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Exploratory concept formation and tool development in neuroscience

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Abstract:

Developing tools is a crucial aspect of experimental practice, yet most discussions of scientific change traditionally emphasize theoretical over technological change. To elaborate on the role of tools in scientific change, I offer an account that shows how scientists use tools in exploratory experiments to form novel concepts. I apply this account to two cases in neuroscience and show how tool development and concept formation are often intertwined in episodes of tool-driven change. I support this view by proposing common normative principles that specify when exploratory concept formation and tool development succeed (rather than fail) to initiate scientific change.

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1. Introduction

The development of tools that allow researchers to measure or intervene on phenomena is a crucial aspect of experimental practice across the natural sciences (Hacking 1983, Rheinberger 1997, Chang 2004, Sullivan 2009). But despite its centrality to the epistemology of experiment, most discussions of scientific change have emphasized theory change over technological change (Kuhn 1970, Laudan 1977, Thagard 1992, Dellsen 2018, but see Baird and Faust 1990).

Recently, Bickle (2016, 2018) has taken issue with this emphasis and argued that tool development is a crucial driver of change in neuroscience. Bickle claims that tool-driven revolutions in neuroscience do not fit Kuhn's theory-centered model of scientific revolutions (2016, 2), that neuroscientists developed experiment tools relatively independently of theories (2018, 1073), and that tool development "comes first"; it is the determining factor that shapes subsequent concept formation and other theorizing (ibid., 1077). A similar and more general view is defended by physicist Freeman Dyson, who argues that "in almost every branch of science […] there has been a preponderance of tool-driven revolutions" (Dyson 1997, 51). Such tool-driven revolutions occur independently of concept-driven (Kuhnian) revolutions (ibid., 50, Dyson 1999, 13; 2012, 1426).

Bickle and Dyson suggest that tool-driven change primarily occurs independently from conceptual change. In this paper, I look at cases from neuroscience to suggest an alternative view: tool development and concept formation are often intertwined during episodes of tool-driven change. Unlike Dyson (1997) and Bickle (2016), I am interested in episodes of scientific change regardless of whether they constitute scientific revolutions or are part of ‘normal’ science.

To elaborate on the role that tools play in scientific change, I analyse how scientists use them in exploratory experiments. A defining negative characteristic of exploratory experiments is that they do not aim to test hypotheses—statements that are derived from a model or body of theoretical knowledge about the domain of inquiry (Giere et al. 2006, 26). Exploratory experiments use various strategies, such as varying many experimental parameters (Steinle 1997), combining experimental techniques (Burian 1997), or applying high-throughput instruments (Franklin 2005). There is no agreed-upon positive characteristic makes all these experimental strategies exploratory (Elliot 2007). Yet, philosophers of science concur that one important—though not the only—outcome of successful exploratory experiments is the *formation of novel concepts* (Steinle 1997, Feest 2012, Haueis 2014). Newly formed concepts constitute scientific change if they allow researchers to describe new discoveries and when they have a lasting epistemic impact on a field of inquiry.

In this paper, I use case studies from neuroscience to develop an account of how researchers use exploratory experiments to form new concepts. On my *exploratory concept formation* account—hereafter the ECF account—scientists use experimental conditions and develop tools to operationally define the meaning and tentatively fix the reference of a concept. My account also provides normative resources to specify when exploratory concept formation succeeds or fails. Such normative resources are necessary to understand when newly formed concepts describe new discoveries appropriately and when they drive change by having a lasting epistemic impact on scientific practice.

While the ECF account includes tool development as an important element of change in neuroscience, it goes beyond the independence of tool development from conceptual change emphasized by Bickle (2016, 2018). I instead argue that in many experiments which changed the course of neuroscience (including most of Bickle's own examples), tool development and exploratory concept formation are intertwined. In my view, there is a common set of normative principles which governs when exploratory concept formation and tool development succeed (rather than fail) to initiate scientific change.

Although I focus on neuroscience, I think the ECF account can be extended to other disciplines where researchers form novel concepts by introducing operational definitions and experiment tools, such as molecular biology (Rheinberger 1997), physics (Chang 2004) and cognitive psychology (Feest 2012). Applied to neuroscientific cases, the ECF account suggests a distinction between the role of new scientific concepts and existing theories which elucidates why tools rather than theories help scientists form novel concepts in exploratory experiments.[1] This distinction is relevant to the general debate about scientific change. While concept formation is often seen as belonging primarily to theory-driven change (Kuhn 1970, Thagard 1992), the ECF account implies that concept formation also plays a crucial role in tool-driven change. The ECF account thereby enhances our general understanding of concept formation in experimental practice beyond existing accounts of tool-driven change (Rheinberger 1997, Chang 2004).

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[1] In the cases discussed, "theory" either refers to a model of the entities or activities in the neural system investigated, or of the class of systems to which it belongs (Colaço 2018). By contrast, scientific concepts are uses of words which depend on the scale at which scientists use a technique to target properties in a domain (Haueis 2021).

The paper proceeds by introducing the ECF account via two important cases of change in neuroscience: the formation of "bug detector" in electrophysiology and of "default mode" in neuroimaging (section 2). Because neuroscientists had to develop new tools to operationally define these terms, concept formation and tool development are intertwined in individual exploratory experiments, which are themselves part of larger tool-concept cycles (section 3). These and other cases of tool development raise the question when an experiment succeeds rather than fails to initiate scientific change. I answer this question by sketching two normative principles of exploratory concept formation. These principles coincide with the characteristics of successful tool development in neuroscientific practice (section 4).

2. The exploratory origin of concepts in neuroscience

2.1 The ECF account

According to the ECF account, researchers form a concept in an exploratory experiment by following the steps displayed in Table 1. I use these steps to analyse cases of exploratory concept formation in neuroscience, and as part of my answer to the normative question when experiments succeed or fail to initiate scientific change (section 4.1).

(C1) Meaning	**(C2) Significance**	**(C3) Reference**
Use experimental conditions to form operational definition	Compare experimental conditions to real-world conditions	Use tools to tentatively fix reference to entity or activity

Table 1: Three steps of concept formation in the ECF account

Experimental conditions in (C1) refer to the material and technical set-up that allows scientists to measure or intervene in an experimental system (Rheinberger 1997, 29). In neuroscience, such conditions include stimulus or response variables used to produce or measure activities of neural entities (Sullivan 2009, 509). These conditions are used to operationally define concepts that characterize the investigated entities or activities.

To assess the significance of an operational definition, researchers (C2) compare experimental conditions to real-world conditions outside the laboratory. Neuroscientists are particularly concerned with *functional* significance, i.e. whether a concept adequately describes neural activity during unconstrained behavior of the organism. Generally, a concept is significant if it allows scientists to achieve an epistemic goal, such as describing, classifying or explaining the entities or activities to which the concept refers (Haueis 2021).

Finally, tools are needed to set up the experimental conditions (C1) and to fix the referent of the concept (C3). The formation of "bug detector" and "default mode" were intertwined with the development of *single-cell recordings* of neuron's receptive field properties and *neuroimaging* of functional brain activity. Both are tools which successfully changed neuroscientific practice (Bickle 2016, 2).[2] The introduction of "bug detector" in electrophysiology and of "default mode" in neuroimaging are thus important cases to understand tool-driven change in neuroscience. I focus on these cases to investigate the relationship between concept formation and tool development in neuroscience (section 3.1).

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[2] Bickle also discusses how the development of optogenetics, gene targeting and the patch clamp revolutionized neuroscience. Section 3.2 discusses the role of concepts in developing the latter two. On optogenetics, see also Robins (2018).

Importantly, experiment tools involve both material devices and *instructions* of how to use them to achieve a specific experimental result (Colaço 2018, 8). Single-cell recording, for instance, instructs how researchers use microelectrodes to find a stimulus parameter which operationally defines a neuron's "receptive field". Thus, developing tools includes building material devices and specifying instructions of how to use them *correctly*. Providing such instructions is an important function of concepts in experimental practice (Feest 2012, Haueis 2021). The need for both devices and instructions thus suggests common norms of tool development and concept formation (section 4.2).

The ECF account can be applied to different types of experiments discussed by philosophers of neuroscience. Some experiments identify previously unknown phenomenon (Silva, Landreth and Bickle 2014, 28–30 call these identity experiments). Other experiments stimulate a neural system to observe activities of entities within that system (Craver 2007, 147 calls these activation experiments). Yet others excite or inhibit activities of entities to observe changes of the neural system (Craver 2007, 147 calls these interference and stimulation experiments, respectively). This paper applies the ECF account to an identity experiment (Raichle et al. 2001) and an activation experiment (Lettvin et al. 1959). An example of exploratory concept formation via interference and stimulation experiments is "central pattern generator" (Wilson 1961), which is analysed in Haueis (2017, ch. 3). Rather than being restricted to one kind of experiment, exploratory concept formation seems widespread in neuroscientific practice.

2.2 The exploratory origin of "bug detector"

The formation of "bug detector" in the highly influential paper "What the frog's eye tells the frog's brain" (Lettvin et al. 1959) is regarded to be a major advance in understanding the neurophysiology of perception (Martin 1994). This case presents a clear example of exploratory concept formation, and tool development played a prominent role in this episode of scientific change.

Lettvin et al. chose an exploratory strategy because they took the existing conceptual framework to be unreliable to formulate hypotheses about optic nerve function. Previously, electrophysiologists used small light spots as stimuli, which assumes that visual neurons respond to light intensity changes in points of the visual field (Barlow 1953a,b). But this assumption is anatomically implausible in the frog optic nerve and thus, "the laws found by using small spots of light on the retina may be true and yet, in a sense, be misleading" (Lettvin ret al. 1959, 1942).

Rather than falsifying previous theoretical hypotheses, the researchers sought to explore what stimuli are *appropriate* to understand what the frog nerve does:

> We should present the frog with as wide a range of visible stimuli as we could, not only spots of light but things he would be disposed to eat, other things from which he would flee, sundry geometrical figures, stationary and moving about, etc. From the variety of stimuli we should then try to discover what common features were abstracted by whatever groups of fibers we could find in the optic nerve (Lettvin et al. 1959, 1942).

To explore optic nerve activity, the researchers placed microelectrodes in individual optic nerve fibers. For stimulation they used a dull black disk and other objects that could be moved with a magnet behind an aluminum hemisphere.

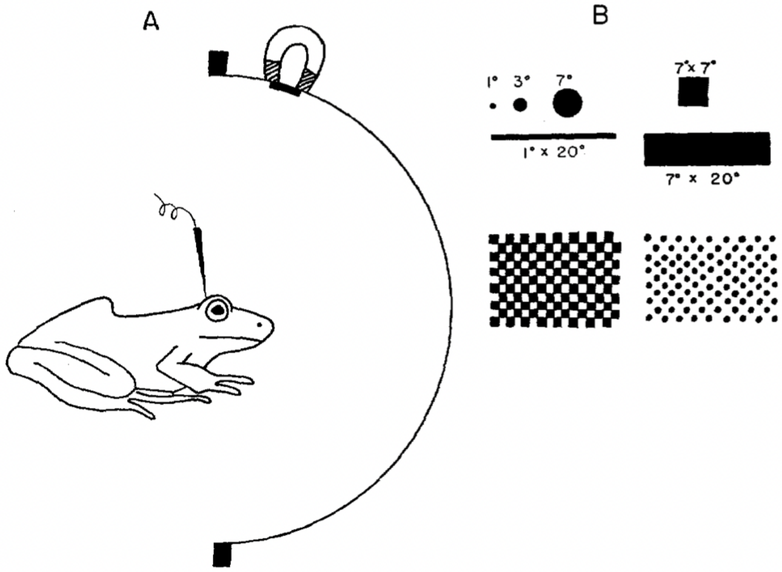

Fig. 1. Experimental set-up (A) and exemplary stimuli (B) used by Lettvin et al. (1959). Adapted from Maturana et al. (1960). Permission to reprint granted by Rockefeller University Press.

The experimental conditions shown in Fig. 1 allowed the researchers to operationally define four fiber types: (i) *sustained contrast detectors*, (ii) *convexity detectors* (iii) *moving edge detectors* and (vi) *net dimming detectors*.

“Convexity detector” operationally defines the bug detector concept. Lettvin et al. formed this operational definition by following the exploratory strategy of parameter variation (Steinle 1997, S70). First, they *varied many stimulus parameters*, e.g., size, shape, velocity, trajectory and overall illumination intensity. Second, they distinguished *indispensable* from *modifying* parameters. Convexity was indispensable to excite type (ii) fibers; non-convex shapes produced no response. By contrast, size was a modifying parameter: convex stimuli smaller than 1° produced responses in some but not other contexts (Lettvin et al. 1959, Fig. 3e-f). Third, the researchers formulated *stable empirical rules* about stimulus-response relationships. For example: 'If a convex object enters the receptive field of a convexity detector, it will fire as long as the object stays within the receptive field.' (cf. ibid., 1945).

Fourth, the researchers searched for *appropriate concepts* to describe the entities in terms of the indispensable parameters (section 4.1). Concepts like ON cells, ON-OFF cells or OFF cells (Hartline 1938, Barlow 1953a,b) were inappropriate to describe groups (i), (iii) and (iv) because light intensity changes were not indispensable to drive their responses. Because group (ii) fibers were previously unknown, "convexity detector" constituted a novel concept formed in this exploratory experiment. Fifth, the published reports contained the *minimal experimental conditions* for eliciting invariant responses from the four fiber types (Maturana 1960, 161, Lettvin et al. 1961, 763). Because Lettvin et al. operationally defined "convexity detector" in terms of these experimental conditions, their experiment implements step (C1) of the ECF account.

The researchers next assessed the functional significance of their operational definitions. They compared the experimental conditions to real-world conditions in which convex shape detection is behaviorally relevant. For example: when a fly-sized object was moved in front of a photograph depicting a frog's habitat, convexity detectors responded strongly, but remained silent when the photograph itself was moved. Lettvin et al. also assessed whether two other experimental conditions diminished ecological validity: (a) covering the frog with moist gauze to ensure a bodily rest position and (b) using the anesthetic tubocurarine to stabilize neural recordings. Condition (a) does not diminish ecologically validity because frogs stay in a bodily rest position in a moist environment when detecting food (Ewert 1987). Condition (b) preserves at least qualitative validity. Although tubocurarine diminishes responses to visual stimuli, the frogs did “move and feed like normal animals” after the experiments (Maturana et al. 1960, 133). The experimental conditions therefore license the inference that convexity detectors process information relevant to catching prey. The functional significance of convexity detectors as “bug perceivers” (Lettvin et al. 1959, 1951) thus implements step (C2) of the ECF account.

To set up the experimental conditions and fix the reference of “bug detector”, Lettvin et al. developed novel tools and applied them to the optic nerve. Their experiment paper appeared alongside a technical paper on platinum black-tipped microelectrodes (Gesteland et al. 1959). Because platinum black has a large surface, it “burns onto itself a shell of very adherent stuff” when used in cell tissue (ibid., 1859). To resolve this problem, the researchers added gelatin to the acid bath when plating the platinum black onto the microelectrode tip. Without that tool, they would have been unable to record triphasic transients as derivatives of spikes in the optic nerve fibers.

Besides microelectrodes, Lettvin’s collaborator Maturana (1959) used electron microscopy to show that the number of fibers was previously underestimated by a factor of 30. He also reported a new kind of small unmyelinated fiber. Since it was unknown which stimuli would drive these entities, Lettvin et al. could not restrict variation to stimuli expected to drive the frog analogues to ON, OFF and ON-OFF cells (Barlow 1953b). The combined use of platinum black-tipped microelectrodes and electron microscopy thus fixed the reference of “bug detector” to small unmyelinated fibers, which implements (C3) of the ECF account.

2.3 The exploratory origin of the “default mode” of brain function

The formation of “default mode” in a widely cited paper by Raichle et al. (2001) initiated a major shift in how neuroimaging researchers investigate and understand functional brain networks (Biswal 2012). This case expands our perspective on what kinds of tools successfully drive change in neuroscience and how they interact with concepts to reshape a discipline over longer periods of time.

The Raichle group engaged in exploratory concept formation because they lacked an appropriate definition of a baseline in neuroimaging experiments. Such a baseline was necessary to understand why a consistent set of areas surprisingly showed a decrease instead of an expected increase during a task (Shulman et al. 1997). To define a baseline for neuroimaging Raichle et al. (2001) introduced the *oxygen extraction fraction* (OEF), which refers to the amount of available oxygen in the arteries that is used by a brain area. The researchers used Positron Emission Tomography (PET) to show that the OEF during the experimental resting state remains *uniform* throughout the entire brain (Fig. 2).

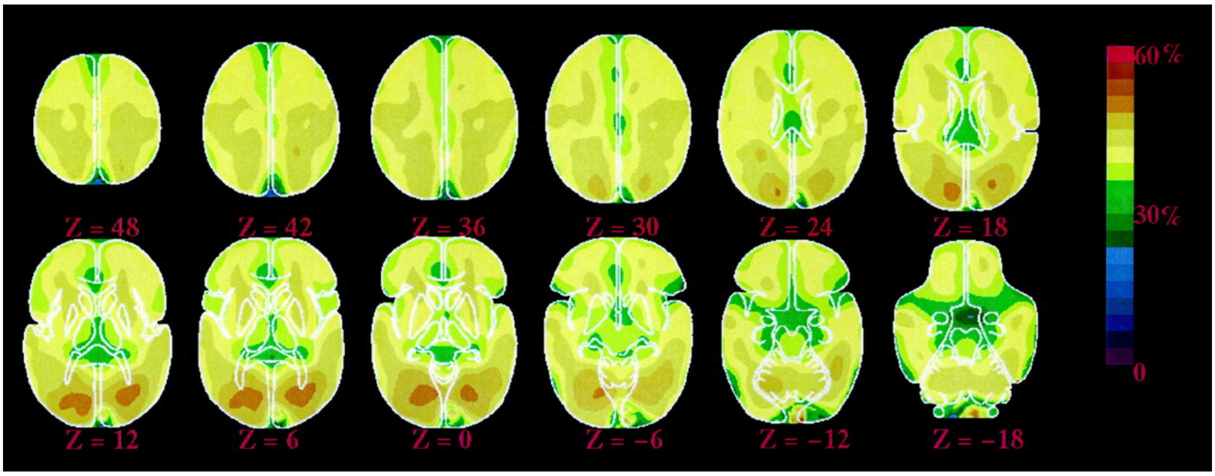

Fig. 2. PET images showing that percentage of available oxygen delivered is relatively constant across the brain during the resting state (subject is lying awake in the scanner, eyes closed). Adapted from Raichle et al. (2001). Copyright (2001) National Academy of Sciences, U.S.A.

This experiment implements step (C1) of the ECF account because the uniform OEF at rest is an experimental condition that operationally defines the *default mode of brain function*. This concept describes the "equilibrium […] between the local metabolic requirements necessary to sustain a long-term modal level of neural activity and the level of blood flow in that region" (Raichle et al. 2001, 677f.). To define this equilibrium experimentally, the researchers divided the OEF value in each local area by the global mean OEF value of a subjects' brain. If this local-to-global OEF ratio equals 1 in all brain areas, then one can ascribe the default mode concept to a given brain at rest.

The experiment furthermore implements step (C2) of the ECF account. The Raichle group evaluated the significance of "default mode" by discussing how the equilibrium between blood flow and oxygen use enables normal brain function outside the laboratory. In cerebrovascular diseases the OEF deviates strongly from uniform values observed at rest (Gusnard and Raichle 2001, Iadecola 2004). This disturbance suggests that in healthy human brains, a homeostatic mechanism maintains equilibrium between blood flow and oxygen. Thus, the equilibrium cannot be specific to the experimental resting state but is “characteristic of all areas of the [healthy] brain at all times” (Raichle and Snyder 2007, 1088). The researchers thus inferred that the operationally defined “default mode” is significant to describe healthy human brain function outside laboratory conditions.

There are three differences to the bug detector case which make the default mode case interesting for a philosophical account of exploratory concept formation. First, unlike the instruments used by Lettvin et al., PET imaging lacks the precision to fix the referent of “default mode” to an activity within the homeostatic mechanism maintaining blood flow and oxygen extraction in equilibrium. Therefore, the experiment does not successfully implement step (C3) of the ECF account. This suggests that not all exploratory experiments are equally successful in forming a novel concept which appropriately describes a new discovery. Judging such cases requires normative principles to determine when concept formation succeeds or fails (section 4.1).

Second, the default mode case highlights that exploratory concept formation can result from an interplay of analysis techniques and material devices. Raichle et al.’s experiment combined an old tool (PET imaging) with the OEF, a known analysis technique to study brain metabolism. What was novel was the use of the OEF to define a baseline for cognitive neuroimaging experiments. Existing accounts of tool-driven change (Bickle 2016, Dyson 1999) entail two reasons to count novel uses of analysis techniques as cases of tool development. The first reason is that novel uses of material devices count as tool development. Gene targeting, for example, was originally developed by developmental biologists, but its use to study memory phenomena is a case of tool development in neuroscience (Bickle 2016). This point generalizes since many tools (e.g., electron microscopy) can be used to study many different phenomena. What counts is that researchers correctly follow the instructions which govern a particular use of the tool. These instructions are both crucial for exploratory experimentation (Colaço 2018) and for tool-driven change in a particular discipline.

The second reason is that like novel material devices, novel analysis techniques drive discovery. An example from outside neuroscience is the astronomer Alexander Wolsczan, who discovered so-called "exoplanets" and "pulsar planets" by combining an old radio telescope with a novel computer program that analysed irregular and weak radio wave pulses (Dyson 1999, 22f.). Besides important differences, these similarities are reasons to count analysis techniques as tools on which the formation of novel concepts depends.[3] According to the ECF account both analysis and experimental techniques can fuel tool-driven change by providing instruments and instructions on how to study unknown properties of entities and activities.

Third, the historical context of the Raichle study reveals how exploratory concept formation promotes the *convergence of two investigative pathways* onto a common entity (Burian 1997). Unbeknownst to cognitive neuroscientists working with PET at Washington University St. Louis, neurophysicists at Medical College Wisconsin also used the

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[3] One may suspect that developing novel analysis techniques is more theory-dependent than building material devices, and so the connection to concepts is less surprising. Despite differences between material devices and analysis techniques, the contrast is overstated because sometimes, building material devices can also rely heavily on theorizing (see Baird and Faust 1990, 169–171).

experimental resting state to study the signal of functional magnetic resonance imaging (fMRI). They found that this signal contained systematic low-frequency fluctuations (<0.1 Hz) and used the concept of “functional connectivity” to describe the temporal correlation of these fluctuations in the motor cortex (Biswal et al. 1995). In 2003, the two pathways converged when Greicius et al. (2003) discovered the *default mode network*, a set of areas in which fMRI activity is highly correlated at low frequencies.

There are crucial differences between “default mode” and “default mode network” which I evaluate in section 4.2. For now, it is crucial that the convergence of investigative pathways onto the default mode network created a novel subfield in neuroimaging: resting state functional connectivity studies (Biswal 2012). This subfield fundamentally changed neuroimaging by providing researchers with novel tools and concepts to study the network organization of the brain. The ECF account thus acknowledges that concept formation happens within, but also reshapes a larger problem agenda composed of interrelated empirical and conceptual questions (Love 2008). The “default mode” arose within and reshaped the research agenda of finding increases brain activity related to cognitive tasks and helped shift the research focus from single areas to brainwide networks and their endogenous activity. I further explicate this agenda-setting aspect when discussing the open-endedness of concepts in section 4.1.

3. Exploratory concept formation and tool-driven scientific change

3.1 The interdependence of tool development and concept formation

The ECF account stresses that forming novel concepts is part of tool-driven scientific change. In this respect I follow accounts which stress that tools play a crucial role in concept formation (Rheinberger 1997, Chang 2004, Bickle 2016, 2018). In this section, I discuss how the ECF account differs from and complements these accounts, first with regard to tool development and concept formation in neuroscience, and second with regard to our general understanding of the epistemology of experimentation.

The ECF account implies that tool development and concept formation can be part of the same process in exploratory experiments. The Lettvin group developed platinum black tipped microelectrodes and applied them to the frog optic nerve to operationally define "convexity detectors", and used electron microscopy to fix the reference of this concept to small unmyelinated fibers. The Raichle group applied the OEF to human resting state brain activity to find a quantitative baseline which operationally defined a "default mode" of brain function. Such operational definitions are grounded by the experimental conditions necessary to produce an effect that is indicative of the entity or activity to be described (Steinle 1997, Sullivan 2009, Feest 2011, 2012, Haueis 2014). If setting up these experimental conditions requires new tools, then tool development and the exploratory formation of concepts are part of the same experimental process.

The ECF account adds a distinction between concepts and theories to debates on exploratory experiments and tool development. The role of theories in exploratory experiments is justificatory because they allow researchers to apply an experimental technique to a particular feature of a target system (Colaço 2018).[4] To use theories in this way, researchers must hold the concepts in which the theory is formulated fixed. For example, when Lettvin et al. (1959) used microelectrodes to record action potentials from axons in the optic tectum, they held the meaning and reference of "axon" and "action potential" fixed.

By contrast, the role of novel concepts in exploratory experiments is to disclose previously unknown entities or activities or solve problems not characterized by the available theories (Steinle 2016, Arabatzis and Nersessian 2015). To use concepts in this way, researchers actively modify their meaning and reference via operational definitions and tool use in exploratory experiments (Feest 2012, Haueis 2014). For example: "bug detector" discloses the function of small unmyelinated axons, which were discovered using electron microscopy and whose function was operationally defined by their response to convex stimuli used in microelectrode recordings. It is the tools which drive the formation of concepts to characterize unknown entities or activities, rather than the theories which direct the application of experimental techniques to known features of the target system.

The difference between the justificatory role of existing theories and the disclosing function of novel concepts is of general relevance because it is not captured by existing accounts of scientific change. Consider first Bickle's account of tool-driven change in

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[4] Theories justify the application of a technique either because they show that the target system is a member of a class of systems (background theory) or because they characterize entities and activities in the system (local theory, Colaço 2018, 4–7).

neuroscience, which does not discuss exploratory concept formation and which emphasizes the independence of tool development from theoretical activity. Bickle (2016 p. 5, fn. 5) admits that his focus on cases of tool-development during relative conceptual stability "might be occluding the discussion of conceptual revolutions" and that "concept development in neurobiology […] might better match Kuhn's account of paradigm shift and anomalies". Like Dyson (1997, 2012), Bickle (2016) puts concept formation and (Kuhnian) theory-driven change on one side and contrasts it with the tool development and (un-Kuhnian) tool-driven change on the other. Because Bickle does not explicitly address conceptual development and dialectically emphasizes the independence of tool development from theory-driven change, his account leaves open what role concept formation plays in episodes of tool-driven change. The ECF account fills this lacuna because it shows that neuroscientists use newly developed tools and newly formed concepts together to discover and describe previously unknown entities and activities in their domain of inquiry.

The distinction between the role of theories and concepts also points out why exploratory concept formation does not fit accounts of theory-driven change in science. These accounts tie concept formation to theoretical change because they assume that the meaning of concepts is determined by their position within a larger theory (Kuhn 1970, 162f.; Laudan 1977, 48). For Kuhn (1970, 29f.), exploratory experiments articulate the paradigm theory because they help scientists to "choose among alternative ways of applying the paradigm to the new area of interest". This overlooks that in experimental practice, concepts can acquire their meaning outside their theoretical contexts when researchers apply them to unexpected phenomena (Arabatzis and Nersessian 2015).

This is also true for neuroscience. For example: “bug detector” acquired its meaning outside the theoretical framework which assumed that visual neurons transmit light changes in a point-by-point fashion. This assumption was unreliable to explore which stimuli drive previously unknown fibers in the optic nerve. Similarly, “default mode” acquired its meaning outside a framework that assumed that brain areas use more energy during tasks than during rest. This framework did not allow neuroscientists to understand task-induced decreases in neuroimaging experiments. Instead of using existing theories, the Lettvin and Raichle groups used experimental conditions and tools to determine the meaning and reference of “bug detector” and “default mode”. The ECF account elucidates why exploratory concept formation, at least in neuroscience, is part of tool-driven change and why this process is distinct from theory-driven change.

The ECF account provides a notion of concept formation that fits the details of neuroscientific practice. Yet it also reveals general features of concept formation that are not prominent in previous accounts of tool-driven change in the physical and life sciences, such as Rheinberger (1997) and Chang (2004). First, the notion of significance captured by condition (C2) of the ECF account is not captured by Rheinberger’s account of concept formation as *material inscription* (Rheinberger 1997, 110–113).[5] Both accounts agree that life scientists use tools to generate material traces that indicate properties of entities or activities within an experimental system. In Lettvin’s experimental system for instance, electrical discharges are material traces which indicate functional properties of small

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[5] Rheinberger does not talk about concepts but about epistemic things, i.e. entities or activities whose properties are partially unknown to scientists. Following Feest (2011) I assume that some concepts are used to describe epistemic things, e.g., “bug detector”, or “default mode”.

unmyelinated fibers. Like Rheinberger, the ECF account defines a concept as *novel* if it characterizes a “spatiotemporal cognitive singularity” within an experimental system (Rheinberger 1997, 23). The formation of “bug detector”, for example, resulted from a unique combination of experimental stimuli, instruments ant technical conditions to detect hitherto unknown activities of optic nerve fibers (see section 3.2).

In contrast to the ECF account, however, Rheinberger claims that the significance of such material traces “ultimately derives from their potential to become, sooner or later, integral parts of future technical conditions” (Rheinberger 1997, 33). The process of material inscription thus has no significance beyond further tool development within experimental systems (ibid., 109). This internal notion of significance, however, does not capture that experimental practice also develops by moving from operational to functional definitions of concepts (e.g., moving from “convexity detector” to “bug detector”; see also Rheinberger 1997, 154; 189). In the behavioral and brain sciences, one approach to functional definition is to determine whether a concept describes a behavior that occurs outside the laboratory (Shamay-Tsoory and Mendelsohn 2019). The ECF account captures this feature by positing that the significance of tool-driven concept formation includes the concept’s significance beyond the laboratory.

Second, the ECF account highlights the role of convergent investigative pathways which is not included in Chang’s account of epistemic iteration (Chang 2004). In epistemic iteration, successive stages of knowledge build upon another to enhance the achievement of epistemic goals (ibid., 45). Chang’s case of the formation and refinement of "temperature" demonstrates that the development of both tools and concepts plays a crucial role in epistemic iteration. Chang's account thus captures how Lettvin et al. and Raichle et al. built on, but also corrected knowledge systems derived from previous experiments (Hartline 1938, Barlow 1953a,b; Shulman et al. 1997) when forming "bug detector" and "default mode".

The ECF account additionally highlights how exploratory experiments from different investigative pathways shape scientific change beyond iterative self-correction in each pathway. Convergent pathways can result in novel concepts ("default mode network") and establish new disciplines such as functional connectivity studies in neuroscience (section 3.3) or modern cell biology (Bechtel 1993). Once we zoom out beyond individual experiments or pathways, we see that tool development and concept formation form interactive *cycles*. The ECF account adds the role of interactive tool-concept cycles from multiple convergent pathways to Chang's account of iterative self-correction within an investigative pathway. The existence of interactive tool-concept cycles suggests that episodes of tool-driven change do not start with tool development which then shape subsequent concept formation. Rather, each of these processes has important conceptual and technological preconditions.

3.2 Objections and replies

This section adresses three objections against the ECF account.[6] The first objection holds that the pre-history of "bug detector" shows that tool development and concept formation are not intertwined in this case. Ethologists had already introduced the concept of an innate release mechanism which allows organisms to immediately and automatically recognize complex stimuli (Tinbergen 1948). In neuroscience, Barlow (1953b, 86f.) already discussed "fly detectors" and identified them with on-off units in the frog optic nerve. The introduction of "innate release mechanism" and "fly detector" occurred separately from the development of tools used by Lettvin et al. (1959).

My response to this objection first points out that Barlow's paper discussing 'fly detectors' appeared *alongside* a paper on technical issues when recording in the frog retina (Barlow 1953a). This suggests that like Lettvin et al., Barlow seems to have developed tools and concepts together. More importantly, despite the similarity in name between "fly detector" and "bug detector", the ECF account shows that the novelty of "bug detector" lies in the unique experimental conditions used to form it. Barlow used small light spots and insulated platinum electrodes on an excised frog retina when identifying on-off units as fly detectors. By contrast, Lettvin et al. used small black discs and platinum black microelectrodes in awake frogs to identify convexity as an indispensable parameter, and electron microscopy to identify small unmyelinated axons in the optic nerve. These conditions, together with Lettvin's skill to record neural activity from awake animals, resulted in a

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[6] Thanks to Edouard Machery for voicing the first and second objection.

cognitive spatiotemporal singularity within the experimental system: the discovery of bug detectors. Despite its novelty, “bug detector” also iteratively corrected “fly detector” because Barlow failed to identify indispensable stimulus parameters and did not know that unmyelinated axons exist in the frog optic nerve. This indicates that “bug detector” was a more successful case of exploratory concept formation than “fly detector” (section 4.1).

The second objection holds that the cases from section 2 only show that the development of *some* kinds of tools in neuroscience—single-unit recording and neuroimaging—depended on concept formation. In other cases, such as gene targeting and optogenetics—tool development *was* epistemically independent from concept formation (Bickle 2016).

I certainly do not claim that *all* cases of tool development depend on concept formation. Yet I want to use the case of gene targeting to show why the role of concept formation is more widespread than Bickle’s account of tool development suggests. Gene targeting works by knocking out a gene for a specific protein product. Bickle assumes that this tool was introduced to the neuroscience of memory during a period of conceptual stability. The idea that memory is connected to plastic changes of the synapses “dominated theorizing and experimental research […] for more than a century” (Bickle 2016, 5, fn. 5). By contrast, gene targeting was a novel tool because it could manipulate long-term changes to synaptic activity without disrupting synaptic function, which was considered a major deficit of previous experimental techniques. Bickle thus construes the introduction of gene targeting by Silva et al. (1992a,b) as independent of concept formation.

This diagnosis is only partially correct, however. The Silva experiments also combined concepts with exploratory origins from two converging investigative pathways. In the first pathway, electrophysiologists introduced “long-term-potentiation” to describe strengthened postsynaptic activity that occurred after presynaptic neurons were stimulated with high-voltage inputs. This phenomenon became linked to learning and memory mechanisms when researchers integrated tools from neuroanatomy and electrophysiology with biophysical models of memory (Craver 2003, 170–79). In the second pathway, molecular biologists discovered that the enzyme called “Ca^{2+}calmodulin-dependent protein kinase II” (CAMKII) is capable of autophosphorylation and is located at the synapse (Kennedy 1983). The biophysical model of Lisman (1985) conceptualized such enzymes as *molecular switches* capable of storing long-term information despite molecular turnover.

Both pathways converged when Silva et al. (1992a,b) confirmed the hypothesis that CAMKII mutant mice are both deficient in LTP and spatial memory performance. While gene targeting made confirmation possible, the researchers would have been unable to *formulate* this hypothesis without the terms “LTP” and “CAMKII” to describe the entities and activities they were investigating. By relying on concepts from the two pathways, the Silva experiments were part of an interactive *tool-concept cycle*. Like Greicius et al. (2003), Silva et al. combined tools and concepts from multiple investigative pathways, which led to the novel subfield of molecular and cellular cognition (Bickle 2016). The ECF account acknowledges the role of tools in this episode while also capturing the conceptual preconditions for their use in neuroscience.

The third objection holds that even if concept and tools are intertwined in tool-driven change, the tools are developed *prior* to the concepts being formed. My response to this objection is that such priority claims point out a possible regress. Take the concept "ion channel", which Bickle (2018, 1074) claims depended on developing the patch clamp in the 1970s and 80s. As Bickle acknowledges, however, Hodgkin and Huxley's model (1952) already proposed the ion channel concept *prior* to the patch clamp. Yet he insists that Hodgkin and Huxley's model in turn depended on Kenneth Cole's development of the voltage clamp (Bickle 2018, fn. 7). One can sense a regress looming here. Cole's work itself relied on the Kelvin cable equation, which conceptualizes nerve conduction as a voltage-based phenomenon (Cole 1983, 314).

Rather than pointing to a priority of either concepts or tools in initiating neuroscientific change, the ion channel case supports the thesis that concept formation and tool development are intertwined. Cole used the voltage clamp to refine the concept "action potential" by discovering that threshold-free currents are responsible for the characteristic shape of action potentials. And Hodgkin and Huxley did not simply apply, but substantially improved Cole's voltage clamp design (Hodgkin, Huxley and Katz 1952), which was necessary to describe the action potential in terms of independent *electrochemical gradients* at the membrane (Hodgkin and Huxley 1952). Bickle is right that later tool development like the patch clamp was necessary to fix the referent of "ion channel". Yet I claim that the regress—although not worrisome by itself—shows that neither tools nor concepts have priority in episodes of tool-driven scientific change.

4. Norms of exploratory concept formation and tool development

In the previous section I argued that when it comes to the history of neuroscience (and comparable cases in other disciplines), exploratory concept formation and tool development can be reconstructed as interdependent processes. But novel concepts and tools are outcomes of *successful* experiments, which raises the normative question of what distinguishes these success cases from failures. Specifically, when does an experiment result in a concept which is appropriate and has a long-lasting epistemic impact? And when does a new tool successfully change neuroscientific practice?

To answer these questions, I introduce two norms that distinguish successful from failed cases of exploratory concept formation (section 4.1).[7] These norms coincide with how Bickle characterizes successful cases of tool development in neuroscience (section 4.2). The result is a picture of tool-driven change in which concept formation and tool development are (at least partly) governed by the same normative principles.

4.1 Two norms of exploratory concept formation: anchoring causes and open-endedness

One goal of exploratory concept formation is to generate concepts which *appropriately* describe the experimental effect in question (Steinle 1997, 2016). In neuroscience, one way to assess a concept as appropriate or inappropriate is to ask whether it identifies an *anchoring cause* in the mechanism that researchers aim to investigate. A cause—understood here as the activity within, or an input/output to a mechanism—is anchoring if it is

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[7] Since I derive them from empirical success of concepts formed in past research, I describe norms that are implicit in experimental practice, rather than imposed *ex cathedra* by philosophers of science (Kaiser 2019).

characteristic of the mechanism as a whole. For example: “convexity detector” identifies an anchoring cause because the activity of detecting convex moving objects is characteristic of the prey-catching mechanism in frogs and toads (Ewert 1987). An anchoring cause allows researchers to tentatively describe that mechanism in terms of a small number of entities and activities that can be manipulated experimentally.

Based on steps (C1)–(C3) of the ECF account, I propose that a concept successfully identifies an anchoring cause if researchers (AC1) operationally define it based on the right experimental conditions, (AC2) correctly evaluate its functional significance by comparing experimental to real-world conditions and (AC3) use tools precise enough to fix its reference to an entity whose activity is characteristic of the mechanism. For example: Lettvin et al. fulfilled (AC1) by distinguishing large and small responses with microelectrode recordings to identify indispensable stimulus parameters that drive optic nerve fibers. For (AC2) the researchers compared experimental to real-world conditions to infer that detecting convex shapes is operative in the prey-catching mechanism. This inference is justified if researchers identify the right experimental conditions in (AC1). Barlow’s earlier inference about fly detectors, for instance, was unjustified because light intensity changes are not indispensable to drive small unmyelinated fibers. Finally, (AC3) electron microscopes and microelectrodes are precise enough to identify unmyelinated axons in the optic nerve, whose electrical responses to convex objects are characteristic of the prey catching mechanism.

Some concepts formed via exploratory experiments only partially succeed to identify anchoring causes. For example, the experiment by Raichle et al. (2001) implements (AC1) by operationally defining "default mode" in terms of the equilibrium between blood flow and oxygen use during rest. This experimental condition identifies an anchoring cause that is characteristic of the mechanism of *cerebrovascular autoregulation*, which maintains constant blood flow despite changes in arterial pressure (Iadecola 2004). The Raichle study also implements (AC2) because the researchers inferred from the disturbance of the OEF in brains with cerebrovascular diseases that the activities which maintain blood flow and oxygen use must be operative in normal, healthy human brains outside the laboratory (Gusnard and Raichle 2001, 687f.). The Raichle study, however, fails to implement (AC3), because PET imaging is not precise enough to image astrocytic endfeet, which control vessel diameter such that blood flow matches the oxygen needed to fuel baseline neural activity (Iadecola 2004). Because the formation of the default mode concept implements (AC1) and (AC2) but not (AC3), the Raichle group was less successful in identifying an anchoring cause than the Lettvin group.

If an experiment does not implement (AC1)–(AC3), the resulting concept fails to pick out an anchoring cause. For example: "default mode network" (Greicius et al. 2003) fails (AC1) because defining the areas it picks out in terms of the uniform OEF does not distinguish them from the rest of the brain (Klein 2014). "Default mode network" also does not capture the (AC2) functional significance of these particular areas since the "default mode is characteristic of all brain areas at all times" (Raichle and Snyder 2007, 1088). What is characteristic of the Shulman/Greicius areas is that they *de-activate* during goal-oriented tasks, which implies the "presence of sustained information processing" during rest (Gusnard and Raichle 2001, 689). The default mode concept does not capture this sense of functional activity because it describes the brain in terms of metabolism and flow of energy, and not in terms of cognition and information processing. Thus, "default mode network" fails to identify an anchoring cause that is characteristic of the information processing mechanism(s) in areas which de-activate during goal-oriented tasks.

Besides identifying anchoring causes, new concepts should also have a wider epistemic significance:

> Concepts and classifications—the very language used to deal with a certain field—determine on a fundamental level the development of the thinking and acting within that field. Any more specific theory necessarily makes use of those concepts and classifications (Steinle 1997, S72).

For concepts to fulfill this role, they must be *open-ended*. A concept is open-ended if it is (O1) applicable beyond the context in which it was formed and is (O2) adaptable to empirical details that differ from that context.

One way to implement (O1) is to show that initial concept is an instance of a more general concept. For example: "Bug detector" is an instance of *"*feature detector*"*, which describes sensory neurons that respond to perceptually significant events. This general concept (O2) is adaptable to any cause that elicits the largest response in those neurons. Consequently, electrophysiologists discovered a wide array of different feature detectors (Martin 1994). Barlow (1972) directly drew on Lettvin et al. when developing the feature detector concept as part of his *single neuron doctrine* of perceptual psychology. Because of its open-ended applicability, the bug detector concept shaped the acting and thinking of electrophysiologists, set the agenda for later theory building, and cemented the role of single-unit recordings as the primary electrophysiology tool to investigate cognitive brain functions.

In contrast to "bug detector", the open-endedness of the default mode concept is limited. One problem is that its operational definition is limited to PET recordings. Consequently, the notion of a *physiological baseline* cannot be directly applied to fMRI experiments (Raichle and Snyder 2007, 1086). The default mode concept describes the relationship between metabolism and electric neural activity. But in systems neuroscience, many researchers study the role of ongoing electric activity in behavior and cognition without considering the role of metabolism (Haueis 2018).

While "default mode" partially succeeds in identifying an anchoring cause, it so far fails to be open-ended. By contrast, "default mode network" (Greicius et al. 2003) fails to identify an anchoring cause but succeeds in being open-ended. This system can be detected in task conditions related to different cognitive functions (e.g. mind-wandering, autobiographical memory, internally oriented attention) and many different neurological and mental disorders (e.g. Alzheimer, autism, anxiety, depression and schizophrenia, Broyd et al. 2008). It also has influenced theorizing about hierarchical information processing in the brain (Margulies et al. 2016). Yet there is no agreed-upon functional description that explains why this system can be detected in these different contexts. This lack illustrates that researchers have so far failed to identify anchoring causes that characterize the information processing mechanism(s) operative in this set of areas.

4.2 How norms of concept formation coincide with successful tool development

The normative principles of anchoring causes and open-endedness coincide with characteristics of successful tool development in neuroscience. According to Bickle (2016), successful tool development proceeds via initial hook experiments which respond to a motivating problem, and second-phase hook experiments which foster the wider dissemination of the tool in the scientific field. For gene targeting, for example, the motivating problem was whether (a) this tool is applicable to mammalian nervous systems and whether it fulfils (b) the experimental demand to block LTP without disrupting synaptic function. Initial hook experiments like Silva et al. (1992a,b) responded to this problem by applying gene targeting to a specific entity in a restricted population (α–CaMKII protein in mice) to address a specific phenomenon in a targeted field of inquiry (LTP in spatial memory research).

In other words, successful initial hook experiments identify an *anchoring cause*. They identify an activity that was poorly understood or unkown before the development of the tools, and which is characteristic of a mechanism investigated (section 4.1). This not only true for the bug detector and default mode case, but also for development of optogenetics, in which experimenters identified hypocretin producing neurons as an anchoring cause in the mechanism underlying sleep-wake transitions (Bickle 2016, 11). In other words: initial hook experiments are successful in part because they develop tools that allow researchers to manipulate and control anchoring causes, just as exploratory experiments are successful in part because they form concepts that appropriately describe causes which are characteristic of a mechanism.

Second-phase hook experiments establish that the newly invented tool is applicable to a variety of experimental contexts. For example, experiments which selectively inhibited the CREB protein established that gene targeting is widely applicable. It showed that gene targeting can be used to manipulate entities that are operative in many different neurocognitive mechanisms and that its spatial and temporal specificity is adaptable to the causal details of these mechanisms (Bickle 2016, 7). Similarly, later experiments showed that optogenetics is widely applicable, for example to mechanisms underlying memory storage (Robins 2018). In other words, second-phase hook experiments establish the *open-endedness* of a newly developed tool. They show that it is applicable beyond the initial experimental context in which it was introduced, and adaptable to the empirical details that differ from that context (section 4.1). It therefore seems that the normative principle of open-endedness specifies when new concepts *and* new tools achieve a wider and long-lasting epistemic significance in experimental practices such as neuroscience.

While the norms of concept formation and tool development are the same at a certain level of abstraction, there are different ways these norms are instantiated in concrete cases. Gene targeting and the bug detector concept both identify anchoring causes. But the former was developed when crucial details about the spatial memory mechanism were already known, whereas the latter was formed when no sketch of the prey-catching mechanism was available. The bug detector concept became open-ended when it was generalized into the feature detector concept (Barlow 1972). By contrast, gene targeting became open-ended when it became differentiated into several subtechniques (Bickle 2016). An adequate account of tool-driven change should recognize both these specific differences alongside the shared general norms of concept formation and tool development.

Although I focused on neuroscience here, I think that anchoring causes and open-endedness may be common norms of concept formation and tool development in other disciplines. Chang's case study, for example, stresses that researchers both formed "temperature" and developed thermometers to measure specific thermal phenomena such as boiling points appropriately (anchoring cause), and to make these concepts and tools applicable to a wide range of contexts (open-endedness). Similarly, Rheinberger (1997, 30) shows how the technique of synthesizing amino acids and the formation of "messenger RNA" helped molecular biologists to appropriately describe characteristics of protein synthesis in particular model organisms (anchoring cause), and to study other phenomena such as the function of ribosomes (open-endedness). These examples suggest that the interdependence of exploratory concept formation and tool development may be a more widespread feature of tool-driven change in the physical and the life sciences.

I think what emerges from all this is a view of tool-driven change in which successful exploratory concept formation and tool development is beholden to the same normative principles. New concepts and new tools advance scientific understanding when they allow researchers to appropriately describe new discoveries. Successful tools and concepts are furthermore applicable to a wider range of distinct but related phenomena (Haueis 2021).

While I argued for a common set of norms governing exploratory concept formation and tool development, I suspect that there are also additional norms that only govern one of these processes. Two norms which only apply to exploratory concept formation is that parameter variation should exhaust the parameter space as much as possible (Rheinberger 1997, 78), and that researchers should conceptualize the investigated objects and phenomena on their own terms rather than using preconceived notions to describe the results (Haueis 2014, 2017). Similarly, there may be distinct norms which govern successful tool development.

5. Conclusion

In this paper, I analysed the role of tools in scientific change by studying how developing tools and forming concepts are intertwined in exploratory experimentation. The ECF account shows that tools and experimental conditions are crucial to the operational definition, functional significance and reference of concepts formed in individual exploratory experiments. Such experiments are also parts of interactive tool-concept cycles, rather than instances of independent tool development. While I focused on neuroscience, the ECF account agrees with philosophers of physics (Chang 2004, Steinle 2016) and molecular biology (Rheinberger 1997) that important episodes of change in the history of science are characterized by the co-dependence of tool development and concept formation.

The ECF account also supports previous writers like Baird and Faust (1990), Dyson (2012) and Bickle (2016) who insist that tool-driven change is easily overlooked by accounts which focus primarily on theory-driven change in science. I elaborated on the role of tools in scientific change by arguing that in exploratory experiments, neuroscientists use tools to form concepts outside their theoretical context. To truly understand scientific change, philosophers of science should acknowledge that "the progress of science requires both new concepts and new tools" (Dyson 1999, 14). My account supports this view by introducing common norms that distinguish successful from failed cases of exploratory concept formation and tool development in neuroscientific research. Insofar as my conclusions generalize beyond neuroscience, they suggest that the interaction between tools and concepts should be at the core of any normative account by which we evaluate their utility in scientific practice.

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