brain, these neurons form dendrites which give rise to cup-shaped structures called calyces [48, 55, 104, 135, 136]. Calyces are only present in insects with antennal lobe [136]. Voltage-dependent subthreshold properties of Kenyon cells bring about a supralinear summation of projection neuron action potentials [81, 109, 110]. Apart from input from projection neurons, Kenyon cells also receive prominent input from GABA-ergic neurons [155]. These GABA-ergic neurons seem to provide both feedback and feed-forward inhibition to the Kenyon cells. Feedback is provided from the output regions of the mushroom bodies, the lobes, where these GABA-ergic neurons contact Kenyon cells axons [17, 45, 49, 50, 60, 86, 104, 135]. Feed-forward inhibition is mediated via local microcircuits within the mushroom body calyces, the so-called microglomeruli. These microglomeruli are presumably composed of a large projection neuron terminal in the center surrounded by dendrites of Kenyon cells and GABA-ergic neurons [45, 108, 155]. Within such a microglomerulus, projection neurons are connected with Kenyon cells either directly or via inhibitory feed-forward loops mediated by the GABA-ergic neurons. Thus, Kenyon cells receive both feed-forward and feedback inhibition.

In terms of its physiology, the insect antennal lobe seems to employ all of the neuronal coding strategies discussed above. A spatial encoding mechanism, i.e. independent coding across a population of neurons using a firing rate code, has been proposed in both the vertebrate olfactory bulb and the antennal lobe in insects [44, 65, 68, 80]. In addition, these spatial patterns of activity across olfactory bulb output neurons have been shown to display odor-specific evolutions which were accompanied by a gradual decorrelation of spatial odor representations [38, 39]. Similar results were obtained in the moth Manduca sexta, in the honeybee, and in the locust where it was recently demonstrated that classification of odor identity and concentration based on spatial vectors of activity across projection neurons improved during the course of stimulus presentation [38, 41, 134].

Regarding the role of the temporal dimension in this system,
two mechanisms are distinguished: information about odor identity and concentration is proposed to be carried in temporal patterns of coherently spiking projection neurons [85, 147] as well as in temporal patterns of activity of individual neurons, measured on a time scale of hundreds of milliseconds [83]. Evidence for the first option, i.e. coordinated coding, comes from a large body of literature showing that projection neurons display stimulus specific temporal synchronization of their activity to a global oscillatory rhythm [80]. Synchronous activity seems to be required for behavioral fine odor discrimination [133] but abolishing coherent activity leaves the animal with an ability to discriminate dissimilar odors. The assemblies of neurons that temporarily synchronize to this rhythm evolve in an odor specific manner with every cycle of the oscillation [79, 81–83, 147]. While there is substantial evidence that these neurons indeed synchronize their firing, however, it is largely unclear to what extent this synchronization improves the accuracy of the encoding of odor stimuli (but see [37]). Hence, we again touch the issue that we discussed above: the pure presence of a particular feature of a neuronal code does not prove the existence of this code unless the information content of these features is assessed and compared to alternative coding strategies. Thus, this emphasizes again the importance of examining the information content of a particular coding strategy.

Apart from synchronized activity, projection neurons also display a modulation of their firing rate on a 100 millisecond time scale, suggesting that these neurons might employ a temporal code. While it is on the one hand speculated that these temporal patterns may not be a code per se but rather a mechanism to optimize the representation of odors over time [80], these temporal patterns seem on the other hand to be dependent on the odor stimulus [38, 39, 80]. However, it is unclear to what extent the temporal structure inherent in these response improves the encoding of odor stimuli beyond what is represented in firing rates alone. Thus, it remains to be seen whether projection neurons indeed employ a temporal code to represent odor stimuli.
1.3 Research question of this Thesis

Building on these considerations about neuronal coding and the olfactory system of insects, we focus in this thesis on the contribution of the temporal dimension to the processing of sensory stimuli. With respect to the role that time plays in this process, we address in this thesis the following three closely related questions: 1) How are dynamic neuronal representations of sensory stimuli generated? 2) What is the information content of these representations? 3) How are they decoded?

In order to follow the logic of an external observer aiming at understanding the neuronal code, we answer these questions in the reverse order (Fig. 1.1). We first address the question of how a temporal code is decoded. This allows us to establish constraints on the properties and the processing of a temporal code as well.
1.4 Organization of this Thesis

as the generation of this code. In a second step, we assess the features of this code that contain the actual information about the stimuli. Finally, we investigate the neuronal mechanisms underlying the generation of such a code.

In the context of these investigations of temporal coding, we want to exclude the possibility that temporal variations in the stimuli themselves interfere with their processing. Thus, we restrict our investigations to static sensory stimuli, i.e. stimuli that are constant in their features over the course of stimulation. Under this condition, we define a neuronal response as employing a temporal code if temporal variations of this response contain information about the stimulus, i.e. we use the second definition of a temporal code we mentioned above. Because the significance of this code is only established if it augments the amount of information carried by instantaneous measures of neuronal activity alone (see above), we compare its information content to the one of instantaneous coding strategies.

In addition to the condition of static stimuli, we investigate the three main questions of this thesis under the hypothesis that a densely laterally coupled neuronal network can generate such temporally dynamic representations. As we saw before, a dense lateral coupling is suggested to play a pivotal role in the context of temporal coding.

The approach we employ here to address our research questions is unique in the sense that it is a combination of both theoretical and experimental techniques, which is possible thanks to a close collaboration with neurophysiologists. The experimental system we investigate in this thesis, the antennal lobe of the moth olfactory system, ideally satisfies both the condition of static stimuli as well as the one of a dense lateral coupling.

1.4 Organization of this Thesis

The main body of this thesis consists of four chapters, which are framed by an introduction in chapter one and a general conclusion
in chapter six. The material presented in the second and third chapter stems from a first-author [74] and a second-author publication [25], respectively. The fourth and fifth chapter are each based on studies submitted for publication in Network: Computation in Neural Systems [72, 73]. Most of the material shown has been presented in talks or as posters at various conferences.

In the second chapter, we assess boundary conditions under which a biologically plausible decoding system can successfully process static sensory stimuli that are represented in a temporal code. Using a recently proposed encoding scheme called "temporal population code", static sensory stimuli are transformed into temporal patterns of activity. For the decoding of these patterns we evaluate a model based on the structure and dynamics of cortical microcircuits that is proposed for computations on continuous temporal streams: the liquid state machine. We demonstrate that the presentation of the temporal patterns in a continuous stream induces a mixing of information across stimuli into a joint spatial representation. This mixing of initially temporally segregated information compromises the success of a linear classifier that reads out these spatial representations. While this result could suggest that the temporal activity patterns may contain information in features that are inaccessible to the decoding network, our investigations of strategies to improve the performance of the decoding network suggest that this is not the case. On the one hand, we show that the mixing problem can be overcome by applying reset signals that initialize the decoding network upon presentation of a new stimulus. This results in an almost doubled accuracy in classifying the temporal patterns. On the other hand, a second and complementary strategy to improve the performance of this encoding-decoding system is to redesign the decoding stage such that it is adapted to decode the specific temporal activity patterns generated by the encoding stage. It is concluded that such an optimization of the decoding system requires elucidating the detailed properties of a temporal pattern that convey the actual information about the stimuli.

The conclusion that a clear understanding of the information-
carrying properties of temporal patterns are crucial for the design of a decoding system set the stage to move to the question of the information content of dynamic neuronal representations. In the third chapter, we assess the specific role that time plays in the encoding of static sensory stimuli, using experimental data from the moth antennal lobe. Under the condition of stationary stimuli, the temporal dimension can play two distinct roles in their processing: on the one hand, spatial response patterns across a population of neurons may display stimulus-dependent dynamics, on the other hand, the temporal dimension of these responses as such may contain stimulus-specific information. In this chapter, we focus on the former question. Using optical imaging of projection neurons, we show that spatial response patterns display indeed stimulus-dependent dynamics. These dynamics are accompanied by a reduction of the similarity between spatial representations of odors, i.e. a decorrelation of spatial odor representations with time. Moreover, results are presented suggesting that the antennal lobe might employ two distinct coding strategies at the same time: one the one hand, it is shown that spatial response patterns across a population of projection neurons are repeatable for the same stimulus but different between stimuli. On the other hand, we show that the temporal evolution of neuronal activity per se could provide an additional substrate to encode odor information. Hence, the hypothesis arises that the antennal lobe could exploit the temporal dimension not only to improve the spatial representation of odor stimuli, but also to employ the temporal dimension itself to represent these stimuli.

This hypothesis that odor stimuli may be encoded in temporal patterns of activity constitutes the focus of the fourth chapter. Using again calcium imaging data of projection neurons, we address the question to what extent the temporal dimension of the projection neuron response contains information about odor stimuli. We derive a biophysical model that accurately describes the projection neuron calcium response and which allows us to completely quantify the amplitude-time course of this response. On the basis of this model, we show in a highly quantitative manner that the spatial and
temporal components of the optical signal contain complementary information about odor stimuli. Specifically, we demonstrate that the temporal change of the optical signal, i.e. the temporal derivative, is stimulus specific and boosts the accuracy of the encoding by 60% compared to a purely spatial encoding using response amplitudes only. Although the temporal patterning evident in the calcium response of projection neurons has been the subject of debate in this and related systems, we provide in this chapter the first quantitative proof that these temporal patterns contain stimulus specific information. The results confirm our initial hypothesis that in the moth antennal lobe system, the temporal dimension also contains information about odor stimuli. Hence, this shows that spatial and temporal properties of neuronal activity contain complementary odor information in the moth antennal lobe.

The fifth chapter closes the circle from experimental results back to theory. We show in a anatomically constrained model of the moth antennal lobe how dynamic neuronal representations of static sensory stimuli are an emergent property of the same underlying network mechanism: a dense lateral coupling of projection neurons mediated by a slow inhibition. First, we show that this dense lateral coupling within the antennal lobe leads in most cases to a decorrelation of spatial representations of different odor stimuli but not repeated trials with the same odor. Second, we demonstrate that the same network mechanism generates projection neuron responses that contain complementary information about odor stimuli in their instantaneous firing rate and in the temporal derivative of the firing rate. Hence, these results accurately reproduce our experimental observations. At the same time, these results also confirm our initial hypothesis that both temporal decorrelation and complementary encoding of static stimuli can be attributed to a dense lateral coupling within a neuronal network. Finally, the identification of information-carrying properties of the projection neuron response allows us to propose how downstream neurons of the olfactory pathway, the Kenyon cells, can read out such a temporal representation of static sensory stimuli.
Chapter 2

Decoding temporally encoded static stimuli

2.1 Introduction

The processing of sensory events by the brain requires the encoding of information in an internal state. This internal state can be represented by the brain using a spatial code, a temporal code or a mixture of both. For further processing, however, this encoded information requires to be decoded at later stages. Hence, any proposal on how a perceptual system functions needs to address both the encoding and the decoding aspects. Encoding requires the robust compression of the salient features of a stimulus into a representation that has the essential property of invariance. The decoding stage, in turn, involves the challenging task of decompressing this invariant and compressed representation into a high-dimensional representation that facilitates further processing steps such as stimulus classification. In this chapter, based on a combination of two independently proposed and complementary encoding- and decoding-models, sensory processing and the properties of a decoder are investigated in the context of a complex temporal code.
Previously we have shown that visual stimuli can be invariantly encoded in a so-called temporal population code [151]. This encoding was achieved by projecting the contour of visual stimuli onto a cortical layer of neurons which interact through excitatory lateral couplings. The temporal evolution of the summed activity of this cortical layer, the temporal population code, encodes the stimulus-specific features in the relative spike timing of cortical neurons on a millisecond time scale. Indeed, physiological recordings in area 17 of cat visual cortex support this hypothesis showing that cortical neurons can produce feature-specific phase lags in their activity [76]. The encoding of visual stimuli in a temporal population code has a number of advantageous features: First, it is invariant to stimulus transformation and robust to both network and stimulus noise [151, 153]. Thus, the temporal population code satisfies the properties of the encoding stage outlined above. Second, it provides a neural substrate for the formation of place fields [152]. Third, it can be implemented without violating known properties of cortical circuits such as the topology of lateral connectivity and transmission delays [151]. Thus, the temporal population code provides a hypothesis on how a cortical system can invariantly encode visual stimuli.

Different approaches for decoding temporal information have been suggested [20, 21, 75, 105]. A recently proposed approach is the so-called, liquid state machine [91, 92]. We evaluate the liquid state machine as a decoding stage since it is a model that aims to explain how cortical microcircuits solve the problem of the continuous processing of temporal information. The general structure of this approach consists of two stages: A transformation and a readout stage. The transformation stage consists of a neural network, the liquid, which performs real-time computations on time-varying continuous inputs. It is a generic circuit of recurrently connected integrate and fire neurons coupled with synapses that show frequency-dependent adaptation [95]. This circuit transforms temporal patterns into high-dimensional and purely spatial patterns. A key property of this model is that there is an interference between
subsequent input signals, so that they are mixed and transformed into a joint representation. As a direct consequence, it is not possible to separate consecutively applied temporal patterns from this spatial representation. The second stage of the liquid state machine is the readout stage where the spatial representations of the temporal patterns are classified.

Whereas most previous studies considered Poisson spike trains as inputs to the liquid state machine, in this chapter, we investigate the performance of this model in classifying visual stimuli that are represented in a temporal population code. Although the liquid state machine was originally proposed for the processing of continuous temporal inputs, it is unclear how this generalizes to the continuous processing of a sequence of stimuli that are temporally encoded. By analyzing the internal states of the network we show that in its original setup it tends to create overlaps among the stimulus classes. This suggests that in order to improve its performance, a reset locked to the onset of a stimulus could be required. We compare different strategies on preparing this network to the presentation of a new stimulus, ranging from random and deterministic initialization strategy to pure continuous processing with no stimulus-triggered resets. We find a large range of classification performance, showing that the no-reset strategy is significantly outperformed by the different types of stimulus-triggered initializations. Building on these results, we discuss possible implementations of such mechanisms by the brain.

2.2 Methods

2.2.1 Temporal population code

We analyze the classification of visual stimuli encoded in a temporal population code as produced by a cortical type network proposed earlier [151]. This network consists of $40 \times 40$ integrate and fire cells that are coupled with symmetrically arranged excitatory connections having distance-specific transmission delays. The inputs to
Figure 2.1: Prototypes of the synthetic “visual” input patterns used to generate the temporal population code. There are 11 different classes where each class is composed of 1000 samples. The resolution of a pattern is 40 times 40 pixels. The prototype pattern of each class is generated by randomly choosing four vertices and connecting them by 3 to 5 lines. Given a prototype, 1000 samples are constructed by randomly jittering the location of each vertex using a two-dimensional Gaussian distribution ($\sigma = 1.2$ pixels for both dimensions). All samples are then passed through an edge detection stage and presented to the network of Wyss et al. (2003) [151].
2. Decoding temporally encoded static stimuli

2.2. Methods

Figure 2.2: Temporal population code of the 11 stimulus classes. Shown are the mean traces of the population activity patterns encoding the number of active cells as a function of time (1 ms temporal resolution, 100 ms length) after rescaling.
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2. Decoding temporally encoded static stimuli

Figure 2.3: General structure of the implementation of the liquid state machine. A single input node provides a continuous stream to the liquid that consists of recurrently connected integrate and fire neurons that are fully connected with 11 readout groups. Each of the readout groups consists of 36 integrate and fire neurons. Weights of the synaptic connections projecting to the readout groups are trained using a supervised learning rule.

This network are artificially generated “visual” patterns (Fig. 2.1). Each of the 11 stimulus classes consists of 1000 samples. The output of the network (Fig. 2.2) is the sum of activities that is recorded during 100 ms with a temporal resolution of 1 ms - i.e. a temporal population code. We are exclusively interested in assessing the information in the temporal properties of this code. Thus, each population activity pattern is rescaled such that the peak activity is set to one. The resulting population activity patterns (which we also refer to as temporal activity patterns) constitute the input to the decoding stage, the liquid state machine (Fig. 2.3). Based on a large set of synthetic stimuli consisting of 800 classes and using mutual information, we have shown that the information content of the temporal population code is 9.3 bits given a maximum of 9.64 bits [115, 151].
2. Decoding temporally encoded static stimuli

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2.2.2 Implementation of the liquid state machine

The implementation of the liquid state machine evaluated here, including the readout configuration, is closely based on the original proposal [91] (see also App. A.1). The liquid is formed by $12 \times 12 \times 5 = 720$ leaky integrate and fire neurons (the liquid cells) that are located on the integer points of a cubic lattice where 30%, randomly chosen, liquid cells receive input, and 20% randomly chosen liquid cells are inhibitory (Fig. 2.3). The simulation parameters of the liquid cells are given in Tab. 2.1. The probability of a synaptic connection between two liquid cells located at $\mathbf{a}$ and $\mathbf{b}$ is given by a Gaussian distribution, $p(\mathbf{a}, \mathbf{b}) = C \cdot \exp(-(|\mathbf{a} - \mathbf{b}|/\lambda)^2)$, where $|.|$ is the Euclidean norm in $\mathbb{R}^3$ and $C$ and $\lambda$ are constants (Tab. 2.2). The synapses connecting the liquid cells show frequency-dependent adaptation [95] (see also App. A.1).

Table 2.1: Simulation parameters of the neurons of the liquid.

<table>
<thead>
<tr>
<th>Name</th>
<th>Symbol</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background current</td>
<td>$I_{bg}$</td>
<td>13.5 nA</td>
</tr>
<tr>
<td>Leak conductance</td>
<td>$g_{\text{leak}}$</td>
<td>1 $\mu$S</td>
</tr>
<tr>
<td>Membrane time constant</td>
<td>$\tau_{\text{mem}}$</td>
<td>30 ms</td>
</tr>
<tr>
<td>Threshold potential</td>
<td>$v_t$</td>
<td>15 mV</td>
</tr>
<tr>
<td>Reset potential</td>
<td>$v_{\text{reset}}$</td>
<td>13.5 mV</td>
</tr>
<tr>
<td>Refractory period</td>
<td>$t_{\text{refr}}$</td>
<td>3 ms</td>
</tr>
</tbody>
</table>

Note: The parameters are identical to Maass et al. (2002) [91].

The readout mechanism is composed of 11 neuronal groups consisting of 36 integrate and fire neurons with a membrane time constant of 30 ms (Fig. 2.3 and App. A.1). All readout neurons receive input from the liquid cells and are trained to classify a temporal activity pattern at a specific point in time after stimulus onset, $t_L$. Thus, training occurs only once during the presentation of an input. A readout cell fires if and only if its membrane potential is above threshold at $t = t_L$, i.e. the readout cell is not allowed to fire at ear-
Table 2.2: Simulation parameters of the synapses connecting the liquid cells.

<table>
<thead>
<tr>
<th>Name</th>
<th>Symbol</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average length of connections</td>
<td>$\lambda$</td>
<td>2 (independent of neuron type)</td>
</tr>
<tr>
<td>Maximal connection probability</td>
<td>C</td>
<td>0.4 0.2 0.5 0.1</td>
</tr>
<tr>
<td>Post-synaptic current time constant</td>
<td>$\tau_{\text{syn}}$</td>
<td>3 ms 3 ms 6 ms 6 ms</td>
</tr>
<tr>
<td>Synaptic efficacy (weight)</td>
<td>$w_{\text{liq}}$</td>
<td>20 nA 40 nA 19 nA 19 nA</td>
</tr>
<tr>
<td>Utilization of synaptic efficacy</td>
<td>$U$</td>
<td>0.5 0.05 0.25 0.32</td>
</tr>
<tr>
<td>Recovery from depression time constant</td>
<td>$\tau_{\text{rec}}$</td>
<td>1.1 s 0.125 s 0.7 s 0.144 s</td>
</tr>
<tr>
<td>Facilitation time constant</td>
<td>$\tau_{\text{fac}}$</td>
<td>0.05 s 1.2 s 0.02 s 0.06 s</td>
</tr>
</tbody>
</table>

Notes: The neuron type is abbreviated with E for excitatory and I for inhibitory neurons. The values of $w_{\text{liq}}, U, \tau_{\text{rec}}$ and $\tau_{\text{fac}}$ are taken from a Gaussian distribution of which the mean values are given in the table. The standard deviation of the distribution of the synaptic efficacy is equal to the mean value, and it is half of the mean value for the last three parameters. The parameters are identical to Maass et al. (2002) [91].
lier times. This readout setup is comparable to the original proposal of the liquid state machine [91]. Each readout group represents a response class, and the readout group with the highest number of firing cells is the selected response class. Input classes are mapped to response classes by changing the synapses projecting from the liquid onto the readout groups. A supervised learning rule changes these synaptic weights only when the selected response class is incorrect (App. A.1). In this case, the weights of the synapses to firing cells of the incorrect response class are weakened, whereas those to the inactive cells of the correct response class are strengthened. As a result, the firing probability of cells in the former group, given this input, is reduced while that of the latter is increased. The synapses evolve according to a simplified version of the learning rule proposed in Maass et al. (2002) and Auer et al. (2001) [10, 91], the main difference being that the clear margin term has been ignored. (Control experiments have shown that this had no impact on the performance).

The 1000 stimulus samples of each class are divided into a training and test set of 500 samples each. The simulation process is split into two stages: In the first stage, the synaptic weights are updated while all training samples are presented in a completely random order until the training process converges. In the second stage, the training and test performance of the network is assessed. Again, the sequence of the samples is random and each sample is only presented once. In both stages, the samples are presented as a continuous sequence of temporal activity patterns where each stimulus is started exactly after the preceding one.

Regarding the initialization of the network, any method used can either reset the neurons (membrane potential), the synapses (synaptic utilization and fraction of available synaptic efficacy), or both. A reset of any of those components of the network can either be deterministic or random. Combining some of these constraints, here, we apply five different methods to initialize the network at stimulus onset. These methods are called entire-hard-reset, partial-hard-reset, entire-random-reset (control condition), partial-random-reset
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2. Decoding temporally encoded static stimuli (as used in [90, 91]) and no-reset (see Tab. 2.3 for the corresponding initialization values). Whereas only the neurons are initialized by means of the partial reset, the entire reset initializes the neurons and the synapses. The initialization values are deterministic in case of the hard-reset methods, and they are random in case of the random-reset methods. The random initialization is used to approximate the history of past inputs. The validity of this approximation will be controlled below. Finally, the network is not reset in case of the no-reset method.

Table 2.3: Initialization values of the liquid variables: membrane potential, synaptic utilization and fraction of available synaptic efficacy.

<table>
<thead>
<tr>
<th>Reset method</th>
<th>Membrane potential</th>
<th>Synaptic utilization</th>
<th>Fraction of available synaptic efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entire-hard-reset</td>
<td>13.5 mV</td>
<td>U</td>
<td>1</td>
</tr>
<tr>
<td>Partial-hard-reset</td>
<td>13.5 mV</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Entire-random-reset</td>
<td>[13.5 mV, 15 mV]</td>
<td>[0, U]</td>
<td>[0, 1]</td>
</tr>
<tr>
<td>Partial-random-reset</td>
<td>[13.5 mV, 15 mV]</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>No-reset</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Notes: Five different methods are used to initialize these variables. The symbol [ , ] denotes initialization values drawn from a uniform distribution within the given interval.

2.2.3 Liquid state and macroscopic liquid properties

The state of the network is formally defined as follows: Let \( z(t) \) be a time dependent vector that represents the active cells at time \( t \) in the network with a 1 and all inactive cells with a 0. We call \( z \in \mathbb{R}^p \) the liquid output vector (with \( p \) the number of liquid cells). The liquid state vector \( \bar{z} \) (usually only called liquid state) is now defined as the component-wise low pass filtered liquid output vector using
a time constant of $\tau = 30 \text{ ms}$.

We introduce three macroscopic liquid properties. In all of the following equations, $\tilde{z}_{ijk} \in \mathbb{R}^p$ denotes the liquid state after the $k$th presentation of sample $j$ from class $i$ where $i = 1, \ldots, n$, $j = 1, \ldots, m$ and $k = 1, \ldots, r$ with $n$ the number of classes, $m$ the number of samples per class and $r$ the number of presentations of the same sample, and $p$ the number of liquid cells. For simplicity we omit the time dependence in the following definitions. We compute a principal component analysis by considering all the vectors $\tilde{z}_{ijk}$ as $n \cdot m \cdot r$ realizations of a $p$-dimensional random vector. Based on the new coordinates $\tilde{z}_{ijk}$ of the liquid state vectors in the principal component system, the macroscopic liquid properties are defined.

The center of class $i$, $c_i$, and the center of a sample $j$ from class $i$, $s_{ij}$, are defined as the average values of the appropriate liquid state vectors:

$$c_i = \frac{1}{mn} \sum_{j=1}^{m} \sum_{k=1}^{r} \tilde{z}_{ijk} \quad (2.2.1)$$

$$s_{ij} = \frac{1}{r} \sum_{k=1}^{r} \tilde{z}_{ijk} \quad (2.2.2)$$

Since these vectors are defined as average values over several presentations of the same sample, the liquid-noise, see below, is not considered in these values if the number of repetitions $r$ is large enough.

The liquid-noise $\sigma_{\text{liq}}$ is defined as the average value of the vectorial standard deviation (i.e. the standard deviation is computed for each component separately) of all presentations of a sample

$$\sigma_{\text{liq}} = \frac{1}{mn} \sum_{i=1}^{n} \sum_{j=1}^{m} \text{std}_k(\tilde{z}_{ijk}), \quad (2.2.3)$$

and can be interpreted as the average scattering of a sample around its center $s_{ij}$.
2.3. Results

In our first experiment, we investigate the performance of the liquid state machine in classifying the temporal activity patterns by initializing the network according to the control condition (entire-random-reset, see Sect. 2.2.2). The readout cell groups are trained to classify a sample at 100 ms after stimulus onset. We run overall 10 simulations, each using the complete training and testing data sets. Each simulation comprises a network where the synaptic arborization and the parameters controlling the synaptic dynamics are randomly initialized (Tab. 2.2). We find that after training 60.6±2% (mean ± standard deviation) of the training samples and 60.2±2% of the test samples are classified correctly. The corresponding values of the mutual information between stimulus and response class are 1.725±0.056 bits using the training data set and 1.696±0.053 bits using the test data set. The maximum value of the mutual information is $\log_2(11) \approx 3.459$ bits. Thus, although the generalization capability of the network is excellent, i.e. the performance on the test and training sets are virtually identical, it achieves only
a moderate overall performance comparing it to a statistical clustering of the temporal activity patterns that shows 83.8% correct classifications [151].

In order to elucidate the mechanisms responsible for this moderate performance, we take a closer look at how the temporal activity patterns are represented in the network. Since we always triggered the training of the readout cell groups at 100 ms after stimulus onset, we are particularly interested in the liquid state (Sect. 2.2.3) at this point in time. Due to the fact that the liquid state is high-dimensional, we employ a principal component analysis to investigate the representation of the temporal activity patterns in the network. The first 50 samples of each class are presented 20 times to the network which results in 20 repeats per sample × 50 samples per class × 11 classes = 11000 liquid state vectors. Each of these 720-dimensional vectors is considered as a realization of 720 random variables. On this data, a principal component analysis is applied. Based on the new coordinates of the liquid states in the principal component system, we compute the three macroscopic liquid properties: the liquid-class-distance, the liquid-sample-distance and the liquid-noise (Sect. 2.2.3). For the projection of the liquid states onto each principal component, these three properties describe the average distance between the centers of the classes, the average distance between the centers of the samples of one class, and the average variability of the liquid states of one particular sample. Thus, by means of the liquid-sample-distance and the liquid-noise, the extent of all samples of one class along each principal axes can be assessed. This extent is limited by the average distance between the samples of one class (liquid-sample-distance) and the sum of this distance with the liquid-noise, the average variability of the liquid states of one sample. Hence, the projection of the liquid states of different classes onto a principal component are separated if the corresponding liquid-class-distance is greater than the sum of the liquid-sample-distance and the liquid-noise. Conversely, the projection of liquid states onto a particular principal component overlap if the corresponding liquid-sample-distance is greater than the liquid-
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Class-distance. On the basis of this interpretation of the macroscopic liquid properties we are able to quantitatively assess the separation among the classes.

![Diagram of liquid state distances versus principal component dimensions](image)

**Figure 2.4:** Liquid state distances versus principal component dimensions. The network is initialized using the entire-random-reset method. The solid line shows the liquid-class-distance, the dashed line the liquid-sample-distance, the dotted line the liquid-noise, and the dash-dotted line shows the sum of the liquid-sample-distance and the liquid-noise. For dimensions greater than 26 the liquid-noise is greater than the liquid-sample-distance, which is in turn greater than the liquid-class distance. For dimensions 1 to 4 the liquid-class-distance is greater than the sum of the liquid-sample-distance and the liquid-noise.

The above analysis of the liquid states is summarized in Fig. 2.4. First, we find that the liquid-noise exceeds the liquid-class- and the liquid-sample-distance for dimensions greater than or equal to 26. Thus, there is little stimulus- or class-specific information but mostly noise in these components. Second, the liquid-sample-distance is greater than the liquid-class-distance for all dimensions greater than or equal to 5, i.e. the liquid states of different classes overlap for these dimensions. Third, for dimensions less than or equal to 4, the liquid-class-distance is greater than the sum of the liquid-sample-distance and the liquid-noise. As a result of this, the
liquid states of different classes have little overlap for these dimensions. Fourth, as a consequence of point three, the liquid-class-distance is also greater than the liquid-sample-distance for dimensions between 1 and 4. Given these macroscopic liquid properties we can conclude, from the third observation, that the projection of the liquid states onto principal components 1 to 4 have little overlap. Therefore, class-specific information can only be found in the first 4 principal components. This finding is somewhat surprising, given the dimensionality of the temporal population code which is of the order of 20 [153] and considering that the liquid states were originally proposed to provide a very high-dimensional representation of the input [91]. Finally, it follows from the second observation that the liquid states projected onto principal components greater than or equal to 5 do not carry class-specific information, with or without liquid-noise. Therefore, the liquid state machine appears to encode the stimuli into a low dimensional representation.

Taking the above observations into account, how can the liquid state machine be modified in order to increase its ability to separate between the stimulus classes? Since the liquid state machine does not a priori contain class-specific information (i.e. class-specific features can not be detected), the liquid-class- and the liquid-sample-distance can not be changed independently. Thus, it is not possible to selectively increase the liquid-class-distance while decreasing the liquid-sample-distance. However, as a result of the entire-random-reset method used to initialize the network, the liquid-noise is independent of the stimuli and could be eliminated by resetting the liquid variables to predefined values at stimulus onset. According to the macroscopic liquid properties, this would therefore lead to an increased separation between the classes which improves the classification performance of the liquid state machine.

We examine the classification performance of the liquid state machine using four reset methods: The entire-hard-, partial-hard-, partial-random- and the no-reset method (Sect. 2.2.2 and Tab. 2.3). We use the same experimental protocol as above, and the results are summarized in Fig. 2.5. First, initializing the network with
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Figure 2.5: Evaluation of different reset mechanisms. a Classification performance and b mutual information of the readout cell groups trained 100 ms after stimulus onset with the input classes. Five different initialization methods are used (Sect. 2.2.2). Gray/white bars show the performance for the training/test data set respectively and 10 simulations are run per reset condition. Error bars indicate the standard deviation ($n = 10$).
the entire-hard-reset method yields a better performance than with the entire-random-reset method as predicted above. Quantitatively, this amounts to approximately a 10% increase in performance. Second, comparing the performance of the entire-hard-/entire-random-reset method to its partial counterpart, we find that initializing the network with the partial-hard-/partial-random-reset method results in a higher performance (Fig. 2.5). Employing a two-way ANOVA on the classification performance using the results of the testing data set, we find for $\alpha = 0.01$, $p_{\text{entire/partial}} \approx 0.0002$, $p_{\text{hard/random}} \approx 4 \cdot 10^{-15}$, $p_{\text{interaction}} \approx 0.11$. Thus, both entire and partial as well as hard and random resets result in significant differences of the average classification performance and the mutual information. The only difference between the partial and the entire reset is that the former does not reset the synapses (Tab. 2.3), i.e. the synaptic utilization and the available fraction of synaptic efficacy are never reset. Thus, this difference has to account for the observed improvement of the classification performance. Third, using the no-reset method, the network yields a performance that is significantly lower than a network initialized with any other reset method (for instance performance comparison of entire-random-reset and no-reset, $t$-test of mutual information of testing data set, $\alpha = 0.01$, $p \approx 2 \cdot 10^{-16}$). Thus, resetting the network is required to achieve a satisfying classification performance.

We investigate in more detail the performance difference yielded by the entire and the partial reset methods. As we found above, entire and partial reset render approximately the same performance. Since the only difference between them is that the synapses are not reset in case of the partial reset method, this suggests that the synaptic short-term plasticity has no effect on the performance of the network. Consequently, the decoding of the temporal activity pattern would be a result of the membrane time constant only. Hence, we effectively remove synaptic short-term depression by setting the recovery time constant, $\tau_{\text{rec}}$, for all synapse types to 1 ms. This results in a training and testing performance of $10.0 \pm 2.8\%$, which is almost chance level. A further analysis of this very low per-
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Performance reveals that it is caused by the saturation of activity within the network. Thus, synaptic short-term depression is required for the proper operation of the network as it balances the amount of excitation.

![Distance vs. Dimension](image)

Figure 2.6: Liquid state distances versus principal component dimensions. The network is initialized using the no-reset method. The solid line shows the liquid-class-distance, the dashed line the liquid-sample-distance, the dotted line the liquid-noise, and the dash-dotted line shows the sum of the liquid-sample-distance and the liquid-noise. Only for dimensions 2 and 6, the liquid-class-distance is greater than the sum of the liquid-sample-distance and the liquid-noise. All other dimensions are dominated by the liquid-noise.

Since a reset of the network has a large effect on its classification performance, we again explore the representation of the temporal activity patterns in the network in order to quantitatively explain this effect (Fig. 2.6). However, here we use the no-reset method to record the liquid states at 100 ms after stimulus onset. We apply the same analysis as before to plot the three macroscopic liquid properties versus the principal components (Sect. 2.2.3 and Fig. 2.4). This analysis shows that the liquid-class-distance is only for dimensions 2 and 6 greater than the sum of the liquid-sample-distance and the liquid-noise. As this difference is only marginal for
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dimension 6, virtually only the projection of the liquid states onto principal component 2 have a small overlap. Hence, only the second principal component carries class-specific information. Comparing this result with the previous analysis of the liquid states obtained using the entire-random-reset method (Fig. 2.4), we find that not resetting the network results in a enormous increase in the overlap of the liquid states between different classes. Thus, in case of the no-reset method, there is a rather critical dependence between the initial state of the network at stimulus onset and the liquid state recorded after stimulus presentation.

![Graph](image)

Figure 2.7: Performance of the liquid state machine at varying temporal length of the temporal population code using different reset methods. a,b Classification performance and c,d mutual information during training/testing as a function of the time of training/testing (chance level in (a) and (b) is $1/11 \approx 0.091$). Up to 50 ms the performance shows an oscillation which results from the strong onset response in the temporal population code.
2.4. Discussion

In all previous experiments we trained the readout cell groups exactly at 100 ms after stimulus onset. Since it was shown that the information encoded in the temporal population code increases rapidly over time and already 60% of the total information is available after 25 ms [151], it is of interest to investigate how fast the classification performance of the liquid state machine rises. Moreover, it is unclear from the previous experiments whether the classification performance is better at earlier times after stimulus onset. In the following experiment, this will be examined by training the readout cell groups at one particular time between 2 ms and 100 ms, with respect to stimulus onset. The network is initialized using either the entire-hard-reset, the entire-random-reset or the no-reset method. For each fixed training/testing time and initialization method, 10 simulations are performed (same as in previous experiments). The results depicted in Fig. 2.7 show that up to 26 ms after stimulus onset the classification performance stays both for training and testing at chance level (0.09) and 0 bits of mutual information. Thus the first two bursts of the temporal activity pattern do not give rise to class-specific information in the network. The best performance is achieved by initializing the network with the entire-hard-reset method, whereas the no-reset method again results in the lowest classification performance. As already shown in Wyss et al. (2003) [151], here, we also find a rapid increase in the classification performance (Fig. 2.7). The performance does not increase anymore after 55 ms but rather fluctuates at a maximum level. Consequently, processing longer temporal activity patterns does not augment the mutual information or the classification performance.

2.4 Discussion

In this chapter we investigated the constraints on the continuous time processing of temporally encoded information using two complementary networks; the encoding network compresses its spatial inputs into a temporal code by virtue of highly structured and dense lateral connections [151] while the decoding network decompresses
its input into a high-dimensional space by virtue of unstructured lateral connections [91]. Our analysis of the decoding network showed that it did not sufficiently separate the different stimulus classes. We investigated different strategies to reset the decoding network before stimulus presentation. While resetting the network leads to a maximal performance of 75.2%, the no-reset method performs dramatically below the other methods investigated, i.e. 35.4 ± 1.9% correct classifications. A quantitative analysis showed that this performance difference is caused by overlaps of the classes in the high-dimensional space of the decoding network. Thus, in order to successfully decode and classify temporal activity patterns with the liquid state machine, the latter needs to be clocked by the presentation of a new stimulus as opposed to using a true continuous mode of operation.

The result that the decoding network can not successfully process the temporal activity patterns generated by the encoding network could indicate constraints on the properties of these temporal patterns. Thus, one might speculate that the temporal patterns may contain information in features that are inaccessible to the decoding network, which would impose constraints on the temporal code. However, our investigations suggest that this is not the case. First of all, the liquid state machine was successfully applied to the classification of a variety of temporal patterns [91, 92]. In this chapter we investigated yet another type of stimulus, a temporal population code. While our input stimuli are continuously varying, most other studies consider spike trains. Given the maximal performance of 75.2% correct classifications of the stimuli, however, we believe that in principle the liquid state machine is capable of processing this kind of temporal activity patterns. Since the liquid state machine was put forward as a general and biologically based model for computations on continuous temporal inputs, it should be able to handle these kinds of stimuli.

The liquid state machine was originally proposed for processing continuous streams of temporal information. This is a very difficult task as any decoder of temporal information has to maintain
an internal state of previously applied inputs. However, continuous streams of information can often be divided into short sequences, i.e. temporally confined stimuli. The knowledge of the onset of a new stimulus would certainly be beneficial for such a network as the single stimuli could be processed separately and the network could be specifically initialized and reset prior to their presentation. Thus, as opposed to a regime where a continuous stream of information is processed, there would be a possibility to avoid interferences of stimuli in the internal state of the network and the network should therefore perform better. However, while the performance difference between continuous or stimulus-triggered processing of temporal information is very intuitive, it is unclear how big its effect would be on the performance and the internal state of the information in the decoding network. Moreover, in previous work on liquid state machines this difference was not assessed [84, 90–92]. Here, we quantitatively investigated this difference in the context of the temporal population code where the input is not a continuous stream but composed of temporally confined stimuli. The initial hypothesis was that the decoding network can process a continuous stream of temporal activity patterns generated by the encoding network. We found, however, that for the decoding network to perform reasonably, it required a reset of its internal states at stimulus onset. The resulting percentage of correctly classified stimuli practically doubled for both hard- and random-reset. A mathematical analysis revealed a critical dependence between the initial state of the network at stimulus onset and its internal state after stimulus presentation. Whereas this dependence is fairly low in case of any reset method, not resetting the network drastically increases it which results in much larger overlaps of the internal states between different stimulus classes. Our analysis suggests that, although the mixing of previously temporally segregated information is of central importance for the proper operation of the liquid state machine, the mixing of information across stimuli leads to an inevitable degradation of its classification performance and the internal representation of the stimuli. In the original study the decoding network was actually initialized with a method
that is similar to the partial-random-reset method used here [90, 91]. This raises the question whether the liquid state machine operated in a true continuous mode in the cited studies. In conclusion, our results suggest that a reset mechanism is an essential component of the proposed encoding-decoding system.

Any reset system consists of two components: A signal which mediates the onset of a stimulus and a mechanism triggered by this signal which allows to reset the components of the processing substrate. Potential candidate neural mechanisms for signaling a new stimulus are for example the thalamic suppression found during saccades [111] or the hyperpolarization observed in the projection neurons of the antennal lobe of moths coinciding with the presentation of a new odor [54]. The temporal population code naturally generates such a signal, characterized by a pronounced first burst that can be easily detected and used to trigger a reset mechanism.

Regarding reset mechanisms, we have distinguished several approaches which differ mainly in how they could be implemented by the brain. While the hard-reset method could be implemented by strongly inhibiting all cells in the processing substrate, implementing the random-reset method appears difficult. It could possibly be approximated by driving the processing substrate into a transient chaotic state which could be achieved by selectively increasing and decreasing the synaptic transmission strength in a short time window after stimulus onset. This approach has similarities with simulated annealing [69] as well as the annealing mechanism presented in Verschure (1991) [143] where chaotic behavior in a neural network is attained by adaptively changing the learning rate. Comparing the classification performance with and without resetting the synapses (entire versus partial reset) reveals that the latter outperforms the former. Thus, not to reset the synapses is rather an advantage than a shortcoming of the proposed mechanisms. Furthermore, these considerations suggest that such a reset system could be implemented in a biologically plausible way.

From a general point of view, not only the liquid state machine but any decoder of continuous streams of temporal information has
to maintain previously applied inputs in an internal state. Thus, inputs applied at temporally segregated times are mixed into a joint internal state. Our results demonstrate that, in the absence of a stimulus-locked reset of this internal state, the effect of mixing strongly degrades the specificity of this internal state which results in a significant decrease of the network’s performance. Thus, since the liquid state machine is seen as a model of cortical microcircuits this raises the question how these circuits solve the problem of the mixing of temporally segregated information. On the basis of our results we predict that it is solved by employing stimulus onset specific reset signals that minimize the mixing of information from past and present stimuli. Although some evidence exists that could support this hypothesis further experimental work is required to identify whether the brain makes use of a form of temporal segmentation to divide a continuous input stream into smaller “chunks” that are processed separately.

A strategy complementary to reset mechanisms which could allow a further improvement of the performance of the decoding network is to specifically adapt it to the type of temporal patterns produced by the encoding network. Consequently, the optimization of the decoding network entails elucidating the detailed properties of the temporal activity pattern that make out the information about the stimuli. In the temporal population code, however, this is as of yet unknown.

In general, the question of the particular format of a neuronal code is relevant to any decoder of this code, and not only the liquid state machine. Detailed knowledge about how a temporal activity pattern represents information would allow the construction of a decoding network specifically aimed at reading out this particular code. Hence, this raises an important question: which properties of a temporal pattern does the brain use to represent information? It would be interesting to address this question experimentally. A promising candidate system could be the first relay of the olfactory pathway of insects, the antennal lobe. Output neurons of this systems were found to respond to odor stimulation with a modulation
of their firing rate on a time scale of hundreds of milliseconds, suggesting that stimulus specific information may be contained in these temporal patterns [80]. Yet, it is currently unknown whether these patterns effectively contain information about odor stimuli. We will therefore address this question in the following two chapters. On the basis of our considerations, elucidating the information-carrying properties of these temporal patterns will facilitate the construction of a more optimal decoding network.
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Chapter 3

Contribution of spatial dynamics to the encoding of static stimuli

3.1 Introduction

We have shown in the previous chapter that the decoding of temporally encoded information by a neuronal network can be optimized following two complementary strategies: first, the decoding network can be reset by the arrival of a new stimulus which thereby provides a form of temporal segmentation, and, as we showed, improves its performance. Second, the decoding network as such can be constructed in a way that it is specifically sensitive to the information carrying properties of the temporal pattern. In order to implement those specific improvements of the decoding network, we concluded that an identification of the properties of the temporal pattern that convey the actual information about the stimuli is required.
3.1. Introduction

From a more general point of view, this conclusion generalizes to any possible format of a neuronal code, which is in its most general form often called a spatio-temporal code. Hence, the question raises of what properties of a spatio-temporal code convey information about stimuli. Space and time can, in the context of static stimuli, contribute to the processing of those stimuli in three different ways [32]. Information about stimuli can exist in the spatial distribution of neuronal activity. Most importantly, these spatial patterns may be temporally static or dynamic. With temporally dynamic we mean that the spatial patterns evolve over time in a stimulus dependent manner – even though the stimulus itself is temporally static. Hence, the first two options are that information about such stimuli is represented in either temporally static or temporally dynamic spatial patterns. The third option, finally, is that information about these stimuli can also exist in the temporal structure of neuronal activity. In order to address these questions experimentally, a preparation is required where both space and time are thought to be involved in representing information about static stimulus features. A standard system where this is the case is the first relay of the olfactory system of insects, the antennal lobe, or its equivalent in vertebrates, the olfactory bulb (Sect. 1.2) [80].

Recently, through selective staining of projection neurons with a Ca\(^{2+}\)-sensitive dye, Sachse & Galizia (2002) [119] recorded odor-dependent spatial activity patterns in the honeybee. In addition, Sachse & Galizia (2002) observed that the activity patterns were not static during the stimulation period but displayed slow temporal dynamics. Using a similar technique, we specifically study in this chapter the spatial as well as these slow dynamic properties of projection neurons in the moth olfactory system.

In this chapter, we use optical imaging data from moth projection neurons to study in the context of static stimuli the three above-mentioned properties of a spatio-temporal code, i.e. whether spatial and temporal patterns of neuronal activity are stimulus dependent, and whether spatial patterns evolve in a stimulus dependent manner with time. We first show that the spatial pattern of projection
neuron calcium activity, averaged over the entire stimulation period of one second, is stimulus specific. Second, we show that the time course of calcium activity of projection neurons is stimulus dependent. Third, we show that spatial patterns of calcium activity, when examined on a shorter time scale than before with a spatial pattern for every 100 millisecond time window, display stimulus dependent temporal evolutions in a way that the spatial patterns to different odors become increasingly dissimilar with time.

3.2 Methods

3.2.1 Animal preparation and optical recordings

3.2.1.1 Preparation of animals

Male *Spodoptera littoralis* were used 2-4 days post-eclosion. The animals have been reared for several generations on a potato-based diet [59]. The pupae were separated according to sex and kept in plastic boxes at 70% relative humidity, 23°C and a 16 h/8 h light/dark cycle. Adult moths were supplied with water ad libitum until the start of experiment.

Animals were restrained in plastic pipette tips, with only the heads protruding. Dental wax was used to secure the animal in the holder and to minimize movements. The brain of the moth was uncovered by opening up a window in the cuticle between the compound eyes and by removing muscles, glands and tracheae. Mouthparts and proboscis were also removed. The brain was superfused with moth saline [27].

3.2.1.2 Dye loading

Retrograde selective staining of projection neurons through the inner antennal-cerebral tract was performed by injection of a dye-coated glass electrode (tip diameter 10 – 20 μm) into the inner antennal-cerebral tract. The majority of uniglomerular projection neurons leaving the antennal lobe have been shown to exit through
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3. Spatial dynamics

the inner antennocerebral tract in *S. littoralis* [7, 8, 121], and about five to six projection neurons of the inner antennocerebral tract innervate a single glomerulus [9]. Crystals of FURA-dextran (10000 MW, Molecular Probes, Eugene, USA) were dissolved in a 2 ml bovine serum albumin (~5% solution) and the tip of the electrodes was coated with the dye. The level of the moth saline was temporarily lowered to prevent the dye from dissolving prior to injection in the brain. To aim for the inner antennocerebral tract the electrode was manually inserted close to the midline of the brain about halfway between the antennal lobe and the mushroom bodies. The dye was allowed to diffuse for 10-20 seconds before the electrode was removed. After rinsing with moth saline the preparation was incubated in a cold (8–12°C) and dark chamber for about 3 hours. This procedure results in a staining of the antennal lobe as well as the inner antennocerebral tract [25]. The optical responses are odor dependent and reproducible with repeated stimulations both within and between animals [25].

3.2.1.3 Optical recordings

We used a TILL Photonics air-cooled imaging system (Gräfelfing, Germany) with a 12 bit slow-scan CCD camera. Filter settings were dichroic: 410 nm; emission LP 440 nm and the preparation was alternately excited at 340 and 380 nm. Exposure times were ~20 and 60 ms, respectively. Sequences of 70 double frames at a sampling rate of 10 Hz were recorded through an upright Olympus microscope with a 20× (NA 0.50; Olympus, Japan) water immersion objective. On-chip binning (2 × 2) was performed, which resulted in a final image size of 320 × 240 pixels. The pixel size at 20× magnification corresponded to ~1 × 1 μm². Execution of protocols was made using Till-vision 4.0 (TILL Photonics).

3.2.1.4 Odor delivery

A moistened and charcoal filtered continuous air stream (30 ml s⁻¹) was ventilating the antenna ipsilateral to the recorded antennal lobe.
through a glass tube (7 mm ID). The glass tube ended ~ 10 mm from the antenna. An empty Pasteur pipette attached to a plastic pipette tip (volume ~ 4.5 ml) was inserted through a small hole in the glass tube, blowing an air stream of about 5 ml s\(^{-1}\). Another air stream (~ 5 ml s\(^{-1}\)) was blown through the odor-loaded pipette by a computer-triggered puffer device (Syntech, The Netherlands) during 1 second (started at frame 20) into the continuous stream of air. During stimulation the air stream was switched from the empty pipette to the odor-loaded one, in order to minimize the influence of mechanical stimulation. Odorants used in the experiment were 1-octanol, geraniol, (+/-)-linalool and phenylacetaldehyde (PAA; 10 animals, one of which was only stimulated with 1-octanol and PAA). The odorants used are biologically relevant to the animal as components of green leaves and flowers of host-plants or emitted from larval frass [6, 66]. The purity of the compounds was between 95 and 99% and they were dissolved in paraffin oil. 10 \(\mu\)l of the solvent containing 50 \(\mu\)g of the respective odorant were applied on filter papers (5 \(\times\) 15 mm\(^2\)). The filter papers were inserted in Pasteur pipettes, attached to plastic pipette tips, sealed with Para-film (American National Can., Chicago, USA) and stored in a freezer (\(-20^\circ\)C) until the start of an experiment. Control stimuli consisted of filter paper with solvent (10 \(\mu\)l) only. Odorants and control were delivered in a randomized order. Each odor was presented between 1 to 12 times, and we allowed at least 60 seconds between stimulations to reduce adaptation effects.

### 3.2.2 Optical projection neuron response

A well known problem with optical imaging using calcium-sensitive dyes is that the data must be corrected for bleaching. In case of FURA-dextran, this correction must be performed independently for both the 340 nm and 380 nm sequences since the time constant of the bleaching is different (as will be shown below). Here, we correct for bleaching by fitting a function to the fluorescence response of all frames excluding the 30 frames after stimulus onset. Subse-
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Consequently, these two functions are used to correct all frames in the sequence. We capture the bleaching effect using an exponential

\[ b(t_i; A, B, \tau_{\text{bleach}}) = A + B \exp \left( -\frac{t_i}{\tau_{\text{bleach}}} \right) \]  

(3.2.1)

where the fitting parameters are the offset, \( A \), the amplitude, \( B \), and the time constant, \( \tau_{\text{bleach}} \). For each illumination wavelength, this procedure results in two exponentials, \( b_{340}(t_i) \) and \( b_{380}(t_i) \) where \( \langle \tau_{340} \rangle = 6.9 \pm 3.1 \) and \( \langle \tau_{380} \rangle = 9.4 \pm 5.9 \) (median and halved interquartile range). The bleaching-corrected ratio, \( F_{\text{ratio}} \), is computed following

\[ F_{\text{ratio}}(t_i, x) = \frac{F_{\text{raw}, 340}(t_i, x) - [b_{340}(t_i) - \min_i b_{340}(t_i)]}{F_{\text{raw}, 380}(t_i, x) - [b_{380}(t_i) - \min_i b_{380}(t_i)]} \]  

(3.2.2)

where \( x \) denotes a pixel, and \( t_i, i = 1, 2, \ldots, 70 \) the frame. \( F_{\text{raw}, 340} \) and \( F_{\text{raw}, 380} \) are the raw responses to illumination with 340 nm and 380 nm respectively, and \( \min_i(.) \) is the minimum value of the argument over \( i \).

Borders of glomeruli are visible in the fluorescence image and quadratic regions of interest of size 10 x 10 pixels (about 10 \( \mu \text{m} \) x 10 \( \mu \text{m} \)) are drawn in the centers of the glomeruli. The size of the regions of interest fits well within the size of a glomerulus (50 \( \mu \text{m} \)) and the position in the center limits light scattering from neighboring glomeruli. Smaller regions render noisier time courses and larger regions do not further improve the signal-to-noise ratio (Fig. 3.1). Subtracting the mean fluorescence before stimulation (frame 2 to 20) from \( F_{\text{ratio}}(t_i, x) \) for each frame, \( i \), and averaging over all pixels, \( x \in S \), of a region of interest, \( S \), yields the optical projection neuron response,

\[ F_{\text{PN}}(t_i) = \langle F_{\text{ratio}}(t_i, x) - \langle F_{\text{ratio}}(t_j, x) \rangle \rangle_{j=2,\ldots,20} \rangle_{x \in S}, \]  

(3.2.3)

where \( \langle . \rangle \) denotes the average value over the specified variables and ranges.
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Figure 3.1: Noise magnitude in arbitrary units as a function of the side length of the region of interest (which is a square). The noise magnitude is the standard deviation of the time course of the calcium response before stimulus onset. The values shown are the mean ± the standard error of the mean (n = 7 animals).

3.2.3 Data analysis

Data analysis is done using Matlab (The MathWorks, Inc., Natick, MA, USA). A principal component analysis (PCA) is performed to compare the distances between the response vectors to different odors. In this analysis, data from a single animal are used and a response vector to an odor is defined as the spatial vector with as many entries as visible glomeruli where each entry is the mean of the optical projection neuron response over frames 21-30. The response vectors obtained from all repetitions with all odors are written in a response matrix of size (number of glomeruli) × (total number of stimulations). A PCA is computed based on this response matrix. Additionally, the average response vectors of each odor are tested for significant differences by means of a MANOVA.

In order to quantify differences in odor-evoked time courses across glomeruli we compare the optical projection neuron responses to a given odor at three time bins (300, 600 and 900 ms after stimulus onset, respectively) in two different glomeruli. The response ampli-
3.3. Results

The results section consists of two parts. In the first part, we examine the spatial and temporal properties of the calcium response of projection neurons. In the second part, we investigate and quantify the similarity between the spatial response patterns across projection neurons to different odors.

3.3.1 Spatial and temporal characteristics of projection neuron calcium response

Previous measurements of the projection neuron calcium response suggested that odor stimulation evokes spatial patterns of activity [119, 120]. In the following, we test whether these spatial activation patterns are repeatable for trials with the same odor but different...
Figure 3.2: Principal component analysis of the spatial response patterns (responses in 14 glomeruli) to four different odors (four or five trials with each odor) in a single animal. 

a. Representations of odors in the space formed by the first three principal components. 

b. The coordinates of the first three basis vectors of the principal component system.

c. Percentage of variance explained vs. principal component dimension.

d. Comparison of the within- to the between-groups distance as a function of the principal component dimension. The between-groups distance is the average distance between the centers of the clusters formed by each odor computed for each dimension in the principal component system. Similarly, the within-groups distance is the average size of each cluster along every principal component dimension. 

Abbreviations: ger, geraniol; lin, linalool; oct, octanol; PAA, phenylacetaldehyde; PC, principal component.
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between odors, based on a principal component analysis in a single animal (four to five repetitions of each odor stimulus). A response pattern to an odor is defined as a spatial vector where the response amplitude in each visible glomerulus (14 glomeruli) represents a single dimension (see Sect. 3.2.3). Figure Fig. 3.2a shows a graphic representation of the first three principal components, which describe 92.6% of the total variance of the data (Fig. 3.2c), and the coordinates of the first three principal components are shown in Fig. 3.2b. Using a comparison of the between-groups distance to the within-groups distance [74] (see also Sect. 2.2.3), we observe that only the first three principal components describe group-specific information, i.e. the between-distance is larger than the within-distance for the first three dimensions (Fig. 3.2d). The organization of the response patterns in this three-dimensional principal component space shows that the responses to octanol and PAA are clearly separated and narrowly clustered. The spatial organization of the responses to geraniol and linalool groups in less defined clusters but are separated from octanol and PAA. Geraniol and linalool are two plant-derived monoterpenes with the same chemical composition and are structural isomers of each other. Finally, a MANOVA shows that the multivariate means of the response vectors are different between odors (one-way MANOVA, $\chi^2 = 119.2, p = 2.5 \times 10^{-9}$; see Sect. 3.2.3). Thus, the spatial response patterns are repeatable for the same stimulus and different between stimuli.

In addition to the stimulus-dependent spatial organization of the projection neuron responses we also observe that the activity patterns show a temporal evolution. We find that when comparing the response amplitude in different glomeruli at different time bins their relative strength differs (Fig. 3.3). The responses of two arbitrary glomeruli shows consistent temporal dynamics across trials. For instance, glomerulus number 2 shows a stronger response to octanol 300 ms after stimulus onset compared with glomerulus number 1. At about 600 ms the time courses cross and at 900 ms the activation of glomerulus 1 exceeds that of glomerulus 2. These differences in response amplitude are statistically significant at 300 and 900 but
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Figure 3.3: Projection neuron response as a function of time. Calcium dynamics for **a** octanol and **b** phenylacetaldehyde (PAA) measured in two glomeruli (see map, **c**). Three repetitions of each are shown. The shaded areas indicate the stimulus period (1 s). With octanol glomerulus 2 consistently reaches the response peak before glomerulus 1. With PAA, on the other hand, glomerulus 2 always responds most strongly. See the text for statistical analyzes.
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not at 600 ms (paired t-test, one-sided at 300 and 900 ms, two-sided at 600 ms, \( p = 0.018, p = 0.88, p = 0.00003 \), respectively, \( n = 12 \)). For PAA, on the other hand, the strongest activity is recorded in glomerulus 2 at all three time bins \( (p \ll 0.001 \) at all three time bins, \( n = 11 \)). Hence, the calcium response of projection neurons displays temporal modulations, and these modulations are dependent on both stimulus and glomerulus.

3.3.2 Similarity reduction of activity patterns evoked by different odors

![Graphs showing correlation between spatial odor responses over time](image)

Figure 3.4: Correlation between spatial odor responses as a function of time. **a** Pearson's correlation indices (median ± standard error of median) for comparisons of responses evoked by either the same odor (octanol or phenylacetaldehyde (PAA), 132 comparisons) or between odors (octanol and PAA, 121 comparisons) in a single animal at each 100 ms bin. **b** Median correlation index (Pearson's correlation) for each pair of odors across animals (± standard error of median; \( n = 9 \) animals) calculated for each 100 ms bin. In the across trial comparison, correlations of all pairs of the same odor are averaged. The grey rectangles indicate the stimulation period (1 s). Significance levels: \( p < 0.05 \) (*); \( p < 0.001 \) (**); not significant (NS), \( \alpha = 0.05 \). Abbreviations: ger, geraniol; lin, linalool; oct, octanol.
Finally, we want to examine whether the similarity of the spatial patterns evoked by different odorants change during the course of odor stimulation\(^1\). We calculate the linear correlation (Pearson’s correlation coefficient) at each time bin between all pairs of activity patterns, both in a single animal (Fig. 3.4a) with multiple trials of two of the odors and across nine animals where we obtained at least two repetitions of all four odors (Fig. 3.4b). The correlations are calculated for all time bins in a sequence. The correlations obtained at the different time bins from response onset (300 ms after stimulus onset) and 900 ms onwards are compared in a statistical test (Friedman’s test; see Sect. 3.2.3). As a control we compare trial-to-trial correlations of patterns evoked by the same odor (all odors pooled). The latter correlations do not significantly change over time (\(p = 0.14\) in the single animal and \(p = 0.64\) across all animals). Correlations of responses evoked by different odorants, on the other hand, change as a function of time (with one exception). The similarity between the responses decreases from 300 to 1200 ms after stimulus onset. Responses to geraniol and octanol also decrease in similarity but, due to a high variance, the difference is not statistically significant (\(p = 0.06\)). This analysis demonstrates a temporal sharpening of the spatial response patterns across projection neurons in the sense that the similarity of the patterns evoked by different odors decreases with time.

### 3.4 Discussion

We investigated in this chapter the spatial and temporal properties of the intracellular calcium concentration in a large population of moth projection neurons in response to plant odor stimulation. We showed that the evoked calcium activity of projection neurons is dependent on the stimuli in both its spatial distribution and its temporal structure. Moreover, we showed that the spatial response

\(^{1}\)The idea for this analysis was contributed by Carlsson. The analysis was performed by both Carlsson and Knüsel.
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pattern across projection neurons triggered by different stimuli became increasingly more decorrelated with time.

A spatial representation of odors in the antennal lobe (or olfactory bulb) is the consequence of the organization of converging olfactory receptor neurons [46, 146]. This spatial organization is at least roughly conserved at the output level of the antennal lobe. When we averaged the calcium responses over the entire stimulus period of 1 second, we found that the odors evoked spatially specific patterns of glomerular activation that were repeatable across stimulations. In a study of both the input and the output of the honeybee antennal lobe, Sachse & Galizia (2002) [119] further showed that the contrast between the global patterns evoked by different odors increased from input to output, which suggests the action of an inhibitory network. In this chapter, a principal component analysis of the global activity patterns averaged over the entire stimulus window revealed that the spatial representation of the odors grouped into clusters. Interestingly, the spatial response patterns evoked by the structurally similar compounds linalool and geraniol were less distinguishable. It should, however, be noted that recordings were performed from a subset of glomeruli (30%) and if we could include responses in non-accessible glomeruli, the spatial response patterns evoked by similar compounds might differ more clearly.

Friedrich & Laurent (2001, 2004) [38, 39] showed that the firing patterns of olfactory bulb output neurons, the mitral cells, evoked by different odors in zebrafish decorrelated over time. Individual mitral cell response profiles remained, on average, constant, i.e. tuning did not narrow over time while the overlap of responding neurons decreased. Similarly, results from locusts, honeybees, and moths have demonstrated that the classification of odor stimuli based on spatial vectors of activity across projection neurons improves over the course of stimulus presentation [38, 41, 134], suggesting an enhanced contrast of these spatial activity patterns to different compounds. Inspired by these studies we set out to investigate how correlations between odor-evoked global activity patterns of projection neurons changed during the course of odor exposure. We found that repre-
sentations of different compounds became increasingly more decor-related with time. The correlations between patterns evoked by the same odor, however, did not change significantly during the course of stimulation. This control showed that this result was not due to an increase of noise in the signals during the period of stimulation and that the spatio-temporal patterns were reproducible. Three of the odorants used (geraniol, linalool and octanol) elicited glomerular activity patterns that were highly correlated shortly after response onset. These three compounds are indeed structurally similar. The two monoterpenes, geraniol and linalool, for example, are structural isomers of each other. In contrast, responses to PAA, an aromatic compound with an attached aldehyde group, clearly already differed from responses to the other compounds at the response onset. Geraniol, linalool and octanol activate overlapping subsets of olfactory receptor neurons in S. littoralis [5, 66]. PAA and other aromatic compounds, on the other hand, activate different subsets of olfactory receptor neurons. Regardless of the original similarity, patterns evoked by different compounds sharpened during the course of exposure. This observation raises the question as to what the behavioral significance would be for the temporal improvement of odor representations. One could speculate that the initial encounter with plant-related volatiles may only require increased attention and a rough discrimination. As the moth approaches a potential food-source there will be enough time to develop a fine discrimination. Behavioral support for our results comes from the honeybee. Honeybees can easily discriminate between structurally similar compounds [78]. Correct discrimination, however, required about 700 milliseconds [34]. In the latter study different blend ratios of nonanol and linalool were used, i.e. two straight-chained molecules with attached alcohol group. In this chapter we also found a high initial similarity between, for example, linalool and octanol which, however, decreased over time. It would thus be very interesting to test the behavioral discrimination time between compounds that are structurally very different, like aromatics and terpenes. Faster discrimination times have been reported from rats (200–300 ms;
3.4. Discussion

[1, 142]) whereas humans may need as long as 2 seconds to discriminate between similar odors [149]. The rats, however, needed several hundred trials to learn the fast discrimination [1].

Similar to other functional imaging studies [43, 119, 131] we found that glomerular activity patterns were not static during the stimulus presentation. The calcium dynamics were temporally complex, glomerulus specific and highly repeatable. All glomeruli responded with a transient increase in calcium concentration at about 100–200 milliseconds after stimulus onset. This response latency is consistent with single cell recordings from olfactory receptor neurons and antennal lobe neurons in *S. littoralis* using the same odor delivery system as used in the current study [5, 7, 8]. A large part of this response latency is due to the delivery method, i.e. the time from triggering the puffer device until the molecules reach the receptor site. A stimulus-dependent temporal variability of the projection neuron responses was observed in the decay to baseline. For example, projection neurons that showed a higher peak amplitude could show a rapid decay and vice versa. As a result the relative relation between amplitudes across projection neurons changed, which means that the global glomerular activity patterns changed. If decay speed and peak amplitude were correlated with each other then spatial patterns would be similar at different time points and only differ in absolute strength. Hence, our data suggest that the amplitude time course of the projection neuron calcium response might be modulated both in its decay speed and peak amplitude. We will investigate this possibility and its implications for the encoding of odor stimuli in the next chapter.
Chapter 4

Contribution of
temporal dynamics to
the encoding of static
stimuli

4.1 Introduction

We already saw that the role of time in the encoding of information by the nervous system has been debated for decades [32]. In this debate, a distinction is usually made between population and single cell encoding. At the level of neuronal populations, it has been argued, going back to Milner (1972), that synchronous neuronal activity could provide the substrate to functionally link information encoded in spatially distributed activity patterns and therefore solve the, so called, binding problem [103, 128, 144]. Synchrony has been observed in a number of neuronal systems [116] including the olfactory system where output neurons of the antennal lobe or the olfactory bulb displayed sequences of synchronized assembly
4.1. Introduction

At the level of single neurons, evidence from various sensory systems indicates that neurons can also show temporally patterned responses to static sensory stimuli [33, 67, 80, 99, 102, 107]. In the olfactory system, the output neurons of the antennal lobe/olfactory bulb display temporally patterned responses on a time scale of hundreds of milliseconds [38, 80]. Previously, we and others have shown that this temporal patterning is accompanied by a decrease of the similarity between spatial odor representations in the antennal lobe/olfactory bulb with time [25, 38] (Chap. 3). Despite elaborate considerations on the putative role of these temporal patterns in neuronal processing [80], their information content in the encoding of odor stimuli has so far not been quantified. In this chapter, we assess and quantify the role of these temporal patterns in the encoding of odor stimuli based on our theoretical investigation of the encoding and decoding of static stimuli into temporal patterns of neuronal activity by a so-called temporal population code [74, 151, 153] (see also Chap. 2). In these studies, we have shown that the temporal structure of the summed activity of a coupled neuronal population provides for a robust and rapid encoding of static stimulus features.

In this chapter, we quantify and assess the accuracy and the speed of the encoding of odor stimuli based on spatial, temporal, and spatio-temporal encoding schemes, using optical imaging from the projection neurons of the moth antennal lobe [25]. Whereas optical imaging analysis methods usually focus on extracting spatial activation patterns [40, 130], here, we propose a model based analysis method that also allows for a quantification of the temporal dynamics of the optical response. The optical response we analyze is measured in the center of the glomeruli visible in the staining of the antennal lobe and shows the response of the projection neurons leaving the antennal lobe via the inner antenno-cerebral tract (Sect. 3.2.1) [25]. As most projection neurons of that tract are uniglomerular [9], we call this response the optical projection neuron response of a glomerulus (or, the optical projection neuron response, Sect. 3.2.2). We fit [132] a biophysically derived model
function [57, 106, 154], a so-called alpha-function, to the optical projection neuron response. On the basis of this model, we quantitatively assess first to what extent the temporal pattern of the optical projection neuron response is modulated by odor stimuli and subsequently which properties of this response contain information on odor stimuli. We show that the spatial and temporal components of the optical projection neuron response to odor stimuli are uncorrelated and that a combinatorial spatio-temporal encoding of odor stimuli renders a 60% improvement in classification as compared to a purely spatial encoding scheme. Hence, our results prove that temporal dynamics of neuronal activity, measured on a time scale of hundreds of milliseconds, contain a significant amount of information about odor stimuli.

4.2 Methods

4.2.1 Animal preparation, optical recordings, and optical projection neuron response

Preparation of animals and optical recordings were described in detail in Sect. 3.2.1. The optical projection neuron response was introduced in Sect. 3.2.2.

4.2.2 Odors

In 6 animals, we used the odors 1-octanol, geraniol, (+/-)-linalool and phenylacetaldehyde (PAA) at doses of 50 µg and 100 µg (except one animal where only 1-octanol and PAA at both doses were tested). In a seventh animal, additionally benzaldehyde, eugenol, E2-hexenal and heptanol were used (all eight odors at 50 µg, heptanol at 17 µg [101]). Odors were dissolved in paraffin oil and applied on filter papers. Control stimuli consisted of filter paper with solvent (10 µl) only. Odorants and control were delivered in a randomized order. Each odor was presented between 1 to 12 times, and we allowed at least 60 seconds between stimulations to reduce
adaptation effects.

### 4.2.3 Model function of projection neuron response

In order to fit the optical projection neuron response we need a biophysical model that accurately describes the intracellular calcium dynamics due to both stimulus- and dye-dependent effects. Usually, single synaptic calcium input currents are modeled using exponential decays or alpha-functions [31]. Here, however, we need to describe the calcium dynamics that results from many synaptic events over a number of seconds. Our model is based on the assumption that first order kinetics govern the increase of the intracellular calcium concentration in the projection neurons upon odor stimulation [132]. In this case, the total ionic calcium input current to a projection neuron is given by an exponential decay

\[
I(t) \propto \begin{cases} 
0 & \text{if } t < s \\
\exp \left( -\frac{t-s}{\tau_I} \right) & \text{else}
\end{cases}
\]  

(4.2.1)

where \( t \) is time, \( s \) denotes stimulus onset, and \( \tau_I \) is the time constant. If the validation of the model function derived here shows that it provides an accurate description of the optical projection neuron response, this suggests that our assumption of first order kinetics may be correct (see below for a validation of our model). Using single compartment models, the dynamics of the intracellular calcium concentration in the presence of a dye have been described with first-order differential equations [57, 106], the general solution of which is that the free intracellular calcium concentration is described as the convolution of the input current with an exponential decay [154]. Here, we assume that all processes of the projection neuron that are imaged using FURA-dextran can be considered as one compartment, i.e., influx, efflux and buffering is uniform throughout. Combining these models of the dynamics of the free intracellular calcium concentration, \([Ca^{2+}]_i(t)\), with our assumption of an exponentially
decaying input current (Eq. 4.2.1) renders

$$[\text{Ca}^{2+}]_i(t) \propto \exp\left(-\frac{t-s}{\tau_D}\right) - \exp\left(-\frac{t-s}{\tau_I}\right). \quad (4.2.2)$$

$\tau_D$ is the decay time constant of $[\text{Ca}^{2+}]_i$ to a brief impulse of calcium input current (impulse response), and $\tau_I$ is the time constant of the projection neuron input current (Eq. 4.2.1). Thus, the free intracellular calcium concentration, $[\text{Ca}^{2+}]_i(t)$, is proportional to the difference of two exponentials with time constants $\tau_D$ and $\tau_I$.

![Alpha-function](image)

Figure 4.1: Alpha-function. The four parameters of the alpha-function are the amplitude-coefficient $S$, the baseline shift $B$, the response onset to, and the decay time constant $\tau$. The amplitude, $A$, is the difference between the peak and baseline activity of the alpha-function, and the duration, $D$, is the width of the alpha-function at half maximum limited by $t_1$ and $t_2$.

For $\tau_D \to \tau_I$, this difference can be approximated by a so-called alpha-function (Fig. 4.1 and App. A.2)

$$\alpha(t; S, B, \tau, t_0) = B + \left\{ \begin{array}{ll} 0 & \text{if } t < t_0 \\ S \frac{t-t_0}{\tau} \exp\left(-\frac{t-t_0}{\tau}\right) & \text{else} \end{array} \right. \quad (4.2.3)$$

if $\tau_D > \tau_I$. In case of $\tau_D < \tau_I$, the difference is $-\alpha(t; S, B, \tau, t_0)$. The four parameters of the alpha-function, the amplitude-coefficient, $S$,
4.2. Methods

The fluorescence intensity after bleaching-correction, \( \hat{F}(t) \), depends linearly on \([\text{Ca}^{2+}]_i(t)\) if the dissociation constant of FURA-2, \( K_D \), is much smaller than the intracellular calcium concentration, that is, \([\text{Ca}^{2+}]_i(t) \ll K_D \) [154]. Indeed, there is evidence that this assumption is satisfied. In *Drosophila* motor neurons, the intracellular calcium concentration was determined to be about 23 ± 11 nM [93] while the dissociation constant of FURA-2 is around 140 nM (Molecular Probes, Inc., Eugene, OR, USA). Thus, since the bleaching-corrected fluorescence depends linearly on the intracellular calcium concentration, it can be approximated with an alpha-function,

\[
\hat{F}(t) = \hat{F}_0 + \alpha(t; S, B, \tau, t_0), \tag{4.2.4}
\]

where \( \hat{F}_0 \) is the constant background fluorescence. (We always use the capital letter \( F \) for the measured fluorescence response whereas the modeled fluorescence response will have a hat, \( \hat{F} \).)

![Figure 4.2: Bleaching-corrected response of an arbitrary glomerulus to geraniol (100 \( \mu g \)) upon illumination of the antennal lobe with light at (a) 340 nm and (b) 380 nm. Note the high background fluorescence (\( F_{0,340} \) and \( F_{0,380} \)), indicated by the grey horizontal line. The shaded area indicates the stimulus.](image)

We now showed that the fluorescence response can be approximated with an alpha-function. In case of FURA-2, the probe is illuminated with two frequencies (340 nm and 380 nm) resulting in two fluorescence responses, one of which has a positive, the other a neg-
4. Temporal dynamics  

4.2. Methods

active peak (Fig. 4.2) [51]. Thus, with \( \hat{F}_{340} \) and \( \hat{F}_{380} \) the bleaching-corrected responses at 340 nm and 380 nm, we obtain

\[
\begin{align*}
\hat{F}_{340}(t) &= \hat{F}_{0,340} + \alpha_{340}(t; S_{340}, B_{340}, \tau_{340}, t_{0,340}) \quad (4.2.5) \\
\hat{F}_{380}(t) &= \hat{F}_{0,380} - \alpha_{380}(t; S_{380}, B_{380}, \tau_{380}, t_{0,380}) \quad (4.2.6)
\end{align*}
\]

where \( \hat{F}_{0,340} \) and \( \hat{F}_{0,380} \) are the background fluorescences defined as the mean fluorescence of frames 2 to 20. The parameters \( S, B, \tau, \) and \( t_0 \) are defined above. Note the minus sign of the 380 nm response which is due to the properties of the dye. The ratio of these sequences is the modeled optical projection neuron response, \( \hat{F}_{PN}, \)

\[
\hat{F}_{PN}(t) = \frac{\hat{F}_{340}(t)}{\hat{F}_{380}(t)} = \frac{\hat{F}_{0,340} + \alpha_{340}(t)}{\hat{F}_{0,380} - \alpha_{380}(t)}. \quad (4.2.7)
\]

For simplicity, we omitted the parameters of the alpha-function. It is important to note that the average background fluorescence is much greater than the stimulus-evoked change in fluorescence (Fig. 4.2), that is, \( \hat{F}_{0,z} \gg \max_t (\alpha_z(t)), z \in \{340, 380\}. \) Thus, Eq. 4.2.8 can be approximated by its Taylor series, resulting in (see App. A.2)

\[
\hat{F}_{PN}(t) \approx \frac{\hat{F}_{0,340}}{\hat{F}_{0,380}} + \frac{1}{\hat{F}_{0,380}} \alpha_{340}(t) + \frac{\hat{F}_{0,340}}{\hat{F}_{0,380}^2} \alpha_{380}(t). \quad (4.2.9)
\]

The sum of the two alpha-functions in Eq. 4.2.9 can be replaced by a single alpha-function if \( \tau \) and \( t_0 \) are about equal. In order to show that, we note that the dynamics of the fluorescence response to illumination with 340 nm or 380 nm only depend on the odor-evoked fluctuations of the intracellular calcium concentration and not on the illumination wavelength. Therefore, the time constants \( \tau_{340} \) and \( \tau_{380} \) and the response onset times \( t_{340} \) and \( t_{380} \) are approximately equal.
and the sum of the two alpha-functions in Eq. 4.2.9 simplifies to

\[ \hat{F}_{PN}(t) \approx \frac{\hat{F}_{0,340}}{\hat{F}_{0,380}} \]

\[ + \frac{\hat{F}_{0,340}S_{380} + \hat{F}_{0,380}S_{340}}{\hat{F}_{0,380}} \alpha(t; S, B, \tau, t_0) \]

\[ = \alpha(t; S \cdot k_2, B + k_1, \tau, t_0). \] (4.2.10)

\[ \alpha \] is an alpha-function with an appropriately chosen set of parameters \( S, B, \tau, \) and \( t_0 \) determined with non-linear regression [124], and \( k_1 = \frac{\hat{F}_{0,340}}{\hat{F}_{0,380}} \) and \( k_2 = \frac{\hat{F}_{0,340}S_{380} + \hat{F}_{0,380}S_{340}}{\hat{F}_{0,380}} \) are two constants. Hence, under the assumption of an exponential calcium influx to the projection neurons of a single glomerulus (Eq. 4.2.1), this analysis predicts that the measured optical projection neuron response, \( F_{PN} \) (Eq. 3.2.3), can be approximated by a single alpha-function (Eq. 4.2.11).

### 4.2.4 Response amplitude and duration

In our further analysis we only want to consider those parameters of the alpha-function that define the temporal dynamics of the response. Hence, out of the four parameters of the alpha-function, we focus here on only two of them, the amplitude-coefficient and the time constant, or their linearly dependent counterparts, the projection neuron response amplitude and duration.

The response amplitude, \( A \), is defined as the maximum value of the alpha-function minus the baseline shift, \( B \). Since the alpha-function is maximal at time \( t = t_0 + \tau \) (Fig. 4.1), we have

\[ A = \alpha(t_0 + \tau; S, B, t_0, \tau) - B = S \exp(-1) = \frac{S}{e} \] (4.2.12)

where \( e \approx 2.72 \) is the base of the natural logarithm. Thus, the response amplitude equals the amplitude-coefficient of the alpha-function, \( S \), divided by \( e \). The response duration, \( D \), is defined as
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the width of the alpha-function at half maximum, that is \( \frac{S}{2e} + B \) (Fig. 4.1). The width is delimited by two points in time, \( t_1 \) and \( t_2 \), where the alpha-function equals \( \frac{S}{2e} + B \). Thus, \( t_1 \) and \( t_2 \) have to satisfy

\[
\alpha(t_{1/2}; S, B, t_0, \tau) = \frac{S}{2e} + B \quad (4.2.13)
\]

\[
\Leftrightarrow \frac{t_{1/2} - t_0}{\tau} \exp \left( -\frac{t_{1/2} - t_0}{\tau} \right) = \frac{1}{2e} \quad (4.2.14)
\]

\[
\Leftrightarrow x_{1/2} \exp \left( -x_{1/2} \right) = \frac{1}{2e} \quad (4.2.15)
\]

where we set \( x_{1/2} := \frac{t_{1/2} - t_0}{\tau} \). Eq. 4.2.15 has two solutions \( x_1 \) and \( x_2 \) that can be found numerically. The duration is then given by

\[
D = t_2 - t_1 = \tau(x_2 - x_1) \approx \tau \cdot 2.45 \quad (4.2.16)
\]

where \( \tau \) is the time constant of the alpha-function. Thus, the response amplitude only depends on the amplitude-coefficient of the alpha-function, and the response duration only depends on its time constant.

4.2.5 Fit validation

The accuracy of the fits is validated by combining both graphical and analytical methods. Model fits that do not satisfy the analytical conditions are rejected.

In order to assess the accuracy of the fit we use three measures, the adjusted R-squared statistic, the amplitude-to-noise ratio and the t-statistic. The adjusted R-squared statistic, \( R_{adj}^2 \), is based on the sum of squared residuals, \( S_{err}^2 \), and the total sum of squares around the mean, \( S_{tot}^2 \). With \( F_i = F_{PN}(t_i) \) the measured optical projection neuron response and \( \hat{F}_i = \hat{F}_{PN}(t_i), i = 1, 2, \ldots, n \) the
fitted optical projection neuron response, the sums are expressed as

\[ S_{err}^2 = \sum_{i=2}^{n} (F_i - \hat{F}_i)^2 \quad (4.2.17) \]

\[ S_{tot}^2 = \sum_{i=2}^{n} (F_i - \langle F \rangle)^2 \quad (4.2.18) \]

where \( n = 70 \) is the number of data points, and \( \langle F \rangle \) is the mean of \( F_i \). Then, \( R^2_{adj} \), which measures the fraction of \( S_{tot}^2 \) explained by the function \( \hat{F}_{PN} \) is expressed as

\[ R^2_{adj} = 1 - \frac{S_{err}^2(n - 1)}{S_{tot}^2(n - p)} \quad (4.2.19) \]

where \( n \) is the number of data points and \( p \) the number of parameters of the model function. The value of \( R^2_{adj} \) is always lower or equal 1, and a value closer to 1 indicates a better fit.

The second measure, the amplitude-to-noise ratio, compares the response amplitude, \( A \), to the standard deviation of the residuals (noise), \( \sigma \). According to the assumptions of non-linear regression [124], the residuals

\[ \varepsilon_i = F_{PN}(t_i) - \hat{F}_{PN}(t_i) \quad (4.2.20) \]

are Gaussian with zero mean and variance \( \sigma^2 \), \( \varepsilon_i \sim \mathcal{N}(0, \sigma^2) \). Thus, we consider the ratio

\[ \eta = \frac{A}{\sigma} \quad (4.2.21) \]

to test whether \( \eta \) is not from \( \mathcal{N}(0, 1) \), the standard normal distribution, at significance level of \( \alpha \). As \( A > 0 \), we use a one-sided test, that is,

\[ Pr(\eta > \theta) < \alpha \quad (4.2.22) \]

defines a threshold, \( \theta \), for which \( \eta \) is from \( \mathcal{N}(0, 1) \) with probability \( \alpha \). \( \theta \) can be computed using the cumulative distribution function of the standard normal distribution. For \( \eta > \theta \), the response amplitude is significantly larger than a value randomly drawn from the
distribution of the residuals, $\mathcal{N}(0, \sigma^2)$. Thus, the projection neuron response cannot be due to random noise in the fluorescence signal with probability $1 - \alpha$.

Finally, we use the t-statistic to verify whether the estimated amplitude-coefficient, $S$, and the time constant, $\tau$, of the alpha function are significantly different from zero. The t-statistic is defined as the ratio between the estimated parameter value and its standard error where $n = 69$ is the number of data points. At a significance level of 0.05, the estimated values are significantly larger than zero if the ratio is larger than 1.67 (inverse of the Student's cumulative distribution function with $n - 1$ degrees of freedom).

### 4.2.6 Data analysis

Data analysis is done using Matlab (The MathWorks, Inc., Natick, MA, USA) and SPSS (SPSS, Inc., Chicago, IL, USA). For analysis of variance (ANOVA), independent variables (factors) are either the glomerulus, the odor stimulus, or odor identity and odor concentration. Dependent variables are either response amplitude or duration. The dependent variables are weighted with the inverse square of their standard deviation in order to correct for different accuracies in their estimates. The significance level is always $\alpha = 0.05$. In case of 2-way ANOVAs, the result is discarded if a significant interaction is detected.

The effect sizes of the two factors odor identity and concentration are measured using eta squared, $\eta^2$. This measure is defined as

$$
\eta^2 = \frac{S^2_{\text{effect}}}{S^2_{\text{total}}} \tag{4.2.23}
$$

with $S^2_{\text{effect}}$ the weighted sum of squares of the effect (odor identity or concentration), and $S^2_{\text{total}}$ the total weighted sum of squares. $\eta^2$ thus measures the fraction of total variability that is accounted for by each factor.

Predictive linear discriminant analysis (LDA) is used to predict the identity and concentration of an odor sample. We assess the
fraction of correct classifications, i.e. the ratio of correctly classified samples versus the total number of samples, with a so-called leave-one-out test. In this test, each sample is left out once and classified based on the discriminant functions derived from all remaining samples. Note that for this test we exclusively use LDA as a linear transformation of the representation of odors from one space to another, without computing any p-values. Thus, testing the assumptions of LDA is not required.

In the classification analyzes, each glomerulus represents the odor stimuli by means of either one of two response parameters or their combination. Missing values of the response parameters are replaced with the corresponding mean. We assess the fraction of correct classifications using the response parameters of subsets of glomeruli. As any read-out process is solely dependent on the information available in a single animal, these subsets of glomeruli are formed for each animal individually. The maximally possible size of these subsets depends on the number of samples and is between 3 and 7 (6 animals). The number of variables for the LDA corresponds either to the size or the doubled size of the subsets of glomeruli (dependent on whether only one or both response parameters represent the odor stimuli). In order to exclude those subsets of glomeruli that provide an insufficient encoding of the odor stimuli, we use for each size of the subsets only those 50 for which the fraction of correct classifications using the combined response parameters is best. The six animals used for the classification analyzes are stimulated with eight odors except one where only four odors are tested and another one where more than one repetition is acquired to five odors. In order to correct for the different number of odor stimuli, fraction correct values are weighted with the according number of odor stimuli divided by the mean number of stimuli. Of these values, the median and the standard error of the median is computed. Tests showed that using unweighted fraction correct values yields similar results.

We carry out two classification analyzes. In a first analysis, odor samples are represented using an encoding based on the response
amplitude, duration, or their combination (i.e. a combinatorial encoding). The second analysis is based on instantaneous counterparts of these encoding schemes where either the instantaneous amplitude of the model function, its derivative (i.e. the instantaneous amplitude change), or their combination represent the odor.

The fraction correct values of the different encoding schemes are statistically compared using Friedman’s test ($\alpha = 0.05$). Post-hoc pairwise comparisons are performed using Wilcoxon’s rank sum test. We use the Dunn-Sidak correction to adjust the significance level for the individual comparisons such that the significance level for the complete set of comparisons is $\alpha_E = 0.05$. The corrected significance level is given by $\alpha = 1 - (1 - \alpha_E)^{(1/N)}$ where $N$ is the number of comparisons.

### 4.3 Results

#### 4.3.1 Fit validation

A standard measure to validate fits is the adjusted R-squared statistic, $R^2_{adj}$. Generally, this measure suffers from a central issue: neither do large values of $R^2_{adj}$ guarantee a good fit, nor do low values of $R^2_{adj}$ allow the conclusion of a bad fit. Thus, verifying fits by only reporting $R^2_{adj}$ is not enough. Therefore, as a first evaluation of the ability of our model to describe the data, we visually inspect the goodness of the fit for a broad range of $R^2_{adj}$-values (Fig. 4.3). We observe that the model follows the optical projection neuron response well for all values of $R^2_{adj}$ while the prediction bounds are wider for lower values of $R^2_{adj}$ compared to the other fits (Fig. 4.3, first column). This demonstrates that the model is good for a broad range of values of $R^2_{adj}$, with lower values corresponding to optical projection neuron responses with lower amplitudes, and, therefore, to fits that are intuitively worse. In order to further validate the sufficiency of our model, we test whether the residuals follow a normal distribution with constant standard deviation and zero mean. The scatter plots of the residuals versus the predictor variable time...
Figure 4.3: Graphical evaluation of goodness of fit. First column: Fitted alpha-function (solid line) including simultaneous prediction bounds (shaded area) overlayed on the optical projection neuron response (dashed line). The grey rectangle indicates the stimulus. Additionally, the adjusted R-squared statistic ($R^2_{adj}$) and the amplitude-to-noise ratio ($\eta$) is given in each plot (Sect. 4.2.5). Second column: Residuals (dots) computed from the plots in the first column versus time. The dashed line indicates zero. The grey rectangle indicates the experimental region. Third column: Normal probability plot of the residuals of only the experimental region (grey rectangle in second column) and line joining the first and third quartiles of the residuals (solid line) including an extrapolation out to the extreme values of the residuals (dash-dotted line). The probability value, $p$, is for testing the hypothesis of a normal distribution of the data (Kolmogorov-Smirnov test). a–e Each row shows the same three plots for a different glomerulus with a descending order of $R^2_{adj}$. 

\[ R^2_{adj} \approx 0.95 \]
\[ \eta \approx 13.8 \]

\[ R^2_{adj} \approx 0.78 \]
\[ \eta \approx 6.5 \]

\[ R^2_{adj} \approx 0.44 \]
\[ \eta \approx 3.4 \]

\[ R^2_{adj} \approx 0.28 \]
\[ \eta \approx 2.5 \]

\[ R^2_{adj} \approx 0.22 \]
\[ \eta \approx 2.2 \]
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(Fig. 4.3, second column) show a constant standard deviation and zero mean. Finally, projecting the residuals against a normal distribution shows that they fall on a straight line, i.e., they follow a normal distribution (Fig. 4.3, third column). This is further confirmed by a statistical test of the goodness-of-fit (Kolmogorov-Smirnov test) of the residuals to a normal distribution (p-values given in Fig. 4.3, third column). In summary, this verification demonstrates that, for a broad range of values of $R^2_{adj}$, our model fits the optical projection neuron responses well while $R^2_{adj}$ scales with the intuitive notion of a good fit.

![Figure 4.4: Analytical evaluation of goodness of fit. a Distribution of $R^2_{adj}$ for all fits carried out. The vertical black line at 0.3 is the threshold above which fits are accepted. b Distribution of the amplitude-to-noise ratio of all fits for which $R^2_{adj} > 0.3$. The values of the amplitude-to-noise ratio are always larger than 2, corresponding to a significance level of 0.023 (Sect. 4.2.5). c,d t-statistic of the estimated values for the alpha-function (c) time constant, $\tau$, and (d) amplitude-coefficient, $S$. The t-statistic is the estimated parameter value divided by its own standard error. The value of the t-statistic is always larger than 10, corresponding to a significance level of about $2.78 \times 10^{-15}$ (68 degrees of freedom).]
4.3. Results

In our further analysis we only want to consider those fits that give a statistically significant value for the amplitude. For this we have to impose a threshold for the $R_{adj}^2$ statistic (Fig. 4.4a). In order to establish this threshold we evaluate the amplitude-to-noise ratio (Fig. 4.4b). We consider an amplitude-to-noise ratio of 2 which gives us a significance level of 0.023. This threshold is equivalent to an $R_{adj}^2$ statistic of 0.3 (i.e. if a fit satisfies $R_{adj}^2 > 0.3$, then $\eta > 2$ is satisfied as well). This procedure results in about 85% of the fits being accepted. Additionally, to confirm that this choice of threshold provides us with a conservative selection of fits, we inspect the t-statistics of the alpha-function time constant and amplitude-coefficient (Fig. 4.4c,d). We observe that all values of $\tau$ and $S$ are significantly above zero. Thus, this demonstrates that our model provides an accurate description of the optical projection neuron response, that $R_{adj}^2$ is a valid measure to verify fits, and that the chosen threshold is reasonable. Hence, the optical projection neuron response can be accurately described in terms of amplitude and duration.

4.3.2 The optical projection neuron response displays a stimulus specific temporal structure

A necessary condition for an encoding scheme that incorporates both the amplitude and the duration of the optical projection neuron response of a glomerulus is that different glomeruli should display distinct values for these response parameters. This condition is satisfied for 7 animals for response amplitude, and for 5 for response duration (total of 7 animals, weighted 1-way analyzes of variance (ANOVAs), factor: glomerulus, between 12 and 18 glomeruli per animal, median p-value for amplitude: $\langle p \rangle \approx 5.7 \times 10^{-22}\ast\ast\ast$, median p-value for duration: $\langle p \rangle \approx 0.002\ast\ast$). Hence, the amplitude-time course of the optical projection neuron response to an odor stimulus is different between glomeruli.

A second condition for an encoding scheme that takes into account both the amplitude and the duration of the optical projection
neuron response of a glomerulus is that different odor stimuli should evoke distinct values for these response parameters. Pooled across all glomeruli of all animals (7 animals, 78 glomeruli), we find that odor stimuli have a significant effect on both the response amplitude and duration (weighted 1-way ANOVAs, factor: odor stimulus, amplitude: \( F(11,1703) \approx 5.7, p \approx 3.7 \times 10^{-9***}, \) duration: \( F(11,1703) \approx 65.6, p \ll 0.001*** \)). When we analyze the data at the level of single glomeruli, we observe that 26 glomeruli show significant simultaneous modulations of both amplitude and duration, while 21 display only modulations of the duration, and 6 show only modulations of the amplitude (weighted 1-way ANOVAs, factor: odor stimulus, \( \alpha = 0.05 \), median of p-values for simultaneous modulation: \( \langle p \rangle \approx 2.6 \times 10^{-4} \), only duration: \( \langle p \rangle \approx 0.007 \), only amplitude: \( \langle p \rangle \approx 0.002 \)). Thus, response amplitude and duration of most glomeruli are modulated in a combinatorial manner.

A third condition for an encoding scheme that is based on the amplitude and the duration of the optical projection neuron response of a glomerulus is that these response parameters should be linearly independent. The distribution of the response duration and amplitude of two arbitrary glomeruli shows that the response parameters to different odor stimuli are clustered and not significantly correlated (Fig. 4.5a–c). Across all glomeruli, we observe that amplitude and duration show an arbitrary correlation structure and are almost as often negatively correlated as positively (Fig. 4.5d). Moreover, in 59 out of 78 glomeruli, the observed correlation is statistically not significant (\( \alpha = 0.05 \)). Thus, amplitude and duration of most glomeruli are linearly independent.

In summary, these results show that for a majority of the glomeruli amplitude and duration of the optical projection neuron response of a glomerulus are uncorrelated and modulated by odor stimuli in a combinatorial manner. Thus, similar to the temporal patterning of the projection neuron or the vertebrate’s mitral cell firing rate [38, 39, 80, 134], the optical projection neuron response of most glomeruli displays a temporal structure that is different between odor stimuli.
Figure 4.5: Correlation between response duration and amplitude. 

**a,b** Response duration versus amplitude for two glomeruli showing no significant correlation between amplitude and duration. The correlation, $r$, and its p-value, $p$, are given in the figure. 

**c** Legend for panels (a) and (b). 

**d** Distribution of correlation coefficients for all glomeruli. Statistically not significant correlations indicate that amplitude and duration are linearly independent (black), while significant correlations indicate a linear dependence (gray). Abbreviations: geraniol (ger), linalool (lin), octanol (oct), phenylacetaldehyde (PAA).
4.3.3 Contribution of stimulus to modulation

![Bar chart showing contribution of stimulus to modulation]

Figure 4.6: Mean effect size ($\eta^2$, see Sect. 4.2.6). $\eta^2$ is averaged for all four combinations of odor identity/concentration with amplitude/duration. In the computation of the pooled averages, only effect sizes are used for which a significant p-value was returned by the weighted two-way ANOVAs of the amplitude and duration of the optical projection neuron response of each individual glomerulus (factors for ANOVA: odor identity and odor concentration, number of corresponding glomeruli that display significant effects given above each bar). Error bars indicate the standard error of the mean.

So far we have demonstrated that odor stimuli can induce significant modulations of the duration and amplitude of the optical projection neuron response. To exclude the trivial result that this modulation can be accounted for by the concentration itself, i.e. a higher concentration could boost the amplitude or the duration of the response, we assess the individual effect sizes of odor identity and concentration using eta squared, $\eta^2$ (Sect. 4.2.6). We observe that the effect size of the odor identity on both the amplitude and the duration of the optical projection neuron response is about twice as large as that for concentration. Moreover, each of these stimulus properties has a practically constant effect on the response parameters (Fig. 4.6, 2-way ANOVA of $\eta^2$, 6 animals, total of 65 glomeruli, amplitude/duration: $F(1,65) \approx 0.7, p \approx 0.41$, odor/concentration: $F(1,65) \approx 40.7, p \approx 2.1 \times 10^{-8}$**, interaction: $F(1,65) \approx 4.3, p \approx 0.043^*$). Thus, the modulation of the response duration is as strong as that of the amplitude and most of this modulation is ac-
4.3. Results

counted for by the identity of an odor.

4.3.4 Encoding of odor stimuli

![Graph: Median fraction of correct classifications versus the size of subsets of glomeruli.](image)

Figure 4.7: Median fraction of correct classifications versus the size of subsets of glomeruli. For each subset of glomeruli, odor stimuli are represented by either the according response durations, response amplitudes, or their combination (yellow, red, and blue line, respectively). The odor stimuli are classified with predictive linear discriminant analysis (LDA), and the fraction of correct classifications is computed with a so-called leave-one-out test (Sect. 4.2.6). Error bars indicate the standard error of the median. The dashed grey line indicates chance level. $n = 6$ animals.

Since both the amplitude and the duration of the optical projection neuron response depend on the odor stimulus we want to assess to what extent these two response parameters contain information on odor stimuli. We compute for subsets of glomeruli the fraction of correct classifications using three encoding schemes: an encoding based on amplitudes, an encoding based on durations, and an encoding based on their combination, i.e. a combinatorial encoding (Fig. 4.7 and Sect. 4.2.6, 6 animals). We find that for subset sizes larger than one the average fraction of correct classifications
for the combinatorial encoding is significantly higher than for the non-combinatorial encodings (Friedman's test for each subset size, between 85 and 300 data points per condition, \( p \ll 0.001 \) for all sizes; post-hoc Wilcoxon rank sum tests of all pairwise comparisons for a fixed subset size, \( \alpha = 0.017 \) corrected for three consecutive comparisons, \( p > \alpha \) for subset size one, but \( p \ll 0.001 \) for all other subset sizes, see Sect. 4.2.6). Moreover, we observe that an increased subset size contributes an additional and significant amount of information in terms of fraction correct (Wilcoxon's rank sum tests for each encoding scheme between consecutive subset sizes, \( p \ll 0.001 \) for all comparisons). Thus, the encoding of odor stimuli into the amplitude and the duration of the optical projection neuron response is complementary in the sense that their combination yields a higher information content than each of these components in isolation.

An important issue in the encoding of odor stimuli into the combination of the amplitude and the duration of the optical projection neuron response is how rapidly the encoded information is available without having to compute the actual response duration which would require integration over hundreds of milliseconds. To investigate this question we use the model function to replace the amplitude and duration with their instantaneous counterparts, i.e. the instantaneous amplitude of the model function and its temporal derivative, the instantaneous amplitude change. The three instantaneous encoding schemes we investigate are the encoding based on instantaneous amplitudes, the encoding based on instantaneous amplitude changes, and the encoding based on their combination, the instantaneous combinatorial encoding. For each of these encoding schemes, we compute the time course of the fraction correct for maximally-sized subsets of glomeruli (6 animals, see Sect. 4.2.6). This reveals that the peak classification performance of the instantaneous combinatorial encoding and the instantaneous amplitude encoding is reached at about 0.8 s and 0.9 s after stimulus onset, respectively (Fig. 4.8a). This time is significantly earlier compared to the peak performance of the instantaneous amplitude change encoding reached at 1.5 s (Friedman's test, \( p \ll 0.001 \), \( n = 300 \text{ data} \)).
4.3. Results

I. Instantaneous amplitude change encoding

I. Instantaneous amplitude encoding

I. Instantaneous combinatorial encoding

Figure 4.8: Speed and accuracy of odor discrimination for subsets of glomeruli. The instantaneous dynamics of the alpha-functions fitted to the optical projection neuron responses are defined by their instantaneous amplitudes and derivatives, i.e. the instantaneous amplitude changes. At each point in time, these measures are used to classify stimuli with predictive LDA using a leave-one-out test to determine the fraction of correct classifications (Sect. 4.2.6). The time course of the fraction correct is computed for an encoding based on either the instantaneous amplitude change, the instantaneous amplitude, or their combination. Based on these time courses, a the average time of the peak and b the peak fraction correct are computed. The time in (a) is relative to stimulus onset, and the dashed line indicates stimulus offset. The dashed line in (b) indicates the chance level. The values shown are the median plus/minus the standard error of the median ($n = 6$ animals, see Sect. 4.2.6). The medians are tested for significant differences (Wilcoxon's rank sum test, significance levels: $p < 0.001$ (***) , not significant (NS), $\alpha = 0.017$, see Sect. 4.2.6).
4. Temporal dynamics

4.3. Results

points per condition, post-hoc Wilcoxon rank sum tests with corrected \( \alpha = 0.017 \). Excluding the latency of about 0.1 s to 0.2 s of the odor delivery system [7], peak classification performance of the instantaneous combinatorial encoding is reached at about 0.6 s to 0.7 s after stimulus onset. Interestingly enough, the time of the peak performance lies well within the stimulation period. In summary, the instantaneous combinatorial encoding is at least as fast as the instantaneous amplitude encoding and faster than the instantaneous amplitude change encoding.

Finally, we want to assess the accuracy of the instantaneous encoding schemes. We base this analysis on the same time courses of fraction correct values as described above to compute the peak fraction of correct classifications. We observe that the instantaneous combinatorial encoding yields a significantly higher fraction correct with a maximum of about 87% compared to 54% for the instantaneous amplitude and amplitude change encodings (Friedman's test, \( p \ll 0.001 \), \( n = 300 \) data points per condition, post-hoc Wilcoxon rank sum tests with corrected \( \alpha = 0.017 \), see Fig. 4.8b). Thus, combining a purely spatial encoding based on a vector of instantaneous response amplitudes with information about the temporal structure as provided by the change of the instantaneous response amplitudes increases the accuracy of the encoding by about 60%.

4.3.5 Relation between optical response of projection neurons and their firing rate

The signal we analyzed, i.e. the optical projection neuron response, is the intracellular calcium concentration of projection neurons as measured from the glomeruli. Each glomerulus is innervated by about five to six projection neurons of the inner antennocerebral tract (Sect. 3.2.1) [9]. We showed that this optical signal can be accurately described by an alpha function. Following this approach we demonstrated that the temporal structure of the optical projection neuron response carries additional stimulus specific information. Hence, this raises the important question of how the pro-
Figure 4.9: Alpha-functions fitted to the projection neuron firing rate. The instantaneous firing rate (grey line) and spikes (vertical lines) of four projection neurons, measured in different animals, is shown. The firing rate is computed by convolving the spike train with a Gaussian ($\sigma = 50 \text{ ms}$). Alpha-functions (black dashed lines) are fitted to the firing rate. The shaded area indicates the stimulus, and $R^2_{adj}$ is the value of the adjusted R-squared statistic (Sect. 4.2.5). Note that the stimulus duration is 0.5 s whereas it is 1 s for all optical recordings. Abbreviation: projection neuron (PN).
4. Temporal dynamics

4.4 Discussion

In this chapter we have shown that the optical projection neuron response to odor stimuli can be described by an alpha-function and that the two key parameters that characterize this response, amplitude and duration, are uncorrelated and significantly modulated by the identity and concentration of odor stimuli. Thus, the optical projection neuron response displays a temporal patterning that is different between odor stimuli. When we combined a spatial encoding scheme with information on the temporal structure of the optical projection neuron response, the performance increased by about 60%.

In our experiments, we measured the optical projection neuron response to make inferences on the information processing by the antennal lobe, that is, we use the intracellular calcium concentration of projection neurons, measured in the glomeruli, as a probe of the dynamics of the antennal lobe network. Our analysis showed that this network, i.e. the conglomerate of olfactory receptor neurons, local neurons, projection neurons, and modulatory projections [9], transforms the receptor response to odor stimuli into a representation where both the instantaneous amplitude and the derivative of the calcium response of projection neurons contain odor information. In order to elaborate whether these two features are part of the actual code employed by the projection neurons, it has to be assessed whether they are transduced by projection neurons and...
4.4. Discussion

4. Temporal dynamics

decoded by downstream neurons.

While the decoding question lies beyond the scope of this chapter, here, we can make inferences on the transduction question, i.e. whether – as suggested by our results – the projection neuron firing rate and its derivative contain odor information. We already presented evidence that the measured calcium dynamics reflect the underlying electrical projection neuron response dynamics. In that case, and because we showed in this chapter that there exists odor information in the instantaneous amplitude of the optical signal, our results suggest that also the projection neuron firing rate contains odor information. Indeed, there is ample evidence supporting this notion [38, 39, 98, 134]. In addition, we demonstrated in this chapter that odor information is also encoded in the derivative of the optical signal. Hence, this suggests that also the derivative of the projection neuron firing rate contains information about odor stimuli. However, this hypothesis has to the best of our knowledge not yet been addressed. It remains to be seen whether future work confirms this prediction.

The goal of this chapter was to assess as an external observer the information content that lies in the temporal dynamics of the optical projection neuron response. This way of “decoding by observers” is distinct from the question of how a biological system does the actual decoding in one crucial aspect: While “decoding by observers” permits us to employ any possible technique to extract all the useful information from the data set, the latter question requires the decoding process to be biologically realistic and thus prohibits many of these analysis techniques. In order to allow a fair comparison between these decoding approaches, we list in the following the techniques that a biological substrate is likely to not have access to and which therefore could give the external observer an advantage. First, we as an observer defined a model of the optical projection neuron response before knowing how the response will look like. Second, again as an observer, we used the alpha-function fitted to the entire response to measure at each point in time the instantaneous amplitude and its change. Third, the classification was performed
piecewise by recomputing the discriminant functions at each time bin. Fourth, these discriminant functions were computed only after selecting those subsets of glomeruli that provided the best results. While it is obvious that these techniques prevent us from concluding that the insect brain decodes those same signals using the same methods, it is important to note again that this question is distinct from the abovementioned goal of this chapter. Hence, our conclusion that temporal patterns of projection neuron calcium signals contain odor information remains valid.

Imaging techniques are a standard and well-established recording method in modern neuroscience [40]. Imaging has contributed an immense amount of information to the understanding of brain function [30, 89], last but not least also to the encoding of odors in the antennal lobe or the olfactory bulb [77]. Several recent studies have investigated encoding principles of projection neurons based on imaging experiments using the same technique as applied in this chapter [25, 41, 119, 120]. The technique we employed has the advantage that it allows to simultaneously measure from an identified neuronal population; the projection neurons. By combining this imaging technique with a model based analysis of the optical signal, we were able to completely quantify its amplitude-time course. This model based analysis of optical imaging data allowed us to show that the temporal dynamics of calcium as measured optically provide a substantial amount of information beyond what is encoded in spatial activation patterns alone. Hence, it will be interesting to see whether model based analysis methods will provide the means to also extract and quantify in other preparations information contained in the temporal dimension of imaging data.

One important aspect of the imaging technique we employed is that the measured optical signal also depends on the intracellular concentration of the dye. This issue, however, is irrelevant to our conclusion because we compared in our analysis of the encoding performance only responses of the same glomerulus to different odor stimuli. Hence, all the responses considered have the same dye-induced distortion, and any differences between those responses can
only be due to the different stimuli.

In previous studies of related system, it has been shown that the temporal sequence of synchrony across projection neurons is stimulus dependent [83, 147] and that their desynchronization causes information loss in downstream neurons [94]. Spike counts or instantaneous (and optically measured) response amplitudes of populations of projection neurons or mitral cells were used to show that the discrimination of odor stimuli improves with time [38, 39, 41, 98, 134]. Moreover, stimulus induced temporal modulations of the projection neuron/mitral cell response have been reported for a range of stimulus durations, from 0.1 s to 2.4 s [25, 38, 39, 80, 85, 134]. In this chapter, we extended these results by showing that both temporal and spatial components of the optical signal contain odor information. Specifically, we demonstrated that the discrimination of odor stimuli can be more accurate if the instantaneous response amplitudes of the optical responses of a population of projection neurons are combined with a measure of their temporal dynamics. Hence, the temporal patterns of the optical projection neuron response contain information about odor stimuli. This encoding of odor stimuli is distinct from an earlier proposed temporal encoding into sequences of synchronized projection neuron assemblies [80].

In general, our results show that temporal modulations of neuronal activity at a time scale of hundreds of milliseconds contain stimulus-specific information. Such a temporal population code was identified earlier using theoretical means [74, 151, 153]. In this chapter we provide empirical evidence that internally generated dynamics of the nervous system – in our case the antennal lobe – transform static stimulus features in a representation where temporal dynamics of neuronal activity could provide an additional channel to transmit information. On the basis of our results we predict that this transformation of static stimulus features into a representation where temporal patterns contain stimulus-specific information is a generic property of densely laterally coupled neuronal structures. In the next chapter, we theoretically investigate this hypothesis in a simulated model of the moth antennal lobe.
Chapter 5

A model of network mechanisms for spatio-temporal encoding of static stimuli and a proposal for the decoding

5.1 Introduction

The experimental results presented in the previous two chapters showed that dynamic neuronal representations can contribute to the processing of static sensory stimuli in two ways: on the one hand, spatial representations can evolve in a stimulus-specific manner over time (Chap. 3), on the other hand, the temporal structure of neuronal activity can itself contain information about these stimuli.
A question that remained unanswered so far, however, is how such dynamic representations could be generated. We address this question in this chapter in an anatomically constrained model of the moth antennal lobe.

We develop a model of the moth antennal lobe that follows the anatomical constraints that we have introduced in Sect. 1.2. Based on this model, we assess first to what extent the similarity between spatial odor representations across projection neurons decreases with time. Subsequently, we quantify the contribution of temporal properties of the response of projection neurons to the encoding of stimuli. We first show in this chapter that a slow inhibition of projection neurons leads to a decorrelation of their spatial response pattern to different odor stimuli but not to trials with the same one. In the second part, we demonstrate that this slow inhibition gives rise to a complementary encoding of odor stimuli in a way that both the instantaneous firing rate of projection neurons and the temporal derivative of the firing rate contain distinct information about the odor stimuli. These theoretical results reproduce our previously reported experimental results of the moth antennal lobe (Chap. 3 and 4) [25, 72], and allow us to make predictions on the functional role of the dense lateral inhibitory network within the antennal lobe.

5.2 Methods

5.2.1 Input

The inputs to the antennal lobe model are synthetically generated. Stimulation with an odor is simulated by activating all receptor neurons with firing rates taken from a uniform distribution on the interval $[0, p_{\text{max}}]$ plus Gaussian noise, the input noise, drawn from $\mathcal{N}(0, \sigma_{\text{noise}})$ (for parameter values see Tab. 5.1). Hence, receptor neurons respond to odor stimulation with a noisy but in average constant firing rate. Such a constant firing rate has been used in previous studies of the olfactory system [87, 88]. Moreover, this
choice of input directly reproduces the experimental result that the correlation between response patterns across receptor neurons remain approximately constant to the initial pattern \[38, 39\]. In the absence of a stimulus, the firing rate of receptor neurons is solely the input noise. A single simulated receptor neuron represents the average firing rate of all receptor neurons expressing the same receptor gene (see Sect. 5.2.2 below). Hence, the noise magnitude \( \sigma_{\text{noise}} \) scales with the square root of the number of “actual” receptor neurons expressing the same receptor gene.

We want to test our model’s decorrelation and encoding properties with inputs having different degrees of similarities. Using the correlation between these inputs as a similarity measure, this means that we have to compute inputs that follow a specified correlation matrix, under the constraint that the firing rates of a single input pattern are uniformly distributed. We achieve this on the basis of a constructive approach. First, we draw random vectors from a multivariate normal distribution with mean zero and a specified correlation matrix. Second, we transform the normal random vectors into uniform random vectors, using the cumulative distribution function of the normal distribution and multiplying the result with \( p_{\text{max}} \), the maximal receptor neuron firing rate. The resulting random vectors have entries that are by construction from a uniform distribution, and the effective correlation matrix of these random vectors is very close to the previously specified one. In order to obtain a more accurate correlation matrix, we repeat these two steps until the correlations between the random vectors are within a previously defined range (see below).

Two types of input data sets are constructed. With the first type of inputs we want to model both different odors as well as repeated trials with the same odor. Because trials with the same stimulus are unlikely to evoke exactly identical sensory responses, here, we model repeated stimulations with the same odor by generating many “samples” of the same stimulus that are all highly similar, but not identical, to each other. In order to implement this property, we impose a constraint on the correlation between inputs. Inputs with
correlations above a threshold of 0.7 are interpreted as belonging to the same stimulus class, and thus represent repeated trials with the same odor stimulus. The value of this threshold is motivated by Fig. 3.4 where we found an average correlation between the calcium response patterns across projection neurons of around 0.7 [25]. For the construction of the trials of one stimulus class, we use a correlation matrix with entries of 1 on the diagonal and entries of 0.85 everywhere else. Using the constructive approach describe above, inputs are generated under the condition that their correlations have to be in the interval \([0.7, 1]\). This choice of parameters ensures that correlations of trials with the same stimulus are high, with correlation indices mostly between 0.8 and 0.95 and a peak around 0.9 (Fig. 5.1, 50 trials). Hence, repeated trials with the same odor stimulus activate receptor neurons in a similar but still systematically different fashion.

The second input type consists of pairs of inputs. We use this type to quantitatively assess the decorrelation of inputs as a function of their correlation. We construct 100000 pairs of stimuli with correlations uniformly distributed in the interval \([0,1]\). In order to obtain an approximately uniform distribution of these correlations, we divide the interval \([0,1]\) into 100 equally sized bins. For each bin \([c_{\text{min}}, c_{\text{min}} + 0.01]\) with \(c_{\text{min}} = 0, 0.01, 0.02, \ldots, 0.99\), 1000 pairs of inputs with correlations in this interval are generated. The correla-
Table 5.1: Parameters of antennal lobe input.

<table>
<thead>
<tr>
<th>Name</th>
<th>Symbol</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximal mean firing rate of receptor neurons</td>
<td>$p_{\text{max}}$</td>
<td>200 Hz</td>
</tr>
<tr>
<td>Standard deviation of input noise</td>
<td>$\sigma_{\text{noise}}$</td>
<td>10 Hz</td>
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5.2.2 Antennal lobe model

The antennal lobe model consists of four types of neurons: olfactory receptor neurons, heterogeneous local neurons, homogeneous local neurons, and projection neurons (Fig. 5.2). The network within a glomerulus is modeled with three neurons, a receptor neuron, a heterogeneous local neuron, and a projection neuron. The number of each of these neuron types is the number of glomeruli $n_{\text{glom}}$ (see Tab. 5.2 for the values of the model’s parameters). The glomeruli are physically arranged in a ring, which allows to avoid discontinuities at boundaries. Each glomerulus receives input from a single receptor neuron, which represents the average activity of all receptor neurons expressing the same receptor gene. Heterogeneous local neurons receive excitatory input from the receptor neuron of the same and of $n_{\text{conn}} - 1$ neighboring glomeruli, and are inhibited by a single homogeneous local neuron which samples from all receptor neurons. Hence, heterogeneous local neurons are sensitive to the difference between the average firing rate of the receptor neurons of their neighboring glomeruli minus the average firing rate of all receptor neurons. In order to assess the effect of this inhibition between local neurons, we will investigate the decorrelation of stimuli both in a network with and without it. Within glomeruli, the pro-
5.2. Methods

5. Spatio-temporal encoding and decoding

Figure 5.2: Structure of the antennal lobe model. The wiring within and between three glomeruli (light gray shaded regions) is shown. Input to the glomeruli is provided by one receptor neuron which synapses onto the projection neuron of the same glomerulus, heterogeneous local neurons of the same and neighboring glomeruli, and onto a single homogeneous local neuron (not shown). Heterogeneous local neurons receive inhibitory input from a single homogeneous local neuron, and inhibit via a slow synapse the projection neuron of the same glomerulus. Abbreviations: olfactory receptor neuron (ORN), heterogeneous local neuron (HetLN), homogeneous local neuron (HomLN), projection neuron (PN), mathematical symbols see Sect. 5.2.2.
projection neuron receives excitatory input from the receptor neuron and inhibitory input from the heterogeneous local neuron. Neuronal activities are represented with firing rates, and all synapses are instantaneous except for the inhibitory synapse between heterogeneous local neurons and projection neurons which is modeled as a slow (GABA\textsubscript{B} type) synapse.

To describe the model in mathematical terms, let $s_i(t_k)$ be the firing rate of receptor neuron $i$, with $i = 1, \ldots, n_{\text{glim}}$ and $t_k$ the time at time step $k$. The firing rate of the homogeneous local neuron, $r_{\text{HomLN}}$, and the excitatory input to the heterogeneous local neuron $q_{\text{HetLN},i}$, is then given by

$$r_{\text{HomLN}}(t_k) = \frac{1}{n_{\text{glim}}} \sum_{j=1}^{n_{\text{glim}}} s_j(t_k) \quad (5.2.1)$$

$$q_{\text{HetLN},i}(t_k) = \frac{1}{n_{\text{conn}}} \sum_{i-[(n_{\text{conn}}-1)/2] \leq j \leq i+[(n_{\text{conn}}-1)/2]} s_j(t_k) \quad (5.2.2)$$

where the symbols $[.]$ and $\lfloor . \rfloor$ denote rounding to the nearest integer towards minus and plus infinity, respectively. Hence, $r_{\text{HomLN}}$ is the average firing rate of all receptor neurons, and $q_{\text{HetLN},i}$ is the average firing rate of receptor neuron $i$ and its $n_{\text{conn}} - 1$ nearest neighbors. Heterogeneous local neurons are activated if their excitatory input exceeds a threshold of $\theta_{\text{exc}}$, which allows to remove input noise. In this case, the firing rate of the heterogeneous local neuron, $r_{\text{HetLN},i}$, is

$$r_{\text{HetLN},i}(t_k) = \frac{1}{10} \begin{cases} \alpha \cdot [q_{\text{HetLN},i}(t_k) - r_{\text{HomLN}}(t_k)] + \beta & \text{Mode 1} \\ \alpha \cdot q_{\text{HetLN},i}(t_k) + \beta & \text{Mode 2} \end{cases} \quad (5.2.3)$$

There are two modes used to compute the firing rate of the heterogeneous local neuron; one with (mode 1), the other (mode 2) without additional inhibition mediated by the homogeneous local neuron. While we use the mode with inhibition for most simulations, the mode without inhibition is a comparison case used to assess the effect of this inhibition between local neurons. The two
parameters $\alpha$ and $\beta$ control the magnitude of the firing rate. While $\alpha$ is a linear scaling of the input to this neuron, parameter $\beta$ serves two purposes: first, it prevents negative firing rates, and second, it is an additional parameter as a function of which we want to test the model’s decorrelation performance. The arbitrary factor of one tenth in front of the above equation scales the firing rate into a physiologically reasonable range.

To model the slow synapse between heterogeneous local neurons and projection neurons, we use a standard synaptic kernel $\exp\left(\frac{t}{\tau_{\text{syn}}}\right)/\tau_{\text{syn}}$ with time constant $\tau_{\text{syn}}$ [31]. The post-synaptic current of this kernel is the low-pass filtered firing rate of the heterogeneous local neuron [31]. Hence, the post-synaptic current, $\rho_i(t_{k+1})$, at time step $k+1$ follows

$$\rho_i(t_{k+1}) = \rho_i(t_k) + \frac{\Delta t}{\tau_{\text{syn}}} (r_{\text{HetLN},i}(t_k) - \rho_i(t_k)) \quad (5.2.4)$$

where $\Delta t$ is the time step of the simulation. The firing rate of projection neurons is then given by

$$r_{\text{PN},i}(t_k) = s_i(t_k) - 10 \cdot \rho_i(t_k), \quad (5.2.5)$$

i.e. the difference of the firing rate of the receptor neuron minus the low-pass filtered firing rate of the heterogeneous local neuron. Hence, projection neurons respond with an instantaneous increase of their firing rate to odor stimulation that is followed by a slow exponential decay. $\rho_i(t_k)$ is scaled with a factor of ten to remove the division by ten introduced in Eq. 5.2.3.

The response of our model to stimulation with three synthetic odors A, B, and C is illustrated in Fig. 5.3. Receptor neurons and heterogeneous local neurons display noisy but temporally constant firing rates. Heterogeneous local neurons are inactive outside the stimulation period because the activation threshold removes the input noise. The activity of the slow synapse between heterogeneous local neurons and projection neurons, as well as the firing rate of projection neurons are temporally dynamic. While the synapse displays
Figure 5.3: Network activity. a Firing rate of receptor neurons, heterogeneous local neurons, and projection neurons, including the post-synaptic activity of the slow synapse between heterogeneous local neurons and projection neurons in response to three odor stimuli A, B, and C. Within the horizontal separator lines, each row shows the time course of the activity of the neurons of a different glomerulus indicated by a gray scale (corresponding scale bar bottom right). The light gray bar indicates stimulation time. b Response to eight trials with each odor stimulus. Each block separated by black horizontal lines shows data of a different glomerulus. Within blocks, rows separated by gray horizontal lines show the responses to trials with the same odor stimulus. Abbreviations: olfactory receptor neuron (ORN), heterogeneous local neuron (HetLN), projection neuron (PN).
5.2. Methods

Table 5.2: Parameters of antennal lobe model and default values.

<table>
<thead>
<tr>
<th>Name</th>
<th>Symbol</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time step</td>
<td>$\Delta t$</td>
<td>10 ms</td>
</tr>
<tr>
<td>Number of glomeruli</td>
<td>$n_{glom}$</td>
<td>25</td>
</tr>
<tr>
<td>Number of ORNs connecting to one HetLN</td>
<td>$n_{conn}$</td>
<td>9</td>
</tr>
<tr>
<td>HetLN activation threshold</td>
<td>$\theta_{exc}$</td>
<td>10 Hz</td>
</tr>
<tr>
<td>HetLN slope</td>
<td>$\alpha$</td>
<td>10</td>
</tr>
<tr>
<td>HetLN intercept</td>
<td>$\beta$</td>
<td>3.5</td>
</tr>
<tr>
<td>HetLN-PN synapse time constant</td>
<td>$\tau_{syn}$</td>
<td>0.3 s</td>
</tr>
<tr>
<td>Inhibition between local neurons</td>
<td>-</td>
<td>yes</td>
</tr>
</tbody>
</table>

Abbreviations: olfactory receptor neuron (ORN), heterogeneous local neuron (HetLN), projection neuron (PN).

both a slow exponentially increasing and decreasing activation, projection neurons respond to odor stimulation with an instantaneous increase of their firing rate followed by a slow decay. As in our experimental work presented in Chap. 4 [72], the response duration of the simulated projection neurons differs between odors. Furthermore, the modeled projection neurons also display a suppression of their activity after response offset, reminiscent to experimental data of projection neurons [134]. Stimulation of the model with repeated trials of the same stimulus shows that the evoked responses are robust to small deviations in the input (Fig. 5.3b).

5.2.3 Analysis of decorrelation

Data analysis is done using Matlab (The MathWorks, Inc., Natick, MA, USA). For analysis of decorrelation, odors are represented with spatial vectors of unfiltered firing rates of receptor or projection neurons. The similarity between spatial odor representations is measured using Pearson's correlation coefficient. Correlations are either computed for every time bin, or for the time bin at response onset and response offset. Response onset is equivalent to stimulus onset. To define response offset, we note that for some stimuli
all projection neurons stop responding before stimulus offset. If all projection neurons are inactive, the according spatial vector of firing rates has only entries of zeros. The correlation of such a vector with another one is undefined. The correlation at response offset is thus computed at the last time bin for which the correlation is still defined. For most stimuli, this time bin corresponds to stimulus offset.

In order to quantify correlations between spatial odor representations across projection neurons at response end, we define two ranges of correlation indices: the range of low correlations is the interval $[-0.2, 0.2]$, and the range of high correlations the interval $[0.7, 1]$. As we will see below, the exact range of these intervals is irrelevant because the correlations at response end display a bimodal distribution with sharp peaks around $-0.1$ and $0.9$ (Sect. 5.3.1.2). The fraction of low/high correlations is defined as the number of pairs of response patterns for which the correlation at response offset is in the according interval, divided by the total number of pairs under consideration.

The optimality of decorrelation is defined as follows. First, the fraction of low/high correlations is computed for all pairs of inputs with a correlation below/above 0.8. (We use here a threshold of 0.8 (and not 0.7 as above) because the correlation between trials is -- as we found above -- in most of all cases larger than 0.8. Input pairs with a correlation above/below 0.8 are interpreted as trials with the same/different odor stimulus.) Then, the optimality of decorrelation is given by the geometric mean of the fraction of high and low correlations. Note that for two positive numbers that are arbitrary except a fixed arithmetic mean, the geometric mean is maximal if these numbers are equal. Hence, this important property of the geometric mean ensures that a decorrelation is judged more “optimal” if both the fraction of high and low correlations are of a similar magnitude (see Sect. 5.4 for a further discussion of this aspect). The optimality of decorrelation is between zero and one, with zero meaning worst and one perfect decorrelation.
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5.2.4 Analysis of encoding performance

As in Chap. 4, predictive linear discriminant analysis (LDA) is used to predict the stimulus class based on projection neuron responses (input type one, see Sect. 5.2.1). We assess the fraction of correct classifications, i.e. the ratio of correctly classified samples versus the total number of samples, by splitting the data into a training and a test set. 80% of the samples are assigned to the training, and 20% to the test set. Samples of the test set are classified based on the discriminant functions derived from all samples of the training set. Note that for this test we exclusively use LDA as a linear transformation of the representation of odors from one space to another, without computing any p-values. Thus, testing the assumptions of LDA is not required.

We use three different encoding schemes for our classification analyzes: stimuli are represented using instantaneous firing rates of projection neurons, the derivative of firing rates, or their combination. The derivative at time bin $t_k$ is defined as the difference of the projection neuron firing rate at this time bin minus the one three time bins earlier, i.e. 30 ms earlier. This delay used to compute derivatives is of the same magnitude as typical membrane time constants of neurons [31]. We assess the fraction of correct classifications using the response parameters of subsets of projection neurons. The size of these subsets is varied from 1 to the total number of projection neurons, i.e. $n_{\text{glom}}$. The number of variables for the LDA thus corresponds either to the size or the doubled size of the subset (dependent on whether only one or both response parameters represent the odor stimuli). For each size of the subsets, we compute for 1000 randomly chosen combinations of projection neurons the fraction of correct classifications (except for subset sizes for which the number of possible combinations is smaller than 1000). Of these values, the median fraction correct and the 20- and 80-percentile are computed.

For most analyzes, fraction correct values are computed at a fixed point in time. For the instantaneous firing rate-based encoding, this is the time bin of peak performance at $t = 10 \text{ ms}$ (see
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Sect. 5.3.2.1 below). For the derivative-based and the combinatorial encoding, the first time bin for which the derivative exists is selected, i.e. \( t = 40 \text{ ms} \).

5.3 Results

The results section is split into two parts. In the first part, we investigate how spatial response patterns across projection neurons decorrelate with time and as a function of the correlation between the inputs. In the second part, we assess the amount of stimulus-specific information that is contained in the temporal and spatial structure of the firing rate of projection neurons. In both parts, we use the same model of the antennal lobe (Sect. 5.2.2) with, unless otherwise noted, the standard parameter set as defined in Tab. 5.2.

5.3.1 Decorrelation of odor representations

5.3.1.1 Example of decorrelation

We first examine the correlation between the projection neuron responses shown in Fig. 5.3. The three odors A, B, and C of this example are presented 20 times each. The average correlation between classes is about 0.69, 0.29, and 0.15, respectively, and the average correlation within classes is about 0.85 (Fig. 5.4; input type one, Sect. 5.2.1). Because receptor neurons respond with a temporally constant firing rate, the correlation of response patterns across receptor neurons remains constant throughout the stimulation period (Fig. 5.4b). The correlation between the spatial response patterns across projection neurons reduces with time for different odors but not for trials with the same (Fig. 5.4a and b). Most notable, this decorrelation also occurs for the two similar odors A and B. We have observed such a decorrelation of the spatial representations of odors in Chap. 3 in the moth antennal lobe, and it was also found in other preparations [38]. Hence, for this particular example, the antennal lobe model accurately reproduces experimental observations.
Figure 5.4: Correlation between spatial patterns across receptor and projection neurons. **a** Correlation matrices for comparisons of the spatial response patterns across projection neurons for trials with the same and different odor stimuli at three points in time (0 s, 0.3 s and 0.6 s after stimulus onset). Note that odor stimuli A and B have a high correlation of about 0.69. **b** Time course of correlation between same and different odor stimuli. The values shown are the medians of all pair-wise comparisons of the 20 trials per odor stimulus either within or between odors. Error bars indicate the 30 and 70 percentile, respectively. The plot is based on the same synthetic odor stimuli as in Fig. 5.3. Abbreviations: olfactory receptor neuron (ORN), projection neuron (PN).
The minimal value of the correlation is reached around 0.7 seconds after stimulus onset (Fig. 5.4b). At this time, only a few projection neurons are still active (Fig. 5.3). However, a large reduction of the correlation occurs already at earlier times when more projection neurons are responding. Hence, this excludes the trivial result that the decorrelation of projection neuron response patterns to different odors is due to the fact that only a single projection neuron is active while all others are silent.

5.3.1.2 Quantitative analysis of decorrelation

The first main question of this chapter is whether the antennal lobe model generates projection neuron responses in a way that their correlation reduces with time for different stimuli but not for repeated trials with the same. The previous paragraph showed one example where this is the case. In order to assess the extent with which this example generalizes, we systematically assess the correlation between response patterns across projection neurons as a function of the correlation between the input patterns (input type two, Sect. 5.2.1). We compute the difference of the correlation between projection neuron response patterns at response onset minus the one at response offset. Negative/positive values of this difference mean a reduction/increase of the correlation. The results show that this difference is mainly negative, and, for a high correlation between the inputs, positive (Fig. 5.5a). Hence, all but highly similar input patterns tend to decorrelate.

In order to quantify this observation in more detail, we compute, as a function of the correlation between inputs, the fraction of low and high correlations between outputs (Sect. 5.2.3 and Fig. 5.5b and c). We observe that the correlations of projection neurons response patterns display a bimodal distribution with peaks at around -0.1 and 0.9 (Fig. 5.5b). The fraction of high and low correlations cross for a correlation between inputs of 0.8 (Fig. 5.5f). Thus, inputs with correlations above this transition point are more likely to remain highly correlated, and inputs with correlation below this value evoke projection neuron response patterns that are more often un-
Figure 5.5: Systematic quantification of correlation between projection neuron response patterns as a function of the correlation between inputs. The stimulus set consists of 100000 pairs of inputs with correlations uniform in [0, 1] (Sect. 5.2.1, input type two). a Color-coded histogram of the difference between the correlation of projection neuron response patterns at response onset and offset as a function of the correlation between inputs. The horizontal dotted line indicates zero. Negative/positive differences mean that the correlation between the response patterns across projection neurons decreases/increases over the course of stimulation. b Example of how the fraction of high and low correlations are computed. The distribution of correlations between outputs is shown for inputs with a correlation in [0.69, 0.7] (green line). The range of high correlations is between 0.7 and 1.0 (red shaded area), the range of low correlations between −0.2 and 0.2 (blue shaded area). The fraction of high/low correlations is defined as the respective area under the green line (as indicated with dark red/blue color; see also Sect. 5.2.3). c Median fraction of high (red) and low (blue) correlations as a function of the correlation between inputs. The shaded area along the curve is the range of median values obtained from drawing 20 distinct sub-samples, each of the size of the twentieth part of the whole data set.
correlated. Interestingly enough, this means that the antennal lobe model only preserves the similarity of highly similar inputs whereas all other inputs are more likely to be decorrelated.

5.3.1.3 Optimality of decorrelation

Figure 5.6: Optimality of decorrelation. a Median fraction of high/low correlation at response offset for a network with and without slow inhibition of projection neurons (Sect. 5.2.3). b Optimality of decorrelation for a network with and without slow inhibition of projection neurons. The dotted line indicates optimality without slow inhibition of projection neurons. Error bars show the range of values obtained from splitting the data set into 20 equally sized subsets and analyzing each separately (i.e. \( n = 20 \)).

We further compress this result in the following by computing the optimality of decorrelation both for a network with and without slow inhibition of projection neurons (Sect. 5.2.3). The mode without slow inhibition serves as a comparison case to assess the extent with which slow inhibition improves the quality of the decorrelation. The results show that with slow inhibition, the fraction of high and low correlations are about balanced, whereas they are unbalanced without slow inhibition (Fig. 5.6a). This equalization of the fraction
of low and high correlation leads to an increase of the optimality of decorrelation (Fig. 5.6b). Without slow inhibition – i.e. without any temporal dynamics in the projection neuron responses – optimality of decorrelation is around 0.5. With slow inhibition, however, optimality increases to about 0.65. Hence, slow inhibition of projection neurons improves the representation of inputs in the sense that it reduces the spatial overlap between responses to similar inputs while it mostly preserves the similarity of highly similar inputs.

5.3.1.4 Parameter search

The antennal lobe model we investigate here depends on a number of parameters. We evaluate the effect of these parameters on the basis of the optimality of decorrelation (see above and Sect. 5.2.3). We vary parameters of the model ($\alpha$, $\beta$, $n_{\text{glom}}$, and $n_{\text{conn}}$) as well as the input noise magnitude, $\sigma_{\text{Input}}$, and the wiring mode (see Sect. 5.2.1 and 5.2.2 for a description of the parameters). For all experiments, we use unless otherwise noted the standard parameter configuration as given in Tab. 5.1 and 5.2. First, we examine the effect of the parameters controlling the firing rate of the heterogeneous local neuron $\alpha$ and $\beta$ (Sect. 5.2.2). This neuron mediates the slow inhibition of projection neurons. We observe that the optimality of decorrelation depends to a large degree both on $\alpha$ and $\beta$ (Fig. 5.7a). For suboptimal values of these parameters, optimality approaches a value of 0.5, corresponding to the case without slow inhibition of projection neurons. Second, we investigate the consequences of the network geometry onto the optimality of decorrelation by changing the number of glomeruli and the number of connections from receptor neurons to heterogeneous local neurons (Fig. 5.7b). The results show that optimality reaches a plateau for $n_{\text{conn}} \gtrsim 9$. Within this plateau, optimality depends hardly on the number of glomeruli or the number of connections. Hence, this illustrates that the decorrelation property of the antennal lobe model generalizes to larger network sizes and is, within boundaries, robust to the number of synapses between receptor and heterogeneous local neurons. In our third experiment, we examine an important parameter of the model: the input noise
Figure 5.7: Effect of antennal lobe model parameters onto optimality of decorrelation. **a** Optimality of decorrelation as a function of the $\alpha$ and $\beta$ parameter of the antennal lobe model that define the magnitude of the slow inhibition of projection neurons. **b** Optimality of decorrelation as a function of the number of glomeruli, $n_{\text{glom}}$, and the number of connections from receptor neurons to heterogeneous local neurons, $n_{\text{conn}}$. In this panel and (a), gray colored squares correspond to values below the optimality of decorrelation without slow inhibition of projection neurons. Color scale bar for both panels is given on the right. **c** Optimality of decorrelation versus input noise. **d** Optimality of decorrelation with and without inhibition between local neurons (see Sect. 5.2.2 for a definition). The values shown are medians, and error bars indicate their ranges ($n = 10$, see Sect. 5.3.1.4). The medians are tested for significant differences (Wilcoxon’s rank sum test, significance levels: $p < 0.001$ (** **), $\alpha = 0.05$). The dotted horizontal line in the lower two panels indicates optimality without slow inhibition of projection neurons. Abbreviations: local neuron (LN).
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(Fig. 5.7c). We observe that the antennal lobe model is highly robust to input noise and that the optimality of decorrelation decreases only slowly with increasing noise magnitude. For noise magnitudes larger than 40 Hz, decorrelation collapses and is below the optimality of a network without slow inhibition of projection neurons. In our last experiment, we compare the optimality of decorrelation of the standard wiring mode with inhibition of heterogeneous local neurons by a homogeneous local neuron to the case without this inhibition between local neurons (Fig. 5.7d, see Sect. 5.2.2 for a definition of the wiring modes). An important aspect that we have to consider in this respect is that the firing rate of heterogeneous local neurons depends on the wiring mode (see equation (5.2.3)). Hence, the optimal values for $\alpha$ and $\beta$ which control this firing rate are different between the wiring modes. We therefore vary for each mode both $\alpha$ and $\beta$, and compute the optimality as the average over the 10 best models. This shows that the wiring mode with inhibition between local neurons yields a significantly higher optimality than the one without. To conclude, these analyses demonstrate that decorrelation of inputs generalizes to different network geometries, and that it is, within boundaries, independent of the magnitude of the slow inhibition of projection neurons and fairly robust to input noise. Our results show that inhibition between local neurons improves the decorrelation.

5.3.2 Encoding of stimuli

5.3.2.1 Accuracy of encoding

We have shown experimentally in Chap. 4 that the instantaneous amplitude and the derivative of the calcium response of projection neurons contain information about odor stimuli [72]. Here, we theoretically investigate whether our antennal lobe model reproduces these experimental results. We use three different encoding schemes in the following analyzes: an encoding based on the instantaneous firing rate of projection neurons, and encoding based on the derivative of the instantaneous firing rate, and an encoding based on their
Figure 5.8: Accuracy of odor discrimination. **a** Median fraction of correct classifications as a function of time for subsets of three projection neurons. The time course of the fraction correct is computed for an encoding based on either the instantaneous firing rate of projection neurons (red), its derivative (yellow), or their combination (blue). The gray line denotes chance level (32 odor stimuli). **b** Median fraction correct for a network with and without slow inhibition of projection neurons. The fraction correct values are measured at \( t = 0.01 \) s for the instantaneous firing rate-based encoding and at \( t = 0.04 \) s for the other encodings (Sect. 5.2.4). The medians are tested for significant differences (\( n = 1000 \) subsets per condition, Wilcoxon’s rank sum test, significance levels: \( p < 0.001 (***) \), \( \alpha = 0.05 \)). The shaded area along the curves in (a) and errorbars in (b) indicate the 20 and 80 percentile.
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combination, i.e. a combinatorial encoding (Sect. 5.2.4). We first inspect the fraction of correct classifications as a function of time for an input data set consisting of 32 odor stimuli of 50 trials each and for a subset size of 3 glomeruli (Fig. 5.8a). We observe that the fraction of correct classifications decays with time, regardless of the encoding scheme used. A comparison of the peak fraction correct values of each encoding shows that the combinatorial encoding yields a significantly higher fraction correct than the non-combinatorial encodings (Fig. 5.8b, $n = 1000$ data points per condition, Wilcoxon’s rank sum tests, $\alpha = 0.05$). The combinatorial encoding boosts the fraction correct by about 30% compared to the encoding based on instantaneous firing rates. A comparison of this results to a network without slow inhibition of projection neurons shows that this boost is entirely due to this slow inhibition (Fig. 5.8b, without slow inhibition). Thus, the encoding of odor stimuli into the instantaneous firing rate of projection neurons and its derivative is complementary in the sense that their combination yields a higher information content than each of these components in isolation.

5.3.2.2 Noise robustness of encoding

A first test of the encoding of odor stimuli into the instantaneous firing rate of projection neurons and its derivative is the question of how robust this encoding is to input noise. We evaluate the fraction correct as a function of the subset size and the noise magnitude for the combinatorial encoding (Fig. 5.9a) and for the difference between the combinatorial encoding and the encoding based on instantaneous firing rates (Fig. 5.9b), using the same stimuli as above. We find that the fraction correct of the combinatorial encoding reaches its maximal value of one even for noise magnitudes of up to 20 Hz if the subsets are large enough. When we inspect the contribution of the derivatives (i.e. fraction correct of combinatorial encoding minus fraction correct of instantaneous firing rate-based encoding), we see that it is largest for smaller subsets and decays with increasing noise magnitude (Fig. 5.9b). Yet, even for higher noise magnitudes, the temporal change of the firing rate still contributes information
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Figure 5.9: Robustness and capacity of odor discrimination. a,b Noise robustness of the representations of odor stimuli. The (a) fraction correct of the combinatorial encoding and (b) the difference between the fraction correct of the combinatorial and the firing rate-based encoding are shown as a function of the subset size and the noise magnitude. c,d Encoding capacity of the model. The (c) fraction correct of the combinatorial encoding and (d) difference between the fraction correct of the combinatorial and the firing rate-based encoding are shown as a function of the subset size and the number of odors. Note that the z-axis and the gray scale are different between panels (color bars to the right of each panel). e Relative contribution of derivatives of firing rates to the accuracy of the combinatorial encoding. The values shown are medians, lower/upper errorbars indicate the 20 and 80 percentile, respectively (n = 1000 data points per condition, but exceptions exist, see Sect. 5.2.4).
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to the encoding of the stimuli. In conclusion, this shows that the encoding of odor stimuli into the instantaneous firing rate and its derivative is robust to input noise, and that the derivative of the firing rate contains information about stimuli also for higher noise magnitudes.

5.3.2.3 Capacity of encoding

A second test of the encoding of odor stimuli into the instantaneous firing rate of projection neurons and its derivative is the question of how the fraction of correct classifications scales with the number of odors. Using up to 1024 synthetic odor stimuli of 50 trials each, we again analyze the fraction correct of the combinatorial encoding and the contribution of the derivatives (Fig. 5.9c and d). The results show that the fraction of correct classifications using the combinatorial encoding reaches perfect performance also for large numbers of odor stimuli. The contribution of derivatives is largest for smaller subset sizes and larger number of odors (Fig. 5.9d). Most notably, derivatives contribute almost up to 30 percentage points to the fraction correct of the combinatorial encoding. In relative terms, derivatives improve the accuracy of the encoding by up to 150% in case of 1024 odors (Fig. 5.9e). Hence, these results demonstrate that a large number of odor stimuli can be represented in our model of the moth antennal lobe, and that derivatives of firing rates can bring about an up to one and a half-fold improvement of the encoding accuracy.

5.4 Discussion

In this chapter we have presented an anatomically constrained model of the moth antennal lobe that provides an explanation for two experimentally observed properties of the moth antennal lobe. First, we provided theoretical evidence that a slow inhibition of projection neurons suffices to decorrelate all but highly similar inputs. Second, we demonstrated that this slow inhibition renders projection neuron
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responses that contain stimulus-specific information in both their instantaneous firing rate and their temporal derivative in a way that these two parameters represent complementary information.

An important aspect of modeling studies is the level of abstraction employed in relation to the hypothesis of the study. Here, the hypothesis was whether a slow inhibition of projection neurons can explain two experimental properties observed in projection neurons: a decorrelation of spatial odor representations with time and a complementary encoding of odor stimuli into both the instantaneous firing rate and its derivative. It is noteworthy that both the decorrelation and also the computation of firing rates are comparably slow processes that operate on a time scale of hundreds of milliseconds. Hence, it is sufficient to base our simulations on a firing rate model as the timing of individual spikes is not relevant to our questions. On top of that, we see this approach having at least two advantages over more complex simulations. First, it also allowed us to work with a comparatively low-dimensional phase space of parameters within which we could perform a systematic quantification of the optimality of the decorrelation. Second, this approach also permitted us to identify computational principles that are of a general nature. Indeed, the abstractness of our model of the moth antennal lobe allows us to predict that decorrelation and complementary encoding are generic properties not only of the antennal lobe but of all densely laterally coupled neuronal structures.

The inputs to almost all models of the antennal lobe (and also the olfactory pathway) have to be synthetically constructed. Here, one aspects of the input we used is worth being mentioned: we simulated a fictional odor stimulus by activating all receptor neurons. The firing rates upon stimulation were drawn from a uniform distribution plus Gaussian noise. Given the noise magnitude of 10 Hz and the maximal receptor neuron firing rate of 200 Hz (Tab. 5.1), about 90% of these neurons are thus activated with a firing rate that is significantly above noise level (i.e. above about 20 Hz). In the antennal lobe, the actual percentage of receptor neurons activated by an odor stimulus is below 90% [53, 139]. On the one hand, our sim-
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Spatio-temporal encoding and decoding simulations thus can be understood to concern only a small fraction of the actual antennal lobe network, i.e. the part of the network that is activated by a stimulus. On the other hand, this construction of inputs also permitted us to test the model's decorrelation and encoding performance under the most difficult condition of almost completely overlapping inputs.

Theoretical predictions about the functional relevance of neuronal structures are a key component of modeling studies. These predictions are especially interesting in case they concern structures that are almost intractable to specifically targeted experimental assays. The very complex and dense local inhibitory network within the antennal lobe, which was proposed to play a key role in shaping odor responses of its output neurons [80], is such a structure. The significance of the results presented in this chapter lie in the fact that they allow us to make three predictions that relate to the structure and function of this local inhibitory network. First, in our model we used fast instantaneous inhibitory synapses between local neurons, and slow inhibitory synapses between heterogeneous local neurons and projection neurons. This particular arrangement of fast and slow inhibitory synapses allowed us to accurately reproduce experimental results of the moth. Hence, it suggests that fast inhibition exists only between local neurons, whereas projection neurons receive slow inhibitory input from local neurons. Most interestingly, there is experimental support for this hypothesis. It was recently found in Drosophila that inhibition between local neurons is only mediated by fast GABA_A receptors, whereas projection neurons are inhibited via both fast GABA_A and slow GABA_B receptors [148]. To what extent also fast inhibition between local and projection neurons plays a role in shaping projection neuron responses on a time scale of hundreds of milliseconds remains to be seen. Second, we found that projection neuron response patterns do not decorrelate when we completely blocked their slow inhibitory input. We therefore predict that completely blocking this slow inhibition would reduce the amount with which odors are decorrelated. Indeed, experimental evidence from Drosophila indicates that ap-
plication of GABA<sub>B</sub> blockers abolishes the temporal patterning of projection neurons [148]. Yet, whether this also affects the decorrelation of spatial response patterns across projection neurons is unclear. Third, when we removed the fast inhibition between local neurons, decorrelation was less optimal. Hence, we predict that blocking fast inhibition between local neurons should reveal a diminished decorrelation of the response patterns across projection neurons. It will be interesting to see whether these predictions can be confirmed.

A key property of any decorrelation process is that it should only reduce the similarity of the response patterns to different stimuli but not to repeated trials with the same one. We have shown in Chap. 3 that the calcium response patterns across moth projection neurons display such a decorrelation [25]. In this chapter, we approximated trials with the same and different odor stimuli by imposing a threshold on the correlation between inputs: while inputs with a correlation above 0.8 represent trials with the same odor, inputs with a correlation below this threshold represent different odors. Based on this construction of the inputs, we showed that repeated trials with the same odor mostly evoked response patterns that stayed highly correlated throughout the response, whereas the response patterns to different odors decorrelated in most cases. It is important to mention in this respect that this result that trials with the same odor stimulus evoke mostly highly correlated responses is distinct from previous studies where it was found that also highly correlated inputs (corresponding to trials with the same odor stimulus) were decorrelated [87, 88].

One aspect related to the analysis of the decorrelation deserves special attention. In order to examine the quality of the decorrelation, we constructed pairs of synthetic odor stimuli. As this construction of inputs results in a dense sampling of the entire input space, we cannot expect the decorrelation process to be perfect, i.e. to reduce the correlation of all input pairs with a correlation below 0.8 while retaining the similarity of all input pairs with correlations above 0.8. Rather, the relevant question in this context is
to what extent the antennal lobe model generates projection neuron responses in a way that the fraction of low and high correlations is balanced (Sect. 5.2.3). Using the optimality of decorrelation, which measures the quality of this re-balancing process, we showed in a network without slow inhibition of projection neurons that the fraction of high and low correlations are unbalanced. When we turned on slow inhibition, these fractions approximately equalized and concordantly, the optimality of decorrelation increased.

We have shown in the previous chapter that the moth antennal lobe generates responses that contain information about odor stimuli both in the instantaneous amplitude of the calcium response of projection neurons as well as the temporal change, or derivative, of this signal [72]. We found that this encoding is complementary, i.e. that the combination of both components yields a higher information content than each of them in isolation. In this chapter, we demonstrated that a slow inhibition of projection neurons suffices to generate such a complementary encoding. We found that this encoding is robust and accurate even for high input noise magnitudes. The encoding has favorable scaling properties and allows for an accurate representation of at least up to about 1000 odors in a network of 25 projection neurons.

The insect antennal lobe, as well as the vertebrate's olfactory bulb, are prominent systems for modeling studies. The experimentally observed oscillatory synchronization of projection neurons as well as the temporal patterning of their responses on a time scale of hundreds of milliseconds [82] have been described with models [14–16, 96, 97, 129]. The temporal decorrelation of spatial odor representations with time [25, 38, 39] has also received attention [14, 29, 87, 88]. As mentioned above, an important aspect of any decorrelation process is the boundary condition that highly similar input patterns, i.e. those representing trials with the same odor, should not be decorrelated. Here, we extended these previous results by showing in a highly quantitative manner that a slow inhibition of projection neurons generates in most cases decorrelated response patterns for all but highly similar inputs. In other words, response
patterns decorrelate between odors but not for trials with the same odor.

The results reported in this chapter showed that information about static sensory stimuli is contained in both the instantaneous firing rate of projection neurons and the temporal derivative of the firing rate. Hence, this raises the question of how Kenyon cells, which receive input from projection neurons, would read out this code, and in particular, what the properties are of a decoding network that can compute derivatives. Regarding the computation of derivatives with neurons, two paths can be taken. On the one hand, temporal derivatives can be approximated with a high-pass filter. A neuron that non-linearly sums inputs arriving in a short time window is in fact a high-pass filter. On the other hand, temporal derivatives can also be computed in a small network consisting of feed-forward excitation and delayed inhibition. In this case, the derivative is directly computed. Interestingly enough, Kenyon cells feature both of these properties [45, 81, 108–110, 155]. Kenyon cells were found to display a supralinear summation of their inputs and thus approximate a high-pass filter. At the same time, the input to Kenyon cells passes through small micro-networks in which projection neurons provide direct excitatory input and – via local GABA-ergic neurons – delayed inhibitory input to the Kenyon cells. Hence, these considerations suggest that Kenyon cells are in principle able to decode information existing in temporal derivatives of firing rates.

In conclusion, our results demonstrate that a temporal decorrelation of spatial odor representations as well as a complementary encoding of odors into both the instantaneous firing rate and its derivative can be attributed to a dense lateral coupling within the antennal lobe. We have hypothesized on the basis of experimental as well as theoretical studies that this dense lateral coupling can transform static stimuli into such temporally dynamic representations (Chap. 2–4) [72, 74, 151, 153]. This chapter provides further evidence for this notion. Hence, this leads us to predict that temporal decorrelation and complementary encoding are generic properties
5. Spatio-temporal encoding and decoding of densely laterally coupled neuronal structures.
Chapter 6

Conclusion

The main objective of this thesis was to study dynamic neuronal representations of static sensory stimuli. Our investigations involved a combined experimental and theoretical approach. This combination of both theory and experiment has one key advantage. As in any recently new scientific disciplines, our understanding about the system in question – in this case the brain – is rather limited. While this situation is very appealing in that it opens a vast amount of interesting directions research can take, it also leaves open many boundary conditions that would constrain the research question as well as the system investigated. In contrast, combining experiments with theory can provide these additional constraints. In the context of this thesis, this means that establishing a neuronal coding strategy requires its validation based on experiments. For this reason, we have employed a combined experimental and theoretical approach, which allowed us to generate specific constraints on the type of a neuronal code employed by the antennal lobe system. These constraints allowed us to establish a coding strategy, fully validate it in the context of an experimental system, and embed it in a theoretical model.

In the discussion of a neuronal coding strategies, the question of
how information is encoded is closely related to the question of how this information is decoded by downstream neurons. In the first part of this thesis, we investigated a complete encoding-decoding system to assess conditions under which the decoding network of this system can read out information represented in a temporal code. We investigated this process in the context of a recently proposed encoding scheme, the temporal population code. In this code, visual stimuli become encoded into the summed activity of a population of densely laterally connected neurons. For its decoding we evaluated a model based on the structure and dynamics of cortical microcircuits that is proposed for computations on continuous temporal streams: the liquid state machine. Employing the original proposal of the decoding network results in a moderate performance. This observation could indicate constraints on the properties of the temporal patterns generated by the encoding network in the sense that these patterns may contain information in features that are inaccessible to the decoder. However, our analysis suggested that this is unlikely. Rather, we found that the temporal mixing of subsequent stimuli results in a joint representation of these stimuli which compromises their classification. To overcome this problem we investigated a number of initialization strategies. Whereas we observed that a deterministically initialized network results in the best performance, we find that in case the network is never reset, i.e. it continuously processes the sequence of stimuli, the classification performance is greatly hampered by the mixing of information from past and present stimuli. We concluded that this problem of the mixing of temporally segregated information is not specific to this particular decoding model but relates to a general problem that any circuit that processes continuous streams of temporal information needs to solve. Considering the biological realism of the encoding and decoding networks, our results suggested that the brain could solve the problem of temporal mixing by applying reset signals at stimulus onset. While a reset signal is a generally applicable strategy providing a solution to this problem, there exists also a specifically applicable strategy with the potential of solving this problem. Key component of this comple-
mentary strategy is to establish the components of a temporal code that carry the actual information about the stimulus. Based on this knowledge, the decoding stage of the encoding-decoding system could be specifically adapted to the particular format of the temporal code generated by the encoding stage, and hence, its performance further optimized. Thus, we concluded that examining the detailed information-carrying properties of a temporal code is a crucial next step.

We studied the question of the information-carrying properties of a temporal code in the second part of this thesis on the basis of both experimental and theoretical approaches. The olfactory system is one of the standard preparations where this issue is experimentally investigated. Output neurons of the first relay of this system display odor stimulus induced temporal modulations of their firing rate on a time scale of hundreds of milliseconds. An important aspect in the discussion of the brain’s coding strategies is that it is often assumed that the different coding strategies are mutually exclusive. In the third and forth chapter, however, we found that this system employs several coding strategies at the same time. When we investigated the optically recorded calcium response of a population of projection neurons, we observed that information about odor stimuli exists in their spatial response pattern, i.e. in the response across a population of neurons. In terms of coding schemes defined in the Introduction, these neurons thus employ an independent coding strategy. At the same time, we found that the these response patterns displayed stimulus dependent temporal dynamics in a way that the similarity between them was reduced with time for different odors but not repetitions with the same one. Finally, when we investigated the time course of the optical signal, we observed that it displayed stimulus dependent temporal modulations. Specifically, we demonstrated that the temporal change of the optical signal, i.e. the temporal derivative, is stimulus specific and boosts the accuracy of the encoding by 60% compared to a purely spatial encoding using a spatial pattern of response amplitudes only. Our analysis suggested that this optical signal reflects the underlying electrical
activity of projection neurons. In this case, information about odor stimuli is contained both in the firing rate of these neurons as well as its temporal derivative. Hence, odor stimuli are represented in a rate code and a temporal code. Thus, while the neuronal code is usually seen as an exclusive set – i.e. rate vs. time and local vs. population, our results suggest that all of these can coexist as complementary aspects of one encoding substrate.

The experimentally established existence of a complementary encoding of odors into both spatial and temporal aspect of the response of projection neurons raised the question of how such responses can be generated. We addressed this question in the last part of this thesis, by developing a model of the moth antennal lobe. Key component of this model is that it ascribes a specific role to the dense lateral connectivity within the antennal lobe. We hypothesized that the complex dynamics required to generated the experimentally observed decorrelation and complementary encoding of odor stimuli are mediated by the dense lateral coupling of neurons in the antennal lobe. Our simulations confirmed that lateral connections are indeed crucial in establishing these two experimental properties of the encoding of odors in the antennal lobe. Specifically, we found that a slow inhibition of projection neurons can explain the decorrelation of spatial odor representations as well as their complementary encoding into the instantaneous firing rate and its temporal derivative. In conclusion, the results of the last part of this thesis suggest that a dense lateral connectivity is required to generate dynamic neuronal representations of static sensory stimuli.

We started this thesis with three connected questions, i.e. how a temporal code can be generated, what the information content of this code is, and how a temporal code can be decoded. The results of the first part of this thesis where we investigated an encoding-decoding system in the context of a temporal code suggested that a clear understanding of the information-carrying properties of this code is crucial to develop any decoder. In our further analysis of the encoding of odors by projection neurons, we identified a temporal code in which the derivative of the firing rate contains information
about these stimuli. Hence, we can now discuss how a neuronal decoder would have to look like to decode this particular instance of a temporal code, i.e. to decode information that is contained in the derivative of the firing rate. In general, computing derivatives with neurons is straightforward. Two different paths can be taken: one option to approximate derivatives is a high-pass filter, i.e. a decoder neuron would only be sensitive to rapid fluctuations in the input signal. Non-linear summation of the inputs to this neuron, for instance, can be used to perform this computation. A second option to approximate derivatives involves a small network of feed-forward excitation and delayed inhibition. In this case, the derivative is directly computed. Most interestingly, the follower neurons of projection neurons, the Kenyon cells, are likely to exhibit both of these features [45, 81, 108–110, 155]: it was not only found that voltage-dependent subthreshold properties of Kenyon cells bring about a supralinear summation of their inputs, but the input to Kenyon cells also passes through complex micro-networks, in which projection neurons also make extensive contact to local inhibitory neurons which provide themselves input to Kenyon cells. Hence, these considerations strongly suggest that Kenyon cells are able to read out the derivative code identified in this thesis.
Appendix A

Supplementary methods

A.1 Details of the implementation of the liquid state machine

We consider the time course of a temporal activity pattern of the encoding network, $I_{inp}(t)$, as a synaptic input current to the decoding network. This current is arbitrarily normalized to a maximal value of 1 nA. The dimensionless weights of the input synapses, $w_{inp}$, are chosen from a Gaussian distribution with mean value and standard deviation of 90 that is truncated at zero to avoid negative values. As only 30% of the liquid cells receive input from the temporal activity pattern (Sect. 2.2.2), a random subset of 70% of the input weights is set to zero.

The recurrent synapses in the liquid show short-term plasticity [95]. Let $\Delta t$ be the time between the $(n - 1)$th and the $n$th spike in a spike train terminating on a synapse, then, $u_n$, which is the
A.1. Liquid state machine

Running value of the utilization of synaptic efficacy, $U$, follows:

$$u_n = u_{n-1} e^{-\frac{\Delta t}{\tau_{fac}}} + U \left(1 - u_{n-1} e^{-\frac{\Delta t}{\tau_{fac}}} \right) \quad (A.1.1)$$

where $\tau_{fac}$ is the facilitation time constant. The available synaptic efficacy, $R_n$, is updated according to:

$$R_n = R_{n-1}(1 - u_n) e^{-\frac{\Delta t}{\tau_{rec}}} + 1 - e^{-\frac{\Delta t}{\tau_{rec}}} \quad (A.1.2)$$

where $\tau_{rec}$ is the recovery from depression time constant. The peak synaptic current, $\hat{I}_{syn}$, is defined as:

$$\hat{I}_{syn} = w_{liq} R_n u_n \quad (A.1.3)$$

where $w_{liq}$ is the weight of the synapses connecting the liquid cells. The excitatory and inhibitory post-synaptic currents $I_{syn,exc}(t)$ and $I_{syn,inh}(t)$ are given by an alpha-function,

$$I_{syn,x}(t) = \hat{I}_{syn} \frac{e^{-\frac{t}{\tau_{syn,x}}}}{\tau_{syn,x}} \quad (A.1.4)$$

where the subscript 'x' stands for 'exc' or 'inh', $\hat{I}_{syn}$ is the peak synaptic current (Eq. A.1.3), and $\tau_{syn,x}$ the time constant of the post-synaptic potential. Finally, the connection probability, $p(a, b)$, of two liquid cells located at the integer points $a$ and $b$ of a cubic lattice follows a Gaussian distribution,

$$p(a, b) = C \cdot e^{-(|a-b|/\lambda)^2} \quad (A.1.5)$$

where $|.|$ is the Euclidean norm in $\mathbb{R}^3$ and $C$ and $\lambda$ are constants. The values of all the synaptic parameters listed above are given in Tab. 2.2.

The liquid cells are simulated as leaky integrate and fire neurons. The membrane potential, $v(t)$, is updated according to

$$v(t + dt) = v(t) + \frac{dt}{\tau_{mem} g_{leak}} \cdot \left( I_{bg} + w_{inp} I_{inp}(t) + I_{syn,exc}(t) - I_{syn,inh}(t) - g_{leak} v(t) \right) \quad (A.1.6)$$
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where $dt$ is the simulation time constant, $\tau_{\text{mem}}$ the membrane time constant, $g_{\text{leak}}$ the leak conductance, $I_{bg}$ the background current, $w_{\text{inp}}I_{\text{inp}}(t)$ the synaptic input current from the temporal activity pattern, and $I_{\text{syn,exc}}(t)$ and $I_{\text{syn,inh}}(t)$ are synaptic currents (Eq. A.1.4). If $v(t) > v_\theta$, i.e. the membrane potential is greater than the threshold potential, a spike is generated and $v(t)$ is set to the reset potential, $v_{\text{reset}}$, and the neuron is quiescent until the refractory period of duration $t_{\text{refr}}$ has elapsed. The values of the parameters listed above are given in Tab. 2.1.

The readout neurons are simulated as leaky integrate and fire neurons. Let $i = 1, \ldots, I$ be the index of a readout group ($I = 11$), $j = 1, \ldots, J$ the index of a readout neuron in group $i$ ($J = 36$), and $k = 1, \ldots, K$ the index of a liquid neuron ($K = 720$). Then, the membrane potential of readout neuron $j$ of readout group $i$, $r_{ij}(t)$, follows

$$r_{ij}(t + dt) = r_{ij}(t) + \frac{dt}{\tau_{\text{mem},R}} (r_{ij,\text{syn}}(t) - r_{ij}(t)), \quad (A.1.7)$$

where $dt$ is the simulation time constant, $\tau_{\text{mem},R} = 30 \text{ ms}$ the readout neuron membrane time constant and $r_{ij,\text{syn}}(t)$ the post-synaptic potential given by

$$r_{ij,\text{syn}}(t) = \sum_{k=1}^{K} s g_{ijk} a_k(t). \quad (A.1.8)$$

$s = 0.03$ is an arbitrary and constant scaling factor, $g_{ijk}$ are the synaptic weights of liquid cell $k$ to readout neuron $j$ of readout group $i$, $a_k(t)$ is the activity of liquid cell $k$ which is 1 if the liquid cell fired an action potential at time $t$ and 0 otherwise. A readout cell may only fire if its membrane potential is above threshold, $r_\theta = 20 \text{ mV}$, at $t = t_L$, i.e. $r_{ij}(t_L) > r_\theta$. $t_L$ is a specific point in time after stimulus onset. After a spike, the readout cell membrane potential, $r_{ij}$, is reset to 0 mV and the readout cell response, $q_{ij}$, is set to 1 ($q_{ij}$ is zero otherwise). The readout group response, $q_i$, of readout
A.2 Mathematical relations

The following shows that the difference of two exponentials can be approximated with an alpha-function in the limit of an infinitesimal difference of the time constants. Consider two exponentials with time constants \( \tau_1 > \tau_2 \) in the limit of \( \tau_1 \to \tau_2 \). Using the series
expansion of the exponential function yields

\[ b(\tau_1, \tau_2) = \exp\left(-\frac{t}{\tau_1}\right) - \exp\left(-\frac{t}{\tau_2}\right) \]  
\[ = \sum_{n=0}^{\infty} \frac{1}{n!} \left[ \left(-\frac{t}{\tau_1}\right)^n - \left(-\frac{t}{\tau_2}\right)^n \right] \]  
\[ = \sum_{n=1}^{\infty} \frac{(-t)^n}{n!} \left[ \frac{\tau_2^n - \tau_1^n}{(\tau_1 \tau_2)^n} \right] \]  

Note that the term for \( n = 0 \) is zero and therefore the sum starts at 1. The term in the square brackets of Eq. A.2.3 can be approximated by setting \( x := \tau_2 - \tau_1 \) and computing its Taylor series around \( x_0 = 0 \) for \( n = 1, \ldots, \infty \),

\[ d_n(x) = \frac{(\tau_1 + x)^n - \tau_1^n}{\tau_1^n (\tau_1 + x)^n} \]  
\[ \approx \frac{n}{\tau_1^{n+1}} x \]  
\[ = \frac{n}{\tau_1^{n+1}} (\tau_2 - \tau_1). \]

Substituting this in Eq. A.2.3 yields

\[ b(\tau_1, \tau_2) \approx \sum_{n=1}^{\infty} \frac{(-t)^n}{n!} \frac{n(\tau_2 - \tau_1)}{\tau_1^{n+1}} \]  
\[ m=\infty \text{ with } t(\tau_1 - \tau_2) \sum_{m=0}^{\infty} \frac{1}{m!} \left(-\frac{t}{\tau_1}\right)^m \]  
\[ = \frac{t(\tau_1 - \tau_2)}{\tau_1^2} \exp\left(-\frac{t}{\tau_1}\right) \]  

Thus, in the limit of \( \tau_1 \to \tau_2 \), \( \tau_1 > \tau_2 \), the difference of the two exponentials is an alpha-function. It can easily be shown that for \( \tau_1 \to \tau_2 \) and \( \tau_1 < \tau_2 \) the difference is an alpha-function multiplied by minus 1.
Finally, we subsequently use the Taylor series expansion to simplify

\[ h(x, y) = \frac{A + x}{B - y} \quad (A.2.10) \]

in the case of \( x \ll A, x \ll B, y \ll A, \) and \( y \ll B. \) The Taylor series of \( h(x, y) \) around \((x_0, y_0) = (0, 0)\) is

\[
\begin{align*}
    h(x, y) &\approx h(x_0, y_0) + \frac{\partial h(x_0, y_0)}{\partial x}(x - x_0) + \\
    &\quad + \frac{\partial h(x_0, y_0)}{\partial y}(y - y_0) + \ldots \\
    &\approx \frac{A}{B} + \frac{1}{B}x + \frac{A}{B^2}y. \\
\end{align*}
\]

(A.2.11) (A.2.12)

Thus, for values of \( x \) and \( y \) that are small compared to \( A \) and \( B, \) the ratio A.2.10 can be approximated by Eq. A.2.12.
Appendix B

Data

In the following we detail how the conclusions of Chapters 2 to 5 can be reproduced based on the data archived together with this thesis.

B.1 Data for chapter 2

The neuronal simulation tool, wSim, used in this chapter is stored in the folder amoth/progs/wSim_dectpc. Instructions on how to use this simulator are in Reto Wyss' PhD thesis [150].

The visual stimuli (Fig. 2.1) were generated using the wSim process stored in the folder amoth/progs/prc/stimGen. The resulting visual stimuli are in the folder amoth/data/dt/stimgen, and the temporal population codes (Fig. 2.2) are computed with the wSim process stored in amoth/progs/prc/simpTempCode. The temporal activity patterns representing the visual stimuli are in the file amoth/data/dt/simptempcode/tpc_11_cl_scaled.dat.

The simulation used for the analysis of the liquid state distances (Fig. 2.4 and 2.6) can be found in amoth/progs/prc/DecTPC_Liq State with the result of the simulation saved in the folder amoth/data/dt/liqstate.
Two simulations were used for investigating the effect of the different reset mechanism (Fig. 2.5 and 2.7). For the no-reset and the two entire-reset methods, the simulation is in amoth/progs/prc/DecTPC_ContTesting. For the two partial-reset methods, the simulation is in amoth/progs/prc/DecTPC_ResetMethods2. The result is stored in the two folders amoth/data/dt/conttesting and amoth/data/dt/resetmethods2.

Finally, the simulation without synaptic short term depression of the synapses of the liquid state machine (p. 33) is stored at amoth/progs/prc/DecTPC_lowdep with the resulting data in the folder amoth/data/dt/lowdep. This data analyzed using amoth/data/matlab/dt_tools/hmcorrectps.m to load the fraction of correct classifications.

Based on the data saved in the subfolders of amoth/data/dt the figures of chapter 2 are drawn using the following Matlab scripts stored in amoth/data/matlab/dt_tools:

<table>
<thead>
<tr>
<th>Figure</th>
<th>Matlab script</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fig. 2.1</td>
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<td>dtmakefig2.m</td>
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<tr>
<td>Fig. 2.4</td>
<td>dtmakefig3.m</td>
</tr>
<tr>
<td>Fig. 2.5</td>
<td>dtmakefig5.m</td>
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<tr>
<td>Fig. 2.6</td>
<td>dtmakefig4.m</td>
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<tr>
<td>Fig. 2.7</td>
<td>dtmakefig6.m</td>
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</tbody>
</table>

### B.2 Data for chapters 3 and 4

Chapters 3 and 4 are based on the same experimental data. The raw imaging data as it was recorded with Till-vision 4.0 (TILL Photonics) is saved in the folder amoth/data/oi/origdata. Raw imaging data was transformed into time-courses of calcium activity and alpha-functions were fitted to these time courses using a series of Matlab scripts stored in the folder amoth/data/matlab/oi_tools and amoth/data/matlab/oi_tools/ui. Configuration files required
B. Data

B.2. Data for chapters 3 and 4

for this transformation are in amoth/data/oi/pnYYMMDD where YY represents the year, MM the month, and DD the day when the recording was taken. Calling for each of these folders the Matlab scripts pst2mat.m, shiftcorr.m, bleachcorr.m, glomsel.m, and respfit.m in this order constructs out of the raw data Matlab archives that contain the amplitude time-courses of the calcium response and the parameters of the fitted alpha functions.

Based on these archives, the figures of chapter 3 are drawn using the following Matlab scripts stored in amoth/data/matlab/oi_tools:

<table>
<thead>
<tr>
<th>Figure</th>
<th>Matlab script</th>
</tr>
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<tr>
<td>Fig. 3.1</td>
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<td>Fig. 3.2</td>
<td>makefig40.m</td>
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<td>Fig. 3.3</td>
<td>makefig39.m</td>
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<tr>
<td>Fig. 3.4</td>
<td>makefig38.m</td>
</tr>
</tbody>
</table>

Further analysis is required for chapter 4. ANOVAs were computed with SPSS, using scripts stored in the folder amoth/data/matlab/oi_tools/spss. ANOVAs for comparisons between glomeruli are computed by calling makefig23.m (folder amoth/data/matlab/oi_tools) and executing the SPSS script anvfitoc.SPS when instructed during the call of the Matlab script. Similarly, ANOVAs for comparisons between odor stimuli are computed by calling maketabl.m and executing anvfit_onewayANOVAs.SPS and anvfit.SPS when instructed on the Matlab console.

Discriminant analysis was done using the scripts ldaprepall.m (folder amoth/data/matlab/oi_tools) to prepare all data saved in the amoth/data/oi/pnYYMMDD folders and subsequently calling ldaproc.m (folder amoth/data/matlab/oi_tools) to compute the discriminant analysis.

Electrophysiological recordings are saved under amoth/data/st/pn_medhat with the raw data as recorded with AutoSpike in the subfolder aspk. Data is exported into Matlab readable ASCII files using AutoSpike's built-in export function. The Matlab archive re-
B.3. Data for chapter 5

required for plotting the data is generated by calling pn2mat.m and pnspikesort.m (folder amoth/data/matlab/st_tools/ui). The first script makes use of a configuration file (pn.sett) stored in the folder amoth/data/st/pn_medhat.

After these preparations, the figures of chapter 4 are plotted using the following Matlab scripts of the folder amoth/data/matlab/oi_tools:

<table>
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<th>Matlab script</th>
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<td>Fig. 4.1</td>
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<td>makefig10.m</td>
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<td>Fig. 4.5</td>
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<td>makefig519.m</td>
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<td>Fig. 4.7</td>
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<td>Fig. 4.8</td>
<td>makefig28.m</td>
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<tr>
<td>Fig. 4.9</td>
<td>makefig36.m</td>
</tr>
</tbody>
</table>

The statistical test results reported in the first and second paragraph of Sect. 4.3.2 were obtained using the console output of makefig23.m and maketabl.m (folder amoth/data/matlab/oi_tools).

B.3 Data for chapter 5

The wSim simulation environment is saved in the folder amoth/progs/wSim. Note that this version is different from the one used in chapter 2. The wSim processes are stored in amoth/progs/prc/alXX where XX is a two digit number between 28 and 40. The input used by these processes is generated using the Matlab scripts alXX inpsyst.m (folder amoth/data/matlab/al_tools) with XX the number of the process. The output of these processes is transformed into Matlab archives using the script aln2mat('alXX').m. For the simulations al36, al37, al38, and al40, discriminant analysis is com-
puted using `alnldastart.m` and specifying the according simulation as a parameter to this function.

After these preparations the figures are plotted using the following Matlab scripts (`amoth/data/matlab/al_tools`).

<table>
<thead>
<tr>
<th>Figure</th>
<th>Matlab script</th>
</tr>
</thead>
<tbody>
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<td>Fig. 5.1</td>
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<td>Fig. 5.3</td>
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<td>Fig. 5.4</td>
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<td>Fig. 5.5</td>
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<td>almakefig27.m</td>
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<td>Fig. 5.9</td>
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Bibliography


BIBLIOGRAPHY


Curriculum Vitae

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Publications


