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Free-Viewing as Experimental System to Test the Temporal Correlation Hypothesis: A Case of Theory-Generative Experimental Practice

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Abstract: Theory-free characterizations of experimental systems miss normative and conceptual components that sometimes are crucial to understanding their historical development. In the following paper, we show that these components may be part of the intrinsic capacities of experimental systems themselves. We study a case of non-exploratory and theory-oriented research in experimental neuroscience that concerns the construction of free-viewing as an experimental system to test one particular pre-existing hypothesis, the Temporal Correlation Hypothesis (TCH), at a laboratory in Santiago de Chile, during 2002-2008. We show that the system does not take well-formulated pre-existing predictions or hypotheses to test them directly, but re-creates them and re-signifies them in terms that are not implied by the theoretical background from which they originally derived. Therefore, we conclude that there is a *sui generis* way in which experimental systems produce proper theoretical knowledge.

Keywords: experimental systems, hypothesis testing, experimental neuroscience, free viewing, temporal correlation hypothesis

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1. Introduction

In the history and philosophy of experimental practice, it is a regular thing to conceive experimentation as distinct from theory. Philosophers of the "practice turn", for instance, tend to highlight experimental activities that are unframed by existing theories (Hacking 1983, Gooding 1990, for reviews, see Soler et al. 2014, Feest and Steinle 2016). One of the most notable cases of experimental practice independent from theory is exploratory experimentation (Burian 1997, Feest and Steinle 2016, Franklin 2005, Elliott 2007). Philosophers like Hans Radder (2003, 2006,

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2009) and Marcel Weber (2005, 2006) consider theory-free characterisations of experimental practice incomplete, insofar as they miss crucial normative components that do not derive from the autonomous functioning of experimentation. Their primary assumption is that "new concepts and theories are not generated by the experimental system itself" (Weber 2005, 148).

This paper considers theory, understood namely as a set of testable predictions, among the intrinsic capacities of experimental systems. We use the notion of "experimental system" in the sense introduced by Rheinberger (1997). Experimental systems are systems of control and manipulation designed to give unknown answers to questions that experimenters are not a priori able to formulate[1]. This paper aims to improve our understanding of how experimental systems materialise these questions, mainly when they concern conceptual or theoretical contents that guide and orientate experimental work. Experimental systems may include exploratory experimentation, but they are not restricted to it. Generally speaking, they are not conflicted with a theory-centred notion of experimentation, even if "the function of the experiment as an instance of testing hypotheses appears to be largely marginal" (Hagner and Rheinberger 1998, 363). To understand how experimental systems generate theory-oriented experimentation we need, in sum, to broaden the view upon experimentation that is dominant among philosophers of the "practice turn" and their critics. This task does not seem to have aroused particular interest in the literature. Waters (2019) has recently proposed a "broad-practice-centred" approach that

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[1] Rheinberger also calls experimental systems the basic units or the smallest integral unit of research (Rheinberger 1997, 28, 224, 238). Rheinberger (2018, 148-151) has recently pointed out that the epistemological validity of the notion of experimental system as basic unit of research finds historical limits. It hardly applies to scientific practice before 18th century or to current Big Science. These historical limitations notwithstanding, we hope to show that several features of the notion may be adequate to understand the process of knowledge production in cases of theory-centred experimental research.

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conceives research as an integration of practices of different kinds, including theory and explanation; however, he does not investigate the specific activities of experimental practice that yield new theoretical knowledge. Chang's idea of a "grammar of scientific practice" (2011) or "system of practices" (2012, 2014) as unifying frame to understand the diversity of experimental activities coherently, is modelled upon the structure of human agency, which seems unfitted to capture the unintentional and unpurposive functioning of experimental systems. We will not be interested here in the agent's decisions that shape the activities associated with the testing of predictions, but in how experimental systems produce concrete testable predictions. In the realm of the history and philosophy of mathematics, Epple (1999) adapted Rheinberger's notion of "experimental system" to explain the formation of knot theory. However, this expanded use of the concept, for which Epple prefers the expression "epistemic configurations" (p. 16), take us away from our focus on experimental science.

In what follows, we study a case of non-exploratory and theory-oriented research in experimental neuroscience that may offer interesting insights about the theoretical capacities of experimental systems. Our case concerns the construction of free-viewing as an experimental system to test predictions concerning one particular pre-existing hypothesis, the Temporal Correlation Hypothesis (TCH), at a laboratory in Santiago de Chile, during 2002-2008. The TCH proposes that the brain uses coordinated firing patterns of groups of neurons as a mechanism to encode visual information (we explain the TCH in more details in section 2.1). Experiments using free-viewing yield results that eventually support, refine and refocus this hypothesis, namely, by showing that eye movements-related neuronal synchrony works as a mechanism for the coordination of the first spikes induced by external visual inputs. However, the functioning of the experimental system does not derive from pre-existing theory associated to the TCH and free-viewing (section 2). The experimental success in designing and implementing experiments and in providing evidence supporting the TCH depends entirely on the specific technical capacities (section 3) developed by the experimental system itself, insofar as they allow researchers to map the free or self-initiated movements of the eyes onto the neuronal processing of visual information (section 4). In sum, the pre-existing hypothesis that motivates and orientates researchers does not shape in advance the predictions that the system tests eventually. We suggest that experimental systems do not take well-formulated pre-existing predictions or hypotheses to test them directly, but re-create them and re-signify them in terms that are not implied by the theoretical background from which they originally derived. There seems to be a way sui generis in which experimental systems generate proper theoretical knowledge. If this is correct, our analyses shall contribute to Rheinberger's characterisation of experimental systems as "reasoning machine[s] in [their] own right" (1997, 20). We agree with Weber (2005, Chapter 5) that an experimental system entails normative and conceptual components, which are necessary to understand its historical development, but we take these components as internally prescribed by the autonomous functioning of experimental systems themselves. We believe, therefore, that our study may also provide some additional evidence in support to John Bickle's claim that "our best-confirmed theory is totally dependent on what our experiment tools allow us to manipulate" (Bickle 2019).

Section 2 of the paper reviews part of the background theory and reasoning that guides and justifies the installation of free-viewing to test the TCH. Section 3 reviews the most characteristic technical achievements enabling the installation of free-viewing as an experimental system. Section 4 shows how the new and autonomous experimental setup creates the normative realm in which specific testable predictions become possible and in which researchers can produce reliable evidence supporting the TCH. Section 5 (conclusion) proposes two general claims about theory generation in experimental systems.

2. Maldonado's experimental proposition

Led by the Chilean neuroscientist Pedro Maldonado, the lab *Neurosistemas* is located in the Faculty of Medicine of the University of Chile. For the last two decades, Maldonado and his collaborators have studied patterns of ocular movement and their neurophysiological correlates. The original motivation of these studies – which have found applications in medicine and industry – was the search for new evidence supporting the Temporal Correlation Hypothesis (TCH). The TCH concerns the mechanisms by which the brain succeeds at rightly and timely coding information from the visual environment. Specifically, it postulates that the brain uses synchronous firing patterns of groups of neurons (see section 2.1 for details about the TCH). In 1993, Maldonado, as a post-doc, joined the laboratory led by Charles Gray in Davis, California. Gray's group was searching evidence supporting the TCH using monkeys staring at moving or stationary stimuli presented on a screen (Friedman-Hill, Maldonado, and Gray 2000, Maldonado, Friedman-Hill, and Gray 2000). Back in Santiago, between 2002 and 2008, Maldonado and his team carried out a series of experiments using awake cats and monkeys freely viewing images of natural scenes.

Maldonado (2007) is a theoretical essay that reveals the background theory justifying the use of free-viewing to study the mechanisms of visual processing. We may recognise at least three premises at stake in that essay. First, it is held that the incorporation of self-initiated ocular movements as relevant experimental parameters responds to a major paradigm shift in the explanation of the visual system. This paradigm shift leads from vision understood as a passive bottom-up process triggered by external physical stimuli, to a broader model that includes top-down processes in which brain plays an active role at building the visual world (see section 2.2). Second, since a primate or human eye performs up to 4 or 5 saccadic movements per second while exploring a natural scene, free-viewing seems a natural marker of the fine temporality in which the brain performs some tasks involved in visual perception, such as feature extraction, scene segmentation and perceptual grouping (see section 2.3). Finally, free-viewing serves as a marker of the high ecological constraints in which the visual system operates typically (see section 2.4).

These three premises are nonetheless all-too abstract to generate experimental protocols, research questions and testable predictions. They do not tell experimenters what they need to do to install an experimental setup capable of reliable results. The point of this section 2, briefly stated, is the following: the reference to pre-existing theoretical considerations is unable to inform the installation and functioning of free-viewing as experimental system. Only the array of tools and skills composing the system (section 3) seems capable of determining the protocols, questions and predictions that give life to the investigation about the TCH (section 4). Protocols, questions and predictions that no pre-existing theory would have ever been in the position to anticipate.

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2.1 Overview of the Temporal Correlation Hypothesis

The visual system is capable of recognising an enormous diversity of shapes, patterns and objects[2]. Constellations of perceptual features such as contours, locations, orientation or luminance combine to form images that our brain is capable of reading in tiny fractions of a second. The processing of visual information involves highly efficacious tasks performed by duly coordinated neurons from different cortical areas. For instance, in the most elementary stage of visual processing, groups of neurons in the primary visual cortex correlate with distributed cells in the retina. These cortical neurons are usually sensitive to particular physical stimuli, e.g. a light bar presented on a screen and oriented at a particular angle. In further stages of processing, neurons become receptive to more complex stimuli within milliseconds. The brain needs to segment and reintegrate the attributes of the objects; it needs to identify whether the response of neurons describes the location, orientation or contrast of a contour; it needs to differentiate overlapping groups of neurons responding simultaneously to nearby objects or the perceptual background. What are the mechanisms allowing the brain to perform these complex tasks? The TCH refers to one of these mechanisms. It joins and improves two other related hypotheses, the convergent hierarchical coding hypothesis (CHCH) and the population coding hypothesis (PCH).

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[2] The presentation we offer of the TCH in this section follows, in general lines, Gray & Singer (1995), Gray (1999) and Singer (1999), Sommer (2014). For evaluation and criticism, cf. Shadlen & Movshon (1999).

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According to the CHCH, visual information is processed through a series of hierarchically organised stages. Neurons in later stages receive and integrate information generated in earlier stages. The more complex the information is, the higher the stage in which the brain codifies it. The CHCH describes an iterative process that eventually forms units highly selective to process specific objects. Evidence obtained from the study of receptive fields at higher levels supports this hypothesis. However, there are solid reasons to doubt that hierarchical convergence is the only mechanism involved in visual processing. Each distinguishable feature and each distinguishable combination of features would need one specialised unit, but the limited number of cells in the system makes this unlikely.

Compared to the CHCH, the PCH has several advantages. According to the PCH, features and combinations of features are represented not by single units, but by concerted firings of different subgroups of neurons distributed in different cortical areas. The same subset of neurons that represent one feature can participate in the representation of a different pattern involving that feature. In other words, identical groups of neurons can represent different objects at different moments. Since the number of firing patterns in cell populations is larger than the number of cortical neurons, this mechanism turns out to be much more efficient than the one described by the CHCH. However, there are at least two problems with the PCH: first, it does not explain how to avoid the overlapping of similar objects coded with the same collective firing pattern. Second, it does not explain how to avoid the interference that may occur when objects coded by different firing patterns are present at the same time. A more flexible mechanism is required to enhance the saliency of a given group of neurons within a millisecond range and in rapid temporal succession. Variations in firing patterns are limited, expensive in terms of units, easily ambiguous, and rely on synaptic transmission, the frequency of which tend to attenuate. The TCH postulates an additional parameter: synchronous activity. Synchronous responses define with precision relationships among neurons. It allows the system to select cell assemblies distinct from others that may be active at the same time.

Synchrony as a mechanism for visual processing was first proposed by Milner (1974) and von Malsburg (1981, 1985). Using microelectrodes in the cortex to register both the spiking activity of individual cells and the extracellular current generated by localised groups of cells, a considerable amount of evidence supporting the TCH began to accumulate since the late 1980s. For instance, Charles Gray and Wolf Singer (1989) found that groups of neurons in cat's visual cortex, when presented with the appropriate stimulus, discharge synchronously at rhythmic intervals of 15-30 ms. Synchronous firing patterns were confirmed by other studies registering the primary visual cortex in cats (Maldonado and Gray 1996) and monkeys (Friedman-Hill, Maldonado, and Gray 2000, Maldonado, Friedman-Hill, and Gray 2000), neighbouring areas of the visual cortex in cats (Engel et al. 1991) and populations of neurons having either different or overlapping receptive fields in monkeys (Engel, Gray, and Singer 1990, Livingston 1996). Critics of the TCH consider the theory incomplete because it does not provide significative clues on how the brain eventually computes and reintegrates the information to represent coherent perceptual wholes (Schadlen and Movshon 1999).

A common feature of all the empirical studies supporting the TCH is that they result from experiments using simple and parametrised stimuli (such as light bars or wave gratings), and that they are performed on anaesthetised or awake but fixating animals. Maldonado's experimental proposition consists in studying synchrony in awake animals freely moving their eyes to explore natural scenes. In the following three subsections, we review three main premises that Maldonado (2007) presents to justify this proposition. We will see that the three are too abstract to specify experimental protocols, research questions and testable predictions. In other words, we find a gap between the theory associated to temporal correlation and the engineering of the new experimental setting, the autonomous functioning of which eventually generates the specific testable predictions guiding research on the TCH using free-viewing (see sections 3 and 4).

2.2 From the classical paradigm in the neurophysiology of visual perception to active vision

Maldonado (2007) refers to a paradigm shift in the explanation of the visual system, from vision understood as a passive bottom-up process triggered by external stimuli, to a new paradigm involving a top-down conditioning process in which the brain plays an active role at predicting the reception of external stimuli. According to Maldonado (2007), the incorporation of "free" or "self-initiated" movement of the eyes as a new experimental parameter is a consequence of this paradigm shift.

Consistent with the old classical theoretical paradigm, the conventional experimental practice in visual physiology involves primarily two actions: on the one hand, mapping single cortical neurons' receptive fields; on the other, registering their response to physical stimuli (see classical studies by Hubel and Wiesel 1959, Hubel and Wiesel 1962, for a general introduction, see Purves 2018, 267-269). In the classical paradigm, researchers concentrate their efforts in studying correlations between the physical properties of stimuli (brightness, colour, contrast,

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orientation, form, and the like) and the spiking behaviour of individual neurons or group of neurons individually measured. Experimenters use external, parametrised and repetitive stimuli that affect the retina of commonly anaesthetised animals.

There seems to be an enormous phenomenological distance between this classical experimental procedure and our ordinary experience of vision. In normal ecological conditions, visual perception involves the constant movement of the eyes. Eye-movements necessarily bring a swift and never-ending change of external stimuli upon the retina. A change of this sort naturally contradicts the physical stability that our perception projects onto the visual world. Therefore, there must be a flaw or an oversimplification in the traditional way of explaining the visual processing of the natural environment. The brain must do much more than coding information passively received. Vision must include top-down processes ensuring the correct, ordered and timely reception of external stimuli.

However, the solidarities between theoretical explanations of vision and the traditional experimental practice are likely not as strong as Maldonado (2007) seems to believe. The *practice* of registering the responses of individual neurons to repetitive and controlled stimuli does not entail the *explanation* of vision as a bottom-up process that integrates physical data. Neurons' receptive fields and their electrical behaviour, simple parametrised stimuli, cells groups in the retina, in the thalamus or the cortex, the optic nerve and the visual pathways, among other factors, are relevant to intervene the visual system in the "classical" experimental paradigm; however, they are not necessarily concepts composing a theoretical explanation. Horace Barlow himself, a pioneer of the classical neurophysiology of sensation and sensory processing (Barlow 1953a, b), admits that "the dogmas" he proposes to explain the relationship between single neurons and sensation "go considerably beyond the evidence" that is derived "by recording from single neurons in sensory pathways" (Barlow 1972, 370, 391). Moreover, the classical experimental paradigm proves to be productive not only for elucidating the bottom-up afferent pathways of visual stimuli, from the retina to the thalamus and cortex. The evidence supporting the TCH itself has been essentially produced within the classical paradigm as well. Research on visual coding may draw on the theory of visual pathways without necessarily been explained by it. This reminds of C. Kenneth Water's manipulationist view on genes (Waters 2004, 2007, 2019): genetics informs research because genes are precious tools for intervening cellular systems, but the new knowledge will fall outside the scope of gene-centred explanations. Similarly, the classical paradigm in the neurophysiology of perception provides experimental and theoretical tools that yield results about the TCH that escape their explicative scope eventually.

Maldonado (2007) seems to build a Kuhnian-like narrative of this paradigm shift in visual physiology. We could reinforce this narrative with some biographical remarks. Maldonado did part of his undergraduate training during the 1980s at "Epistemología Experimental", a legendary Santiago laboratory that brought together two leading figures of Chilean neuroscience, Humberto Maturana and Francisco Varela. Therefore, young Maldonado began his career immersed in the idea that visual perception is first and foremost a way of constructing the world (Maturana and Varela 1987, 141-178, 1991, Varela, Rosch, and Thompson 1992), not a mere integration of external stimuli. Maldonado's focus was from the beginning placed on explaining biological functions as emerging in the interactions of organisms with their environment (Maldonado, Maturana, and Varela 1988). Within the frame of this Kuhnian-like narrative about the emergence of free-viewing as experimental system, we may indeed say that Maldonado's skills and training contribute to explain how come he did "see" potential connections between free viewing and neuronal synchrony. "What a man sees depends both upon what he looks at and also upon what his previous visual-conceptual experience has taught him to see" (Kuhn 1970, 173). But getting to see things differently does not ensure that we develop the ability to study them. We need instruments and skills enabling their control and manipulation (section 3), not "armchair reflection[s] about 'how the brain works'" (Bickle 2019).

2.3 Free-viewing as a marker of the fine temporality of brain's tasks in visual perception

Maldonado (2007) states: "if we are to examine the temporal properties of the neuronal discharges, then it is also reasonable to think that we have to pay attention to the temporal structure of the visual stimuli we use to study cortical function". This inference is meant to lead directly to the installation of free-viewing as experimental system. Free-viewing is a natural marker of the fine temporality in which the brain performs the tasks required for visual perception (such as feature extraction, scene segmentation and perceptual grouping). When a primate or human eye explores a natural scene, it may perform up to 4 or 5 saccadic movements per second, which means that the brain performs all the tasks required for visual perception in periods within the range of 100-300 ms (Thorpe, Fize, and Marlot 1996).

However, we think that no logical or experimental necessity leads directly to materialise research about "the temporal properties of the neuronal discharges" in a system that correlates the neuronal activity with self-initiated eye-movements. In other words, nothing in the discussion about temporal correlation or the speed of visual information processing entails the incorporation of eye-movements as a new experimental parameter. In section 4, we will formulate this by saying that only a "conjuncture" brings together eye-movements and research about synchrony. We think that free-viewing appears as a contingent "supplement" (for this notion, cf. Rheinberger 1997, Derrida 1973, Chapter 7, 1976); a "supplement" that recontextualises eventually the whole investigation, namely by offering a new space for representing the fine temporality of neuronal coding and providing testable predictions concerning the correlations between synchrony and eye movements (see section 4).

As we have seen (section 2.1), neither the combinatorial problem of the CHCH, nor the overlapping and interference problems of the PCH, relate to the temporal constraints of visual information processing. Both the CHCH and the PCH satisfy the processing speed requirements (Rolls and Tovee 1995, Gray 1999). Free-viewing is indeed a marker of the highly sophisticated and accurate synchronisation of spikes within extremely short temporal windows, but the 200 ms window in which occur a rapid movement of the eyes followed by a fixation period, is a much too long period for the processes that we need to spell out. The literature had already established that the expected duration of meaningful neuronal interactions and synchronous firing occurs on a time scale of less than 5 ms (Von Der Malsburg 1981, 1985) and that the informationally relevant periods for discrimination of visual stimuli in the inferior temporal cortex last 20 ms (Rolls et al. 2006). Moreover, as already recalled, Gray and Singer's experimental results supporting the TCH almost do not deviate from the "classical" experimental setting: they consisted in recording the neuronal response to moving light bars in sleeping or awake but fixing cats (Gray and Singer 1989, Gray et al. 1989). Therefore, so far, there seems to be no theoretical necessity leading from "the temporal properties of the neuronal discharges" to an experimental system using free-viewing.

2.4 Free-viewing as a marker of the high ecological constraints in which the visual system operates

It is not under discussion that a primary goal of visual neuroscience consists in explaining the neuronal basis of vision as it occurs under normal ecological conditions. What is under discussion is the technical feasibility and experimental effectiveness that natural stimuli and free viewing may have (Rust and Movshon 2005). Without the conditions for its proper manipulation, free viewing may appear as an arbitrary, not to say a whimsical, heteroclite and multiform process, impossible to measure and study. By inhibiting the free movement of the eyes, the classical experimenter allows some specific correlations to appear (such as those between an external physical stimulus and the receptive field of a neuron). Researchers tend to avoid free viewing not because of their theoretical or ontological commitments, but because of the technical and methodical constraints that limit its productive use.

Nevertheless, free-viewing is not entirely meaningless in the classical experimental paradigm. It functions namely as a marker of the high ecological constraints in which the visual system operates typically. This function of free-viewing is relevant when we are concerned with the validity of our claims about synchrony in visual processing. Validity concerns seek to know "whether the context, stimuli employed, and responses elicited in the experimental context are similar to those that would be found in the world" (Sullivan 2015, 41). What if synchrony were an artefactual construct of laboratory conditions, particularly of the simple, repetitive and controlled stimuli? In the classical paradigm, it is possible to show that synchrony is not, for instance, an artefact of the anaesthesia, by observing neuronal responses in awake animals and over a range of different kinds and levels of anaesthesia. However, the classical system does not produce data about the behaviour of neurons when eyes are free to explore complex stimuli. As long as a new experimental setup having eye movements as a parameter is not in place, there is no way to yield reliable answers to these validity concerns. The problem is that the simple idea of free-viewing is not precise or concrete enough to indicate how to engineer research questions and experiments. Free-viewing has not yet gained the experimental capacity of "assessing what we do not know" (Rheinberger 1997, 47). All we have is a system that generates non-testable data: when eyes are free to move, neurons behave unpredictably.

3. Free-viewing's experimental setup

"The history of neuroscience," Rafael Yuste writes, "is the history of its methods" (Yuste 2015). An entire array of tools is needed for the electrophysiological recording of multiple neurons and the extracellular potentials, to track the positions and movements of the eyes, to register spike synchrony in 5 ms windows. If Maldonado and his collaborators had not used specific tools and techniques to intervene segments of free eye-movements, the life span of which barely reaches 200 milliseconds, then the experimental system would unlikely have produced new knowledge about neuronal synchronization.

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In this section, we review some of the most characteristic technical components of the system of free-viewing, namely: awake capuchin monkeys (*Cebus apella*) freely moving their eyes (section 3.1), pictures of natural scenes (section 3.2), magnetic scleral coils for monitoring the position of the eyes (section 3.3), and tetrodes (section 3.4). We choose these examples because they are part of the system physically mounted in Santiago with the specific purpose of finding evidence supporting the TCH. We will see that motivating problems guide the design, selection or adaptation of each of these tools. We use the concept of "motivating problem" in the metascientific sense introduced by Bickle (2016). It refers to specific experimental problems responsible for the development or the adaptation of new tools. We will later see (section 4) how the new array of tools (not a pre-existing theory) creates the normative space in which specific testable predictions become possible and in which researchers will be able to produce reliable evidence. Testable predictions do not precede, but result "from the development and ingenious uses of experiment tools" (Bickle 2019).

3.1 The model organism

Magnetic search coils for tracking the position of the eyes (see section 3.2) and tetrodes for recording electrical activity in the cortex (see section 3.4) are both invasive methods. Methods of this kind turn unethical the use of healthy human beings for experimentation purposes. Experiments reported in Friedman-Hill, Maldonado and Gray (2000) and Maldonado, Friedman-Hill and Gray (2000) used Rhesus monkeys (*Macaca mulatta*). When Maldonado began his experiments in Chile, it was only possible to work with Capuchine monkeys (*Cebus* *apella*). This change of organism was unproblematic because it did not imply significant alterations in surgical procedures and training. The search coils implant procedure was similar in both cases; as for the implantation of tetrodes, experimenters used available knowledge about the topography of the visual cortex (Gattass, Sousa, and Rosa 1987).

The choice of non-human primates awake and freely moving their eyes seems functional to the new paradigm that seeks to study active perception (see section 2.2). The fact that visual scanning of natural scenes in the case of primates, as in the case of human beings, is composed of a similar number of rapid saccadic movements per second, turns the choice of this organism also functional to the study of the fine temporality of synchrony (see section 2.3) and to the recreation of more natural ecological conditions (see section 2.4). The experimental problem that motivates the use of primates, however, does not seem directly concerned with any of these premises, but only, or at least primarily, with generating an efficient and reliable device for data production. The object under study consists of short (100-300 ms) segments of visual scanning. Each of these segments results from the composition of a saccadic movement and the immediately following fixation period. Experimenters' jargon calls one segment of this nature a saccade-fixation (S-F) trial. Figure 1 shows eight S-F trials. Primates are suitable animals for data production because they mark the segmentation of self-initiated S-F trials unambiguously during the visual scanning of a natural scene. Unambiguous marking of vision segmentation makes the production of statistically relevant numbers of S-F trials easier. Two primates were used in the experiments; one generated a total of 2452 S-F trials and the other a total of 2686 S-F trials. Previously, Maldonado & Babul (2007) worked with cats. The use of cats is usual in the neurophysiology of visual perception. However, for studying free-viewing, cats seem less suitable than monkeys. They produce a lower number of S-F trials during visual exploration, and the training to perform the visual task (to scan freely natural scenes) is more complicated.

3.2 Tracking eye movements

“In the free-viewing part, the animals were allowed to freely explore the monitor screen with self-initiated eye movements” (Ito et al. 2011). Eye movements are part of our natural way of perceiving our visual environment. It is something our brain “does” in order to make the visual world happen, as much as the movements of our hands over a surface seem a necessary condition for touching. We can quote an old remark by German physiologist Hermann von Helmholtz: “We let our eyes roam continually over the visual field, because that is the only way we can see as distinctly as possible all the individual parts of the field in turn” (Helmholtz 2005, quoted in Duchowski 2007, 4). Accordingly, we may expect that the course that the eyes follow while exploring a visual scene translates the subjective and invisible experience of the agent who perceives. Eye-movement provides relevant psychological information. Eyes’ direction and the selection of visual stimuli in our environment mark visual attention. If accompanied with pupillary dilation, it may also mark the subject's interest, desire or emotion. For instance, using non-invasive up-to-date techniques of eye-tracking, Maldonado’s group has carried out studies about the visual behaviour of website’s users (Loyola et al. 2015), the pupillary response to negative emotional stimuli in meditation practitioners (Vasquez-Rosati et al. 2017), and the pupillary response to non-photorealistic representation in stereoscopic cinema (Fajnzylber et al.

2017). In sum, eye position and pupillary behaviour represent – if we use Michael Hagner's expression – "the mind at work" (see Hagner 2006).

However, the experimental motivating problem that leads to the operationalization of eye movements differs significantly from considerations about their psychological value. On the one hand, we need to identify saccade-fixation trials unambiguously. A saccade-fixation trial begins with a saccade-onset (corresponding to the end of the preceding fixation), is followed by a saccade-offset (equivalent to the new fixation-onset) and ends with a fixation-offset. Saccades are defined as movements with an angular velocity higher than 100°/s lasting for at least 5 ms and a minimum acceleration of $170°/s^2$. Fixation periods are defined as lasting at least 100 ms with eye position fixed within 1° of the gaze location reached at the end of a saccade. On the other hand, to extract meaningful statistical events, we need to identify trials with similar duration. Researchers used the onset of an eye-movement as reference for defining the standard duration of trials. For fixations, data were included from -25 ms before fixation onset to 325 ms after fixation onset, and for saccades, from -25 to 75 ms.

3.3 Natural scenes

In one of the experiments, monkeys explored sets of 13 pictures of different natural scenes. A "natural scene" consists of pictures of animals, human faces or landscapes (see an example in figure 1, A). Images were displayed on a computer monitor located 57 cm in front of the animals. The utilization of natural scenes does not respond primarily to requirements of higher ecological validity. As Maldonado, Ossandón, and Flores (2009) explain, "what normally

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is considered free viewing in experimental designs (presentation of static images on a monitor) has little resemblance to natural vision, in which most of the time vision is engaged in goal-directed behaviour”. Laboratory conditions using free viewing are, in fact, only slightly more “natural” than in the classical experimental paradigm. For instance, to extract eye movements unambiguously, we need the animal to have the head artificially fixed (for that purpose, during the surgeries to implant tetrodes and search coils, researchers also implanted a cranial post).

The most important function of natural images consists in inhibiting the arbitrariness of researchers’ interventions during the visual tasks. In the classical experimental paradigm, experimenters decide the kind of stimuli that were presented and the timing of their presentation. But now, the intervention of experimenters is among the factors that would thwart the manifestation of relevant variables. By letting animals explore freely natural scenes, we make sure eye-movements are self-initiated. Moreover, while freely exploring a scene, animals never fixe their gaze longer than needed by the brain to process visual information, so that eye-movements mark brain states during this processing. As Maldonado (2007) explains, “[t]his approximation intends to enable the brain to carry out a task under dynamics not interrupted by the experimenter, but that are, at the same time, capable to deliver appropriate markers to analyse and to correlate neuronal activity with behaviour” (448).

The incorporation of more complex stimuli – the replacement of light bars or wave gratings with natural images, and of simple colour with intricate colour patterns – is not relevant because of the physical and statistical properties of images (for natural scene statistics and visual perception, see Gallant 2004, Stansbury, Naselaris, and Gallant 2013). In the new experimental setting, natural images are used because they allow self-initiated eye-movement to appear as

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relevant variables. We are in a context that is considerably different from the "classical paradigm", where the aim was to study the correlations between the physical properties of stimuli and the receptive field of cortical neurons. The new setting makes disappear one of the typical objections raised against the use of natural images in visual neurosciences. Traditionally, it is objected that natural images are statistically too complicated to be used fruitfully in the neurophysiological study of visual perception. For instance, Rust and Movshon (2005) state: "The main – and in our view, crippling – challenge is that the statistics of natural images are complex and poorly understood. Without understanding the constituents of natural images, it is imprudent to use them to develop a well-controlled hypothesis-driven experiment". However, in the new experimental setup using free-viewing to test the TCH, the use of natural images does not require us to specify their constituents.

3.4 Tetrodes

In the neurophysiology of perception, the classical or standard tool to register the electrical activity of neurons in the visual cortex are single wired microelectrodes. It is reasonable to think that the use of this tool explains in part the traditional focus on individual neurons. As Rafael Yuste puts it, the "focus on the properties of individual neurons was a natural consequence of the use of single-cell anatomical and physiological techniques" (Yuste 2015, 487).

In experiments with free-viewing, Maldonado uses compounds of 4 micro-electrodes, also called "tetrodes". The use of tetrodes was introduced by O'Keefe and Reece (1993) and

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Wilson and McNaughton (1993) to improve the identification of cells in the hypoccampus. The method was shown to be much more effective than microelectrodes in both their reliability and the yield of units recording of cells performing the same function. During his stay at Gray's laboratory in the 1990s, Maldonado collaborates in the adaptation of this technique, originally applied to the hippocampus, to register the activity of the visual cortex (Gray et al. 1995). In his experiments with monkeys freely viewing natural scenes, Maldonado uses arrays of 8 tetrodes positioned in circle, with a center-to-center distance of about 400 μm. One of the four channels of each tetrode was filtered to register local field potentials (LFPs). LFP is an extracellular signal reflecting the synaptic activity of neurons that are localised in the close vicinity of the recording micro-cable (more details about LFP in section 4.2).

The advantage of these arrays of tetrodes was not their ability to register groups of nearby cells and the dynamics of their interaction, namely the synchronous discharge during visual tasks, as if they were a tool for registering synchrony "at work". The utility of this method is much less spectacular, although highly functional for research on synchrony. Tetrodes overcome two typical errors induced by single microelectrodes. When using microelectrodes, it is easier to overlook that different events may be generated by the same neuron and that the same event may be generated by different neurons. Tetrodes are much more efficacious and accurate in registering singular events. This is important for a more fruitful application of statistical methods, namely the Unitary Event (UE) Analysis method, which takes pairs of neurons firing simultaneously to calculate synchrony in short time windows (Grün, Diesmann, and Aertsen 2002a, b, Grün 2009).

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4. Free-viewing as a theory-generative experimental system

It may well be true that pre-existing empirical and theoretical knowledge about neuronal synchrony did guide researchers during the installation of free-viewing as an experimental system to test the TCH, and that this pre-existing knowledge did even command experimental design. However, this guidance has, at most, a "heuristic" value, and in no case, is a necessary condition for the kind of testable predictions that the system eventually materialises. A contingent conjuncture brings together eye movements and research about synchrony (for the notion of "conjuncture", see Rheinberger 1997, 133-135). But this conjuncture eventually creates its necessity, deep enough to re-direct experimental research about the TCH in directions that no pre-existing theoretical or empirical knowledge could have predicted. We may state our point in the following terms. Contingent or not, the installation of free-viewing as experimental system creates ex-post a normative realm that yields TCH-associated testable predictions. Roughly described, this normative realm is based on the mapping of saccade-fixation trials onto the neuronal processing of visual information (section 4.1).

We need to consider an objection to our thesis. If it is true that an experimental system entails a sui generis capacity of generating testable predictions, then one may wonder about the conditions under which inter-system knowledge progression is possible. The system of free-viewing eventually produces knowledge that pertains to a specific subfield in visual neurosciences and this knowledge is said to confirm the TCH. Therefore, experimental systems might not be as autonomous as we think concerning pre-existing knowledge. How could we say that the system of free-viewing yields evidence for a pre-existing hypothesis, if this pre-existing hypothesis did not shape in advance the predictions that will be tested? We address this objection in section 4.2. We claim that conceptual continuity and progression of TCH-related research rely ultimately on the technical and methodological capacities that experimental systems generate by themselves. Knowledge produced by an experimental system describes properties and processes that are tightly referred to a set of experimental procedures. The extrapolation of this knowledge to describe properties and processes that are referred to other experimental procedures is possible only within the narrow limits of partially shared technical and methodological conditions.

4.1 The production of testable predictions

By articulating free viewing with neuronal synchrony, however contingent this articulation should be considered, a new normative realm emerges, and, along with this, new directions for research about the TCH take place. As we have seen (section 3.3), one of the most significant consequences of free-viewing was not so much the incorporation of more complex stimuli – natural images –, but the incorporation of eye movements as a variable that is experimentally relevant for representing brain's processing of information. This incorporation is important for at least three reasons. First of all, due to the simplicity of its structure, eye-movements are one of the most studied and best-known mechanisms of the motor system (Purves 2018, 449-450). Accordingly, incorporating it as a relevant variable allows to incorporate background theory highly valuable for experimental purposes: knowledge about ballistic eye movement, innervation of non-ocular muscles, metrics of saccades, micro-saccades, and fixation, and the like, become mighty and promising instruments for controlling and manipulating the visual system. The second relevant consequence of incorporating eye-movements is that free-viewing becomes a natural marker of brain states during visual processing. When they freely scan a natural scene, eyes move and fix as needed by the brain to process the information. Free-viewing as experimental system allows experimenters to operate upon invariant correlations in which the changes in eye movement are conceived of as a function of the changes in neuronal processing. On the one hand, experimenters map the sequence of saccade-fixation trials onto the sequence of brain states during visual processing (see fig. 1, A-B). On the other hand, within each saccade-fixation trial, it is also possible to establish a micro-periodisation (saccade-onset, saccade-offset, fixation-onset, fixation period, fixation-offset) that experimenters map onto the fine temporality of neuronal interactions, thereby creating an internal differential order that represents functional micro-phases of the process. In sum, the normative realm that free-viewing creates is essentially based on the mapping of saccade-fixation trials onto the neuronal processing of visual information.

As experimental system, free-viewing becomes a device to materialise questions and to formulate testable predictions that it would not have been possible to derive abstractly and directly from previous theoretical constructions about the TCH. Eye-movements operationalize the temporal order in which spike synchrony occurs. The highlighted fact that synchrony operates according to an extremely precise timing acquires a new meaning; namely, that synchrony must be compatible both with the short periods of saccade-fixation trials and with their internal order. The fine temporality of visual processing does not refer merely to the duration and rhythm of synchronous events but also refers to the extensive and intensive functional orders that eye-movements map. On that basis, experimenters can predict correlations between internal saccade-related extracellular signals and the first spikes responding to external visual stimuli (Ito et al. 2011). They find that the peak of spike synchrony (see fig. 2, bottom panel) coincides with the steepest negative slope of the saccade-related LFP modulations (fig. 2, top panel) and with the fastest firing rate increase of externally evoked spikes (fig. 2, middle panel). Without having installed free-viewing as experimental system, this prediction would have made no sense.

The third consequence of including eye-movements in the new experimental setting is that free-viewing now provides a concrete point of departure to investigate “active vision”, i.e. the part that the brain takes at actively configuring the visual environment. In the classical paradigm (that uses sleeping or awake but fixating animals), animals cannot predict when the stimuli could appear. If instead eyes freely scan natural scenes, then we may conjecture that the visual system might generate predictive information about when externally induced activity reaches the cortex. By moving the eyes, changes of external stimuli “come at times where the brain expects or provokes them” (Maldonado et al. 2008, 448). This action of the brain refers now to a testable process. The brain begins to prepare the reception of external information as soon as the eyes move. “The phase-locking of the first spikes [produced by the external stimulus] is highly likely a reflection of the interaction between the visual input-related signal and the eye movement-related signal” in the primary visual cortex (Ito et al. 2011, 2488).

4.2 Knowledge progression based on data-recording and data-analysis methods

Experimenters obtain new evidence supporting the TCH in a new experimental paradigm that uses animals freely exploring natural scenes. In other words, research about the TCH using this experimental setting yields results that increase our knowledge about synchronous firing in visual processing. It adds a new perspective to the one that uses simple and parametrised stimuli in anaesthetised or awake but fixating animals (the "classical paradigm") and also to previous research using self-initiated eye-movement performed in the dark (Rajkai et al. 2007). This inter-system and inter-paradigm complementarity shall not surprise. Part of the work of investigators consists in showing how their results contribute to growing bulks of knowledge in their research fields. Scientific papers always need to contextualise the results they report within pre-existing research questions and hypotheses. This ordinary fact, however, could be used to undermine the central thesis of our essay. If we accept that free-viewing yields results that confirm and refine or even redirect previous research on TCH, shouldn't we accept as well that the system's testing activities are not as autonomous as we have pretended throughout our analyses? Shouldn't we admit that pre-existing knowledge about the TCH determines in advance the functioning of free-viewing as experimental system, especially if the stated purpose of this system consists in generating evidence in favour of that pre-existing hypothesis?

One way to work out this problem is by examining how the integration of results across different experimental systems takes place. We suggest that this integration does not require given conceptual contents acting as common referents for descriptions that investigators reach through experimentation. We believe that shared technical and methodological tools, which rely on the intrinsic capacities of experimental systems, ensure knowledge integration by providing common grounds for the operationalization of conceptual contents. To show this, we will take a closer look to how the two experimental paradigms that we have contrasted throughout this essay, i.e. the classical paradigm and free-viewing, produce, using different sets of variables and manipulation paths, connected evidence about the TCH. We claim that they produce this connected evidence insofar as TCH-related concepts are operationalized by using shared techniques and methods for data-recording and data-analysis.

Following Sullivan (2009, 2015), an experimental paradigm is a set of standard methods and procedures that specifies how to produce a phenomenon of interest in laboratory conditions. In the case we are studying, we identify two (at least) different experimental paradigms tackling synchrony as a neuronal mechanism for visual processing. Between the two paradigms, there are significative differences both in methods to produce data (e.g. the visual tasks and the stimuli) and in detection procedures (e.g. physical properties of stimuli and the statistics of natural images are replaced with protocols defining saccade-fixation trials). Variables of experimental intervention in one paradigm move or disappear in the other paradigm. In the first case, the physical properties of visual inputs are relevant variables; in the second, the timing of saccade-fixation trials. In one paradigm, the relevant experimental paths begin with the simple and parameterised stimuli that are controlled by the experimenter; in the other, they begin with self-initiated eye-movements. In sum, the two paradigms end up materialising visual processing quite differently.

However, both paradigms share crucial tools for data-recording and data-analysis, and this eventually allows the integration of results. We will consider one example: the correlations between local field potentials (LFPs) and the spiking behaviour of individual neurons. Electrophysiological techniques for detecting neuronal processes reach a very high temporal

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resolution, but a very poor spatial resolution. While researchers have the means to record and inspect electrical activity in a few milliseconds, they lack instruments to observe continuous variations through different spatial scales. In other words, what they see it happens at micrometre scale (for instance, the electrical activity of neurons' spines) has no apparent connections to what simultaneously happens at a millimetre scale (for instance, the field potentials in the visual cortex). Modelling correlations between different spatial scales poses severe difficulties. As far as research on synchrony is concerned, it would not be exaggerated to say that there exists evidence about the coordinated behaviour of neurons in the cortex for more than one century, i.e. ever since researchers created the means to record self-regulating oscillatory rhythms in the brain (Caton 1875, Sommer 2014). Nevertheless, to understand the function of these oscillatory movements in the neuronal processing of visual information, it would be necessary to find stable correlations between them and the behaviour of individual neurons responding to controlled stimuli. How could one do that? As previously recalled (section 3.4), LFPs are extracellular currents recorded by implanting microelectrodes in cortical tissue. LFP modulations are supposed to receive synaptic currents from multiple neurons located in less than 1 mm from the tip of the microelectrode (Destexhe and Bédard 2014). Therefore, significant variations in the amplitude of the signal's average likely reflect synchronised activity of localised sets of neurons. Finding stable and repetitive correlations between the rhythms of individual spikes and specific phases of LFP signal would constitute a valuable indicator of the function of synchronised activity in the brain's information processing. For that reason, experimenters study the relationship between spike behaviour, measured using methods for unit recording, and the modulations of potential fields (Denker et al. 2011). For example, Gray and Singer (1989) shows

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that when light bars are in the right position, changes in neuron's firing pattern coincides with changes in the amplitude of LFP oscillations, and more specifically that spikes are locked to the negative peaks of the LFP signal. Maldonado et al. (2008) and Ito et al. (2011) found a correlation between spike synchrony and saccade-onset-related LFP modulations (see above, section 4.1). In one case (Gray and Singer 1989), LFP modulations are dependent on the external input; in the other case (Maldonado et al. 2008, Ito et al. 2011), it originates along with saccades. The phase-locking of synchronous spikes to LFP modulations creates, therefore, a unified spatiotemporal ground in which the electrical processes described by the two experimental paradigms with their different set of variables and of causal paths take place. From that moment on, what investigators describe in one system can be integrated to or confronted with what they describe in the other.

To understand knowledge progression across different experimental systems, we do not need to presuppose pre-existing conceptual referents to which these systems refer. The autonomous functioning of an experimental system contributes to the progression of pre-existing conceptual contents insofar as it shares, with other experimental systems, techniques and methods for data-recording and data-analysis. In the case we are examining, shared electrophysiological methods and techniques - the operativity of which depend on the intrinsic capacities of experimental systems - create a unified spatiotemporal ground for the operationalization of TCH-related concepts. We agree with Jacqueline Sullivan's claim that multiplicity of experimental paradigms may favour the progression of knowledge in experimental neuroscience (Sullivan 2009, Sullivan 2018); this is likely due to the ability of these different paradigms to integrate results based on shared methodological and technical strategies.

5. Conclusion

As experimental system, free-viewing becomes a device to materialise questions and to formulate testable predictions that it would not have been possible to derive abstractly and directly from previous theoretical constructions about the TCH. Theory-centred experimental research is not at odds with the autonomous functioning of experimental systems. Quite the contrary, as we have seen in this paper, experimental systems have intrinsic normative capacities to generate the theory on which experimental research comes to be eventually centred in practice. Free-viewing creates the conditions for its development as a theory-centred experimental system.

To conclude, we propose two general claims about theory-generative research in experimental systems. In the first place, we claim that meaningful and experimentally plausible predictions are those that an experimental system is capable of materialising. In other words, meaningful and plausible predictions are those that incorporate in their own formulation the instructions for their testing. For instance, the conjecture that eye movement-related changes in neuronal excitability may work as a mechanism for the precise coordination of the timing of early visually evoked spikes during free viewing is meaningful and experimentally plausible only if it prescribes how we must prove it. This conjecture prescribes two actions indeed: on the one hand, to measure the spiking activity and the simultaneously recorded LFP in visual cortex while

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monkeys freely view natural images, and, on the other hand, to correlate the timing of externally evoked spikes to the LFP modulations related to the initiation of voluntary eye-movements. If we paraphrase a well-known motto of logical-empiricism, we could say that the meaning of testable predictions is the method of their experimental verification (Schlick 1936). As we have seen, even an experimental system that has been installed with the explicit purpose of verifying predictions derived from a pre-existing hypothesis - a hypothesis that was constructed in the language of pre-existing theory and confirmed by pre-existing experimental results -, ends up generating testable predictions that are specifically referred to the new experimental procedures that experimenters were capable of building. In this sense, we may say that experimental systems are machines that generate propositional knowledge in their own right.

If this is correct, then we may add, in the second place, the following claim: the truth value of a hypothesis – also of a set of hypotheses or, in general, of a set of propositions that we may call a “theory” – do not preexist the process that tests it (them), but is the outcome of this process. In this sense, we should agree with John Bickle (2019) in that our best confirmed theories are totally dependent on what experimental systems allow us to manipulate.

Figures

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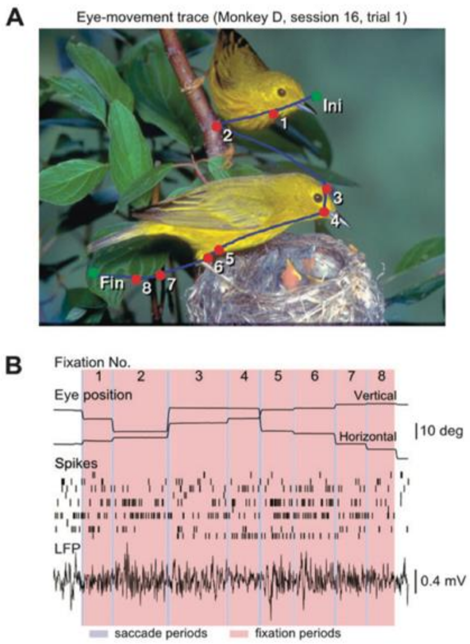

Figure 1. Eye movements and visual cortex activity during free viewing of a natural image. (A) Trace of eye movements. Red dots indicate fixation positions and blue curves represent the traces of saccadic eye movements. Green dots indicate the initial (Ini) and final (Fin) eye positions in this trial. (B) Traces of the horizontal and vertical eye positions (top) are shown together with the simultaneously recorded single unit spike trains of 10 neurons (middle) and an LFP trace from one of the four cables of a tetrode. Periods of fixations and saccades are indicated by red and blue shaded areas, respectively. *Source* (Ito et al. 2011)

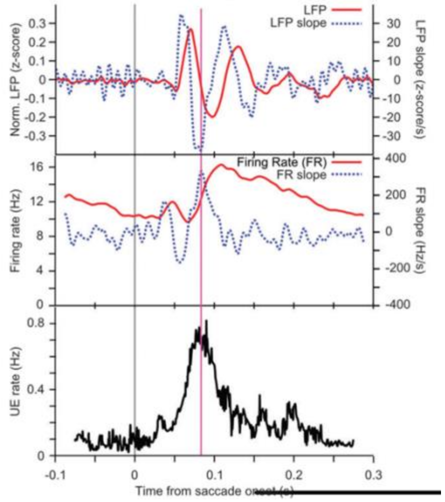

Figure 2. Temporal relationship between LFP (top), firing rate (middle), and rate of Unitary Events (bottom). Red solid and blue dashed curves in the top panel represent saccade-onset-triggered average LFP and its first temporal derivative (dashed blue), respectively. The pink vertical line indicates the position of the negative peak of the derivative, which corresponds to the steepest negative slope of the LFP. *Source* (Ito et al. 2011)

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