



# How to be rational about empirical success in ongoing science: The case of the quantum nose and its critics

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## ABSTRACT

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Empirical success is a central criterion for scientific decision-making. Yet its understanding in philosophical studies of science deserves renewed attention: Should philosophers think differently about the advancement of science when they deal with the uncertainty of outcome in ongoing research in comparison with historical episodes? This paper argues that normative appeals to empirical success in the evaluation of competing scientific explanations can result in unreliable conclusions, especially when we are looking at the changeability of direction in unsettled investigations. The challenges we encounter arise from the inherent dynamics of disciplinary and experimental objectives in research practice. In this paper we discuss how these dynamics inform the evaluation of empirical success by analyzing three of its requirements: data accommodation, instrumental reliability, and predictive power. We conclude that the assessment of empirical success in developing inquiry is set against the background of a model's interactive success and prospective value in an experimental context. Our argument is exemplified by the analysis of an apparent controversy surrounding the model of a quantum nose in research on olfaction. Notably, the public narrative of this controversy rests on a distorted perspective on measures of empirical success.

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## 1. Introduction

Empirical success is a central criterion for scientific decision-making. Competing models and methods are considered pursuit-worthy if they produce tangible and quantifiable results. In this context, empirical success is seen as a necessary if insufficient condition for the truth or, at least, the adequacy of scientific explanations. Advocates of both scientific realism and anti-realism have centered on empirical success as a criterion of the progressiveness of models (Van Fraassen, 1980; Psillos, 1999). Generally these accounts define empirical success by the requirements to fit the experimental data, be instrumentally reliable, and represent a good predictor of new phenomena (Doppelt, 2005).

Yet philosophers have also recognized many issues that underlie the epistemic value of empirical success for the assessment of scientific explanations. Empirical success admits of degrees, and a central challenge facing its explication is the difficulty of justifying the primacy of support from multiple methods or incommensurable models. A well-known problem in the history of science is that many successful theories in fact turned out to be false, resulting in the classic argument of pessimistic meta-induction (Laudan, 1981). Inevitably, this furthers the question of how stable and durable the criterion of empirical success really is for attributions of adequacy to rival scientific explanations. Given the frequency of appeals to empirical suc-

cess, especially in rational accounts of theory choice (Solomon, 2001), the notion itself thus deserves renewed attention.

This paper focuses on potential challenges to the philosophical understanding of empirical success when we assess the appraisal of current, as in unresolved, research strategies. Almost all of the central ideas in the philosophy of science have been developed and tested against the background of concluded case studies, routinely also involving discussions about their historical accuracy (Schickore, 2011). Fundamentally, the question arises: Should philosophers think differently about the advancement of science when they are looking at continuing research questions instead of past episodes? Our central concern here is that normative accounts appealing to empirical success can indeed produce unreliable conclusions if we think that the appraisal of ongoing science builds on the same understanding as our treatment of historical episodes. A central difficulty we will encounter involves the changeability in disciplinary objectives that determine what constitutes empirical success.

What are the considerations that philosophers must take into account before engaging with contemporary issues in a normative fashion? As it has been pointed out, real science is rather messy and its methods do not always coincide with the epistemic ideals of philosophers (Medarwar, 1999; Schickore, 2008). We will discuss the challenges that arise from the inherent dynamics of disciplinary and experimental objectives in ongoing research practice, and we analyze how these dynamics inform the evaluation of empirical success by looking at three standard requirements of empirical success: data accommodation, instrumental reliability, and predictive power. Our argument is exemplified by the analysis of a feigned controversy sur-

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rounding the model of a quantum nose in research on olfaction. Notably the public narrative of this controversy rests on a strongly distorted perspective on the practitioners' debate and its measures of empirical success. We conclude that the assessment of empirical success in developing inquiry is set against the background of a model's interactive success and prospective value in an experimental context. Further, we suggest an outline of network criteria by which to identify and qualify the relevance of empirical evidence in ongoing science.

## 2. Problem: Confrontational narratives of model choice

For large parts of the history of science, research on the nose was a playground for eccentrics, and the science of smell did not attract broader scientific or philosophical attention. However, this has changed recently, and research into the molecular and neural basis of smell has increased exponentially over the last thirty years. Today olfaction constitutes an experimental system that promises greater insight into ligand-receptor interactions and the organization of higher-level brain processing (Firestein, 2001; Shepherd, 2004, 2012; Axel, 2005; Barwich, 2015b, 2016). Meanwhile, its current dynamics and susceptibility to the revision of its core premises make olfactory research an excellent example to study the ambiguity of determining what a reliable research strategy is.

The process of smelling is an interpretation of chemical information in the environment through a specialized sensory system. Our nose detects volatile airborne molecules (odorants), and our brain makes sense of their physical information by turning them into perceptual qualities. While research on olfaction has progressed fundamentally over the past years, a number of major questions remain open, in particular, concerning the molecular recognition of smell. In comparison with the visual or auditory systems, the physical stimulus of smell has not been captured in a comprehensive classification. Yet this is not a result of the seemingly subjective nature of smells, but the molecular characteristics of the olfactory stimulus. Instead of being based on a low-dimensional parameter such as wavelength, the chemical basis of smell is multidimensional, encompassing several thousands of parameters (Ohloff, Pickenhagen, and Kraft 2011; Keller & Vosshall, 2016). This complexity of the stimulus challenges experimental approaches detailing the molecular machinery of odor recognition. To date, molecular biologists lack a sufficient understanding of odor coding and how the olfactory receptors interact with their ligands (Barwich, 2015b; Firestein, 2001).

About a decade ago a popular science book shone a spotlight onto olfaction and this open question of how the nose detects scents: *The Emperor of Scent*, a story about a quantum model of the nose that detects infrared vibrations of airborne chemicals and its charismatic inventor Luca Turin (Burr, 2004). The book presented the story of a fierce competition between two rival theories regarding the molecular mechanism of smell recognition. It introduced the "vibration theory of odors" against the orthodox model of the so-called "shape theory." While the shape theory refers to geometric and spatial properties as the causal features of odorants, the vibration theory states that the odor of a molecule is linked to its intra-molecular vibrational frequency. The shape theory is considered inadequate by vibration proponents, as it fails to provide robust regularities, let alone laws, which link the smell of a molecule to its structure. Too many exceptions, the reasoning goes, suggest that there may not be a rule. In contrast, the quantum smell idea sounds neat and clear in its claims: there is one key feature responsible for the odor of a molecule that allows classifying smells according to their molecular basis (Turin, 1996, 2006, 2009). Turin's theory mirrored the dream of fragrance chemists and perfumers throughout the 20th century, that there may be some-

thing like a code in the nose that allows you to predict the smell of molecules from their chemical structure. The vibration theory made predictions. It accommodated irregular chemical data. Notwithstanding, it is judged as being wrong.

Although firmly rejected by the majority of olfactory researchers, this story was prefaced as an authentic controversy. Popular science was quick to declare a potential victory for this idea, despite continuous and consistently negative evaluation of the model by the olfactory research community. After Turin's January 2013 publication of a positive but only preliminary and singular study (Gane et al., 2013), several media outlets prophetically declared the following: *'Quantum smell' idea gains ground* (Palmer, 2013, for BBC News); a *Study Bolsters Quantum Vibration Scent Theory* (Anderson, 2013, for Scientific American); and the *Controversial theory of smell is given a boost* (Ball, 2013, for Chemistry World). Some academic channels also proclaimed that the *Secret of scent lies in molecular vibrations* (Ryan, 2013, for UCL News). Even Nature News had been unable to resist the temptation to herald an imminent paradigm change in *Rogue theory of smell gets a boost* (Ball, 2006).

Interest in this apparent controversy in olfaction also entered philosophical analysis. In particular, the eminent social epistemologist Miriam Solomon upheld the quantum model of the nose as a great example to analyze what she calls "norms of dissent" in scientific controversies (2006a, 2006b, 2008). Solomon champions a normative role for the philosophy of science that is not bound to a descriptive adoption of the scientists' perspective on the implications of their work. Throughout her works, involving both past as well as present inquiry, Solomon has emphatically cautioned about the idea of an "invisible hand" in science as a self-governing system of epistemic values. She advises a guide for non-practitioners, such as philosophers or policy makers, to assess the appropriateness of dissent in scientific debates. The primary concern is to establish a normative model that identifies fruitful competition and encourages discussion in situations of scientific dissent. In this context, Solomon lists a measure of empirical, epistemic, and social "decision-vectors" as criteria for the success of a theory:

1. Theories on which there is dissent should each have associated empirical success.
2. Empirical decision vectors should be equitably distributed, i.e., in proportion to empirical success.
3. Non-empirical decision vectors should be equally distributed, i.e., the same number for each theory. (Solomon, 2006a, 2008, 6).

The controversy about the molecular basis of smell offered a great opportunity for putting her model to the test. Notably the central criterion that any scientific model must fulfill before qualifying for a non-relativistic but rational decision-vector analysis is "empirical success" (Solomon, 2001, Ch. 2). According to Solomon, empirical success is not defined by a single criterion, however. Drawing on arguments in the broader discourse in the philosophy of science, she references empirical success as a conglomerate of different contributions that must be evaluated on a case-by-case basis, ranging from "predictive accuracy (Van Fraassen's paradigm), explanatory power (Laudan), technological success (Latour) or manipulative success (Hacking)" (Solomon, 2001, 27). Henceforth, Solomon followed the public narrative of an olfactory controversy in Burr (2004) and Turin (2006), and she contrasted the vibration with the shape theory of odors, where the latter was judged to be unable to provide robust shape-smell correlations. The inherent narrative on which her approach built is grounded in a "confrontational model" of theory-choice, analogous to the ideal of the scientific method in the empirical sciences. It states, not without problems, that philosophical gener-

alizations about scientific theories can be tested against case studies (traditionally historical ones, see Schickore, 2011, Kinzel, 2015). On this account, Solomon weighted what she identified as the underlying decision-vectors in this scenario and concluded that the olfactory community's dismissal is empirically unjustified and premature but based on mere social bias.

Did Solomon's assessment do the scientific context and its empirical basis justice? We all like a good story, of course, especially one about a renegade scientist dismantling old-fashioned ideas of an ossified establishment. From an outsider's point of view, Turin's model and the accompanying popular science narrative were indeed greeted with fierce polemics, and the story was brushed off by the scientific community (Nature Neuroscience Editorial, 2004; Vosshall, 2015). A quote by the neurogeneticist Leslie Vosshall is perhaps the bluntest expression in this context: "I like to think of the vibration theory of olfaction and its proponents as unicorns. The rest of us studying olfaction are horses. (...) The problem is that proving that a unicorn exists or does not exist is impossible. This debate on the vibration theory or the existence of unicorns will never end, but the very important underlying question of why things smell the way they do will continue to be answered by the horses among us" (Vosshall quoted in Palmer, 2013). But what this quote really expresses is a general frustration by olfactory scientists with the public misrepresentation of their work. Scientists operating with the standard model were seeing themselves portrayed as "incompetent villains," and they saw the need to defend their work against audiences that have "love[d] controversy (...) ever since David and Goliath" but "who were ill qualified to judge its scientific content" (Nature Neuroscience Editorial, 2004). It would be misleading to reduce the story of this pseudo-controversy to mere entertainment value, though.

In essence, the main problem with Solomon's perpetuation of an olfactory controversy is that there is no "shape theory of odors" (as evoked in this narrative), nor does current olfactory research fail to explain the chemical data. Something in the science narrative went wrong here, and this should be taken seriously if we aim to pursue philosophical studies of science with integrity. Scientists feeling themselves portrayed as villains may be one thing, but *incompetent* villains? What we encounter is a glaring dissonance between a scientific community and its public portray. Is this simply a philosophical misunderstanding of a single scientific episode? Unfortunately not.

The central narrative amplified here is of a homogeneous scientific community that shuns the individual outsider, and the popularity of this narrative draws support from increasing emphasis on the social dimensions of scientific dissent in science studies. Only recently, the philosopher Huw Price also wondered about a fringe controversy in physics: *Is cold fusion truly impossible, or is it just that no respectable scientist can risk their reputation working on it?* (Price, 2015)? Price sees no primarily rational explanation for the biased choice against the idea of cold fusion in favor of the standard explanation ("reputation traps"). Instead, he sees it as rooted in social tensions. This perspective of the social marginalization of radically new ideas resonates with the story of Turin in Burr's and Solomon's narrative. It also is the story of Aubrey de Grey and his theory of longevity. There are a variety of similarly framed disputes in which a controversy seems to endure largely outside the expert community. To be sure, sometimes a good theory really is neglected based on social prejudice. Notwithstanding, not every one of these stories turns out to be a genuine Barbara McClintock. Therefore, we should likewise ask ourselves that if almost every expert in a field assures us that a model is wrong – or at least highly problematic – what in our perspective from the philosophy and social studies of science justifies the impression that it could be otherwise?

What the confrontational vector-model fails to address, as we will see in what follows, is how to assess the empirical problem in question and, consequentially, how to *qualify* the empirical success of research strategies. Any appropriate weighing of competing explanations is conditional on whether a scientific conflict is resting on the same objective of what it means to solve a problem successfully. On this account, it is worth pointing out that Solomon's assessment stands in stark contrast to the evaluation of data in the scientific community and, as we will show, has not been supported by any experimental developments either. Henceforth, we now are engaging with three key measures of empirical success, discussing how Solomon sees them instantiated in the case of the olfactory example, before elaborating on the grounds for what turns out to be a misevaluation.

### 3. Analysis: Three measures of empirical success

#### 3.1. Empirical adequacy: Data accommodation and fit

The minimal requirement for any model to count as empirically successful is that it accommodates the observational data (Van Fraassen, 1980; Psillos, 1999). However, the qualification of such explanatory fit is not unproblematic; that is "we need to distinguish between meritorious fit and 'fudged fit'" (Forster, 2007, 588). In particular, this issue mirrors the distinction between truthful explanation or the 'saving of phenomena' through the adjustment of model parameters and ad hoc hypotheses. How do we assure and assess the appropriateness of data accommodation?

In scientific practice, the dilemma pointed at here is, in fact, twofold. These two factors often run together but ought to be mentioned separately. First, consider the challenge of data selection. Scientific models do not fit all possible data, but apply to particular sets of data instead. How do we choose the relevant sets and, moreover, prioritize between them? Second, scientific models usually do not manifest a clear-cut accommodation of the relevant data sets either. The preference for one empirically messy model over another may thus be redirected to epistemic virtues, for example, concerning its parsimony, unifying capacity, completeness, internal consistency, scope, elegance, and so forth. That said, the value and assessment of epistemic virtues open up a range of separate philosophical problems.

A detailed look at the olfactory controversy soon exemplifies the underlying problem: Data accommodation does not imply empirical adequacy and, in turn, observational fit cannot warrant explanatory accountability or success. According to the decision-vector model (Solomon, 2006a, 2006b, 2008), the shape theory does not account for the vast structural diversity of odorous molecules and, therefore, fails to fit the observational data accurately. From this viewpoint, the empirical adequacy of the shape theory is highly selective and compromised in its fit with the chemical data. By contrast, the vibration theory appears to accommodate a range of irregular structure-odor relations (SORs) that pose an inherent issue for a shape-selective explanation of smell. One salient example for this is the case of isosteric molecules, which have the same shape yet different odor qualities (Sell, 2006). The model of the quantum nose claims to provide an explanation for such irregular cases of SORs (Turin 2006, 2009).

Failure of data accommodation implies some form of a measure for success. What is the decisive factor in the evaluation of SORs? The main problem with the narrative of an olfactory controversy is that it debates a straw man. The irregularity of SORs does not constitute a failure of the shape theory of odors - simply because such a theory does not exist today. So how did this idea come about? According to Solomon, the "traditional model" of olfaction appeals to a shape-selective mechanism, where a molecular interaction takes place

when a molecule has a correct fit with a complementary shaped receptor: "The generally accepted theory of scent is that particular scents are detected by shape receptors in the nose, which detect the shape of the molecules (or parts of the molecules) that make up those scents (Solomon, 2006a, 28, 2008, 9)." This simplified characterization of olfaction refers to the old lock-and-key model for enzyme reaction, originally proposed by Emil Fischer in 1894.

Historically, Fischer's lock-and-key model indeed provided the central heuristics for research on smell throughout the 20th century and up to the discovery of the olfactory receptors in 1991. Drawing on the presumed specificity relation between a substrate and its binding receptor, it was none other than Linus Pauling (1946) who proposed a similar mechanism for olfactory recognition by suggesting a correlation between the shape and size of a molecule and its smell. In this context, systematic investigations into the molecular basis of odors only started in the mid-20th century (Barwich, 2015a). The explanatory centrality of molecular shape and size was reinforced by contemporary technological innovations, such as X-ray crystallography, liquid gas and affinity chromatography, and mass spectrometry. These technologies allowed for more detailed knowledge of the structural arrangement of molecular compounds. One might even say that these technological innovations facilitated the golden era of fragrance chemistry.

Under the premise of a shape-sensitive mechanism, Robert Moncrieff (1949) worked out a more detailed hypothesis, referring to steric (i.e., geometrical) properties of molecules underlying odor detection. Labeled the "Steric Theory of Odors," John Amoore (1964, 1970) furthered this approach by stipulating a range of odor types in relation to their space-filling properties. As a rule of thumb, molecules with a similar geometrical and spatial configuration were supposed to smell alike. Amoore also tested these odor classes with psychophysical experiments on anosmic patients (people unable to smell specific kinds of odors). Nonetheless, stereochemical classifications of odor types were riddled with exceptions, and Amoore's idea of primary odors appeared too simplistic to explain the huge structural diversity of odorants (Ohloff et al., 2011).

These historical developments provide the backdrop against which Solomon places her assessment. According to her, the dominance of the standard model is justified not by its empirical fit but greater historical endurance, and the prevalence of the standard model is explained by reference to social decision-vectors that entail a "[c]onservativeness in the academic community. There is a general resistance to changing the theory that has had a monopoly for at least 30 years (Solomon, 2006a, pp. 30, 2008, 15)." Such conservativeness of the scientific community, she insinuated, obscured the inherent empirical problem of data accommodation in current scientific debate.

Alternatively, "the vibrational theory of odor" was introduced as providing a resolution to the irregularity of SORs. At first, this narrative seems to find support in examples from earlier studies on a precursor to the vibration theory of odors. One of the first explicitly chemical hypotheses, mentioning molecular vibrations, was proposed

by Malcolm Dyson in the late 1920s and 1930s (Dyson 1928, 1938).<sup>1</sup> However, at the time it was unclear how molecular vibrations might be detected by a biological system. Dyson's theory was taken up and expanded a few decades later by Robert Wright in the 1960s and 1970s. Wright (1964, 1977) found that a range of bitter almonds exhibited a regular correspondence of vibration patterns and odor quality. Envisaging a possible mechanism for the transduction of molecular vibrations, the theoretical vision of a "spectroscope made out of flesh" drove Wright's creative but unsuccessful efforts to revive a vibration theory of odor.<sup>2</sup>

It is against this historical background that Turin (1996, 2006) questioned the premise of the so-called shape theory with its premise of a causal similarity between olfactory responses and stereochemistry. In essence, he saw the so-called shape theory as posing a flawed structural assumption to begin with. Drawing on the earlier invention of a device involving electron spectroscopy by Jaklevic and Lambe (1966), he proposed a mechanism that stipulated the detection of molecular vibrations through inelastic electron tunneling spectroscopy (IETS). This is a quantum phenomenon in which electrons can jump small gaps between a donor and an acceptor. The IETS-model stipulates that such tunneling occurs in ligand binding. Turin's model is creative, and his presentation of it makes for occasionally compelling reading, but it has not been provided with any experimental links to protein studies to date. For the plausibility of his speculative model, Turin explicitly roots his model in the failure of the standard shape-selective account to accommodate the structural diversity

<sup>1</sup> Dyson's idea originated from his early studies involving element substitutions of chlorine compounds with heavier bromine and iodine elements. Two observations had caught his attention. First, molecules of the same shape can smell dissimilar whilst molecules with different shapes can smell alike. Second, the smell of a molecule gradually and constantly changes in relation to substitutions with heavier atoms. Could this mean that there is a causal connection between the odor of molecules and their molecular mass? Yet Dyson's emerging hypothesis about molecular vibrations remained vague, as there was no form of measurement available at the time. Only with the discovery of the Raman effect of light diffraction and photon emission did his hypothesis acquire empirical meaning. Following this, Dyson suggested that molecular vibrations in the Raman spectrum correlate with odor quality.

<sup>2</sup> Optical spectroscopy seemed out of the question, as one problem of an infrared light source is that it would roast its organic surroundings. The only alternative, he reasoned, was to postulate a mechanical interaction—a strategic move with major theoretical implications. It meant that the only energy source exciting the hypothetical receptors must be thermal motion. As a result, the energy involved is small, and the detectable range of molecular vibrations is restricted to a maximum of 1000 wave numbers ( $\text{cm}^{-1}$ ). Unlike Dyson, Wright identified far-infrared frequencies to underlie odor perception, but excluded near-infrared ones. Notwithstanding his exemplary studies on bitter almonds, exhibiting a regular correspondence of vibration patterns and odor quality, Wright's frequency restrictions posed insoluble problems. His mechanical model failed to explain the strong smell of small molecules whose frequencies lie outside the theoretically detectable range such as ammonia ( $\text{NH}_3$ ) or hydrogen cyanide ( $\text{HCN}$ ). Another obstacle impeding the success of Wright's idea was the instrumental requirement for the measurement of far-infrared frequencies, as a spectroscope was not a readily accessible instrument for contemporary researchers. As a consequence, most of Wright's experimental results could not easily be reproduced. The final straw that led contemporaries to abandon his theory was the case of enantiomers (i.e., mirror-imaged molecules). Enantiomers are identical in shape and vibration spectrum, the only difference is their spatial orientation. Studies of enantiomers in the 1970s, showing that some enantiomers with identical vibrations have a different smell, were seen as the most irrefutable objection to the vibration theory (Barwich, 2015a). By the 1980s, sporadic interest in the vibration theory of odors had passed. In light of the rapidly growing accumulation of synthetic materials and the improvement of statistical techniques for the comparison of molecular parameters, olfactory research in fragrance chemistry proceeded to pursue the study of odorants through an extension of the concept of chemical similarity (Ohloff et al., 2011).

of chemical data. From this perspective, Solomon judges the current strategies to accommodate irregular chemical data through flexible receptor behavior to represent a case of having ‘fudged the fit.’

What this evaluation overlooks is a fundamental change in the scientific understanding of the causal principles in primary odor recognition. This paradigmatic change has impacted the prioritization of data sets as well as the underlying understanding of empirical fit. Research on olfaction in the 20th century is divided into the time before and after the discovery of the olfactory receptors in 1991 (Buck & Axel, 1991; Firestein, Greer, and Mombaerts 2014). Yet this key event in olfactory science gets heavily sidelined in the narrative about the quantum nose controversy, which instead details a receptor model with insights from the 1940s to the 1970s; notably, a time where the general existence of cell surface receptors was a highly speculative idea (Barwich & Bschor, 2017). As a result, Solomon's assessment fails to account for the huge impact this discovery had on the field.

The significance of the receptor discovery cannot be overstated, and Linda Buck and Richard Axel received the 2004 Nobel Prize in Physiology or Medicine for their breakthrough. Until recently, biologists were unable to conclusively determine the precise molecular features responsible for smell perception simply because the mammalian olfactory receptors were unknown. Before the receptor discovery, research on the molecular basis of odors mainly took place in fragrance chemistry. Fragrance chemists sought out regularities between the structure of molecules and their odor quality, leading to the development of rules for structure-odor relations. After the receptor discovery, molecular biology and neuroscience became more prominent for the explanation of smell (Barwich, 2015a). On that account, the doctrine of the lock-and-key model does not only present a simplification, but it is also considered to be an outdated description of molecular mechanisms and odor chemistry today. While the lock-and-key analogy remains a useful idealization, it is not considered an adequate account of the biological mechanism, nor is it deemed to provide a shortcut to robust structure-odor rules. Moreover, the relation between structure and odor is much more complex than the notion of shape indicates. From a chemistry perspective alone, the concept of chemical similarity between odorants encompasses a multitude of features “like molecular weight, functional groups, polarity, acidity, basicity, and steric interactions” (Hettinger, 2011). Besides, before the receptor discovery, it was also uncertain in the context of molecular biological research whether odors were even detected by anything such as “shape receptors.” Although growing evidence indicated the potential involvement of a G-coupled protein in the olfactory transduction mechanism by the late 1980s, some studies had also been pursuing alternatives to receptor models; for example, by considering odor detection via the activation of ion channels (Buck, 2004). Thus, Solomon's narrative that alludes to a theoretical conservatism in the scientific community, as always favoring “shape receptors” to be the paradigm, is rendered historically untenable and fictitious.

Overall the experimental implications of Buck and Axel's findings for research on smell were wide-ranging. When Buck and Axel (1991) discovered a multigene family encoding the olfactory receptors in the mammalian genome, their findings integrated research on the olfactory pathway into mainstream neurobiology because they identified smell receptors as G-protein coupled receptors (GPCRs). GPCRs constitute the largest receptor gene family in the mammalian genome; they take part in a variety of fundamental physiological processes and bind to a variety of structurally different ligands, including hormones, peptides, neurotransmitters, odorants, and even photons (Snogerup-Linse, 2012). The discovery of the olfactory GPCRs now allowed for the functional analysis and detailed studies

of odor activation on sensory neurons. These studies established the combinatorial nature of receptor activation, meaning that one receptor recognizes several ligands and one ligand can be detected by several receptors (Malnic, Hirono, Sato, & Buck, 1999). Rather than “overall shape,” the causality of odorants is defined through a component analysis of various molecular features in interaction with conformational changes of the olfactory receptors (Barwich, 2015a). Consequently, this insight into the combinatorial nature of receptor activation made the search for straightforward structure-odor rules seem like an intuitive but naïve miscalculation. Meanwhile, the receptor discovery further allowed for the tracing of stimulus activation patterns from the sensory neurons in the nasal epithelium to the olfactory bulb. It thereby paved the way for the integration of olfaction into the advancing experimental content of sensory neuroscience (Axel, 2005).

The upshot of this detailed analysis is that the appropriateness of data accommodation entails more than a comparison of idealized observational fits between two models. Rather, it necessitates a *qualification* with regards to the mutable disciplinary objectives and (dis)continuities that define an empirical problem. The receptor discovery signified a benchmark event and change in the disciplinary objectives that turned olfaction from a domain in analytic chemistry to a promising new subject in neurobiology. Here, olfaction emerged as a new model for understanding the strong evolutionary ties of signaling proteins. Previously irregular structure-odor irregularities were now subject to flexible receptor behavior. Instead of a rigid lock-and-key premise from the 1970s, modern biology considers energy profiles and conformational changes as pivotal to understanding binding behavior and activation (Barwich, 2015b). Comparative observations of shape-selective and vibrational SORs thus do not map onto the central issue of modern olfactory research, namely the interaction-governing receptor behavior.<sup>3</sup> In this context, Solomon's analysis of what constitutes the empirical fit in both theories is not representative of contemporary research but references an understanding of olfaction prior to 1991, more precisely the science of smell of Amoore from the 1960–70s.

### 3.2. Instrumental reliability: Reproducibility and robustness

The empirical success of a model is further conditional on whether it reliably generates and replicates the observational data in an experimental setting. Such reliability is ensured in two ways. On the one hand, it hinges on the reproducibility of data through similar methods and across comparable settings. On the other hand, instrumental reliability designates the robustness of findings. Solomon praises robustness as an essential requirement for model choice, as it indicates that the evidence in question is sufficiently independent of a particular theory or the theory-ladenness of observations (2001, 28).

First, beginning with the reproducibility of research, the various challenges that accompany this issue have received a vast amount of attention in the natural and social sciences in the ensuing “replication crisis” lately (Ioannidis, 2005). Three kinds of reproducibility stand out in this context, namely “method reproducibility,” “results reproducibility,” and “inferential reproducibility” (Goodman, Fanelli, and Ioannidis 2016). Essentially, method reproducibility implies the stability of results from the same technologies and kinds of data analysis. It is closely linked to results reproducibility, which involves the

<sup>3</sup> The claim of a recent machine learning study to predict odor from molecular structure (Keller et al., 2017) must, therefore, be seen with caution (Gilbert, 2017), especially in light of empirical results that stand in contrast to Keller et al.'s approach (Poivet et al., 2016).

corroboration of results from previous studies with new data. Lastly, inferential reproducibility means that the same data gives rise consistently to the same theoretical conclusions. To be sure, a variety of factors can affect the implementation of these reproducibility measures, for example, the signal to measurement-error ratio or the complexity of the experimental design.

Second, robustness is another instantiation of instrumental reliability that is considered to facilitate better evidence. Robustness refers to datasets that are derived from multiple, independent investigative sources (Wimsatt, 2007). Nonetheless, appeals to robustness yield practical problems as well. Sometimes, multiple techniques may not be available. Conversely, the generation of commensurable data from various and independent methods can be difficult. This poses a particularly tricky problem for the philosophical analysis of contemporary scientific developments, as “concordance is easier to see in retrospect, with a selective filter for reconstructions of scientific success” (Stegenga, 2009, 655).

The epistemic concern arising from these methodological issues is the question of how to ensure that our scientific conclusions are validated consistently through continuing experimentation. In ongoing research, this concern is heightened by the fact that both the data and its interpretations are subject to repeated revision (Chang, 2006; Elliott, 2012). Hence, how can we recognize the coherence of a research strategy in flexible research contexts? The identification of a robust research strategy entails more than a quantification of the multimodal lines of evidence. It also requires the explication of inconsistency in data production, changing selection criteria, and incompatible techniques. Plus, coherence in data production may not even be the best sign of an empirically successful model either.

What we must consider before any quantification of experimental evidence is its qualification. Cartwright (2007) has argued for the significance of grading evidence regarding the quality and the relevance of data production. According to her, there are experiments of high quality but low relevance and, vice versa, there can be experiments of low quality but high relevance. In turn, we face two related yet separate considerations. On the one hand, we must ensure the articulation of data pertinence for a specific hypothesis. On the other hand, there is the assessment of the actual quality of the data. So, what are the criteria for justifications of data relevance?

In our example of the olfactory controversy, Solomon grants Turin's theory sufficient instrumental reliability by stating that “most of his smell observations are replicated by chemists or fragrance scientists” (Solomon, 2006a, 30, 2008, 14). This expectation has – at least so far – not been confirmed. Or in the more candid words of Gilbert (2017): “In a grand substitution of ego for psychophysics, Turin claims that Turin's theory successfully predicts odors because they smell the way Turin says they do.” There have not been any successful replications of Turin's observations to date, and it is unclear to which replications Solomon refers. To the contrary, a study by Keller and Vosshall (2004) at Rockefeller University set out for an explicit test of one of the central claims of Turin's model, involving the smell of isotopic variants. Given that isotopic variants have a similar stereochemistry (shape) but different intra-molecular vibrations (i.e., different wavenumbers), they ought to smell different to the human nose. Keller and Vosshall (2004) recorded that test panelists were unable to tell a difference in the odor of deuterated acetophenone and its parent compound. Solomon, aware of this negative study, marked it as proof of the antagonism Turin faces through the establishment (Solomon, 2006a, 30, 2008, 12). Nonetheless, even Turin's subsequent reproduction of Keller and Vosshall's experiment came to the same negative results (Gane et al., 2013). Here, we find multiple studies testing the same premise with a similar experimental design,

aiming at the reproducibility of the results. It thus stands to reason that the dismissal of the underlying hypothesis cannot be based mainly on social or publication bias.

In reply to the negative outcome of his replication of Keller and Vosshall's experiments, Turin reinterpreted the findings. Alternatively, he now entertained the option that the difference in frequency between the isotopes might be too weak to result in an odor difference strong enough to be perceived. To test this ad hoc hypothesis, another study with an altered experimental design was conducted. For this, his team specifically designed a musk molecule with enhanced features (i.e., deuterated cyclopentadecanone). These isotopes contained more hydrogen and deuterium bonds that, if Turin's assumption about the nature of isotope perception is right, must surely result in a perceptible odor difference. The assumption turned out to be supported by the experimental results; the human subjects in this study were able to tell the isotopes apart (Gane et al., 2013).

Similar to his earlier studies, Turin's latest results were considered insufficient and not supportive of the vibrational theory. One main reason is that psychophysical studies are rarely conceded to be a decisive factor in settling theoretical disputes. Sensory measurements, especially of olfactory performance in humans, are notoriously difficult and thus do not provide the most reliable source for the reproducibility of methods and results because of their causal multidimensionality and limited degree of control (Barwich & Chang, 2015). For this reason, the quality of Turin's data is viewed as too meager to warrant its strong theoretical conclusion at present. The observed perceptual effect could have been affected by too many variables that, furthermore, may not have been accounted for in the experimental set-up. In light of this, Turin's 2013 study only has high relevance with respect to his own theory, and not in the context of olfactory research in general. Moreover, the inferential fit between the explanation and the experimental design was found as either too weak or inconsistent by his colleagues. In reply to Turin's study, the chemist Eric Block responded that “Turin can't have it both ways: either noses can smell deuterium or they can't” (Anderson, 2013). Block's verdict may be revisable in light of future developments, but – in Cartwright's terms – Turin's data thus far has only carried supportive implications for his own framework with menial qualitative strength and limited connections to the general context of olfactory research.

So what kind of evidence is needed to reinforce the vibration theory? Responses to Turin in the olfactory community have been univocal in that respect: The problem with Turin's model is its sheer absence of protein-related experimental data. His psychophysical studies merely represent indirect observations, which test inferences from a highly speculative mechanism but fail to address the empirical feasibility or implementation of said mechanism. In Richard Axel's view: “Until somebody really sits down and seriously addresses the mechanism and not inferences from the mechanism ... it does not seem a useful endeavour to use behavioural responses as an argument. [...] Do not get me wrong, I'm not writing off this theory, but I need data and it has not been presented” (Axel quoted in Palmer, 2013).

Therefore, what fosters scientific caution against the strong claims of vibrationists is that Turin's model lacks any evidence that deals with the empirical data required to assist its core claim. Because if you want to make an argument against the striking evolutionary ties of GPCRs and say that olfaction works contrary to everything we know about biology thus far (Palmer, 2013), then you had better show it with data of the receptors as the key causal entity in your claim. Meanwhile, a recent multi-method and multi-lab study by Block et al. (2015) proceeded to test Turin's claim of the differential detection of isotopic variants by examining whether the protein-re-

ceptors do respond differently to isotopic variants. Again, the result was negative. In response, Turin mitigated the relevance of this test by stating that Block et al.'s *in vitro* study may not account for *in vivo* effects. That said, the IETS-model itself lacks any experimental tests on GPCRs to this date (i.e., a conceivable study could have been an explicit functional comparison in the detection of vibrational features, as it has been done with stereochemical parameters in Malnic et al. (1999).)

In fairness, Solomon could have hardly anticipated results of more recent studies. However, her framework did fail to correctly distinguish and estimate the relevance and quality of the evidential data that was available at the time of her analysis. We saw that the scientific community had already strongly criticized Turin's model as being too anecdotal and inappropriate in light of the central causal entity of odor recognition: the protein receptors. Furthermore, the support for Turin's model was considered to lack sufficient quality regarding the reproducibility and strength of its methods and inferences. By contrast, when other laboratories offered negative evidence subsequently, it was both in the form of causal relevance (Block et al., 2015) and reproducibility (the replication of Keller & Vosshall, 2004 in Gane et al., 2013).

In recap, we saw that appeals to empirical success in theory choice can yield incorrect conclusions if we neglect to specify the reliability and robustness of data *in parallel with its relevance*. Such qualification of data involves not only the articulation of its importance for a particular hypothesis, but also its embeddedness in a broader disciplinary context. Besides, the *differential weight* of positive and negative evidence must be not be forgotten in this setting either.

### 3.3. A good predictor of new phenomena

The last feature of empirical success we want to discuss is predictive power. 'Prediction' is a future-oriented term that refers to the acquisition of knowledge not previously associated with a target system. Predictive models or theories facilitate accurate expectations about the properties or behavior of the investigated materials. Nonetheless, what counts as a prediction can imply different things (Barrett & Stanford, 2006). One understanding of successful prediction resonates with the procedure of inductive inference in the empirical sciences. If we confirm a hypothesis about an entity based on previous, similar findings, this may count as a successful prediction in a wider sense. Another understanding of prediction rests on the deductive-nomological model. On this account, we derive hypotheses about an entity from general laws as knowledge about the structural features of a target system, rather than empirical observations.

Epistemic challenges regarding the value of such predictions address the question of how novel the findings from these procedures must be. In other words, is it sufficient for a predictive model to connect previously separate observations, or do the findings need to yield unencountered data? Some philosophers, like Lakatos, applied a strict notion of prediction that requires findings to be "improbable" or "impossible" according to current understanding (Lakatos, 1970). Others, like Musgrave (1974) and Leplin (1997), allowed for a weaker notion of prediction as data accommodation but with a strict measure of success in a competitive scenario. From their view, a theoretical framework is superior to its rival only if, when one directly compares their assumptions, both cannot entail the same result of a possible test. 'Not entailed' in this case means that either the observations conflict with one of the rivals or present a result on which the rival remains silent. The difference in these two appeals to prediction mirrors the

distinction of historical and logical relations between theory and evidence (Barrett & Stanford, 2006; Musgrave, 1974).

Philosophers of science have commonly preferred logical relations over historical ones since the former provide a greater independence from the contingency of observational methods. Nevertheless, logical relations do not necessarily produce an explanation (Rosenberg, 1994). Also, in light of the multiple realizability of phenomena, especially in the biological sciences, we are further confronted with an equivalent of the problem of the underdetermination of theories by observational data (Stanford, 2006). Therefore, in light of potentially ambiguous correlations, predictive relations must be somewhat *characteristic* of their target system. Notwithstanding, the definition of such characteristics as modeling constraints inevitably brings us back to a historical account of evidential relations.

Starting with the stricter notion of predictive success, the appeal of the vibration theory in Solomon's narrative is a distinct discovery on which Turin builds his case. Challenging widespread objections to his idea of smell as a spectral sense, Turin set out to make a prediction of odor from a molecule's vibrational spectrum. He went looking for two molecules that correspond in both odor quality and vibration frequency but that exhibit a different stereochemical configuration. To remove doubts about their perceptual similarity the odorants needed a distinctive smell. The choice fell on sulfur where the frequency of the SH-bond was outside the vibrational range of most known odorants. Calculating vibration patterns of diatomic molecules a frequency close to the SH-bond (2500 wave numbers ( $\text{cm}^{-1}$ )) was found in the BH-bonds of boranes (2550 wave numbers ( $\text{cm}^{-1}$ )). The sulfurous smell of boranes had been remarked prior to Turin (Stitt, 1941). What caught Turin's attention is that "Borane and Sulfur are not in the same column of the periodic table. They have no shape and no chemistry in common" (Turin quoted in Burr, 2004, 416). In turn, the geometrical configurations and electronic properties of molecules composed of borane bonds differ significantly from those of sulfur. The question is whether sulfur and boranes really smell similar. Unfortunately, a simple smell test would not do, as boranes are rocket fuels and explode spontaneously on contact with air. A test with a less temperamental but toxic decaborane ( $\text{B}_{10}\text{H}_{14}$ ) seems to confirm Turin's idea; boranes smell sulfurous. In support of Turin's perception, Alfred Stock, the inventor of boranes, commented on their smell as being "reminiscent of sulfur" as early as 1912 (Berger, 2012). The sulfur-borane prediction is intriguing as part of a collection of structure-odor examples where Turin (2009) sees a failure of the traditional stereochemical model. It further presents an unlikely correlation of data that fulfills the above criteria of Laudan, Musgrave, and Leplin. Nonetheless, why is this prediction insufficient to grant the IETS-model satisfactory empirical success or epistemic equivalence? Does the lack of appraisal for this prediction ground in the conservativeness of the scientific community, as Solomon suggests?

When we return to the examination of olfaction in section 3.1, it is evident why structure-odor rules were at the heart of olfactory theorizing before the receptor discovery. SORs provided the sole empirical source for any hypothesis about the molecular detection mechanism. However, we also found that the question of chemical similarity was revised in light of receptor behavior (for details see Barwich, 2015a). For this reason, Turin's prediction offers an interesting correlation that remains too coincidental. As a single observation, it lacks a sufficient empirical grounding for its causal explanation and remains a coincidence that may be due to a variety of other causal factors. And no further predictions were provided since 1996; notably not even 20 years later when Solomon took on this case. The logical relation between the IETS-model and its evidence thus remains incidental and has yet not been furnished with the appropriate links to the

characteristics of the receptors. These characteristics refer to an evolutionary understanding of the olfactory receptors as GPCRs. GPCRs share a strikingly large amount of conserved amino acid sequences, pointing at their shared evolutionary roots and development of a ligand-binding mechanism (Snogerup-Linse, 2012).

Meanwhile, it would be a mistake to understand the significance of the receptor discovery as a mere confirmation of what Solomon took to be the orthodox model (i.e., prediction in the weaker sense), largely because there had been no orthodox model. Before the mid-1980s, olfaction was not considered to operate on a molecular mechanism comparable to other sensory signaling processes (Buck, 2004). The heuristic analogy of the lock-and-key mechanism may have instructed discourse in fragrance chemistry, but its molecular implementation was speculative and not entirely without skepticism until the discovery of the actual receptor genes. Consequently, this finding presented novel empirical knowledge and embedded olfaction into the wider experimental context of neurobiology, establishing its molecular ties with other cell membrane proteins.

In effect, the receptor discovery itself yielded unexpected insights into the details of odor recognition that fundamentally revised scientific understanding of the molecular basis of odor. Just consider: Before their discovery, the number of olfactory receptors was estimated to be around 30–100. Surpassing these estimations by far, Buck and Axel found over 500 receptors; and this number has exceeded 1000 today. (To put this into perspective, the largest known receptor family at the time was serotonin with a less than impressive number of 15 members!) Their sheer size in parallel with a highly diverse genetic make-up opened up a plethora of new questions about these receptors and their ligand-binding behavior,<sup>4</sup> further changing our understanding of the molecular recognition process: "The problem is thus to account for a binding pocket that is analogous to that of other transmitter receptors and photoreceptors but can interact differently with different molecules. Thus, in contrast with the traditional lock-and-key metaphor for enzymatic and receptor specificity, the olfactory receptor is hypothesized to function by a broad affinity mechanism. *This is an example of a new concept of receptor activation involving broad receptor-signal interactions*" (Shepherd, 2012; emphasis added).

What reads like a dogmatic slumber of the biological community in Solomon's analysis was, in fact, the awakening of olfaction as a modern molecular model system for neurobiology. With this corrected understanding of the olfactory "controversy" in mind, we can now come to a conclusion about the challenges that philosophers face in their analysis of contemporaneous scientific research.

#### 4. Discussion: Why there is no real scientific controversy in olfaction

Although empirical success is the foundation of scientific advancement, we have seen that its explication is not without obstacles. Our analysis of the olfactory pseudo-controversy brought to light that scientific evaluations of a model's empirical success are structured by the disciplinary objectives of what counts as the empirical problem in question. Notably these objectives are inherently dynamic and subject to change. In fact, what counts as an empirical problem is subject to continuous developments, so much so that what might be considered an issue at one time, can convert into a representation of data complexity only a few years later. While these changes rest partly on his-

<sup>4</sup> These significant empirical developments and their theoretical implications have yet to be addressed by Turin and his supporters – who still seem to prefer beating up an undeserving John Amoore with his best intentions to understand the invisible molecular world of smell in the 1970s.

torical contingencies, they were also shown to reside in developments that are of relevance for the general philosophical study of science. We saw that the quantification of empirical success inevitably builds on a specification of relevance in observational attribution.

What are the concrete philosophical consequences we can draw from this particular episode? The first point we must acknowledge is that the story of the quantum nose does *not* constitute merely an isolated episode or misrepresentation of a scientific discourse. Many advocates of fringe science have relied heavily on the narrative of an oppressive establishment that ignores and excludes the spirited pioneers and the evidence for their work (e.g., Price's account of scientific dissent about cold fusion followed a similar pattern, so does the public hype around Aubrey de Grey, and other comparable cases;<sup>5</sup> for specifics on fringe science narratives with the example of gravitational waves see also Collins (2014)). The fact that certain lines of research did not take place as part of mainstream science requires more careful examination for *why* it is not considered mainstream or, alternatively, what might be required for its integration into mainstream research. (For instance, we might ask, how can a speculative model proactively contribute to current experiments and concepts without being used exclusively to apply only to its own framework; like in the case of the currently self-referential tests of the IETS-model).

A particular issue with too many public narratives on scientific controversies is that they sometimes emphasize the social dynamics as the decisive element over the empirical evidence without, however, engaging sufficiently with said social contexts.<sup>6</sup> This can result in highly distorted narratives of scientific disputes. And those readers not sharing my interest in the olfactory community might be reminded of the impact that such overemphasis on social dynamics in research had on the perception of climate science (Collins, 2012). Indeed, Collins & Evans, (2009) in *Rethinking Expertise* have provided a profound analysis about why there is more to scientific expertise and competence than social credibility.

Perhaps the strong appeal to accepting a social perspective is a problematic heritage of the psychological mob dynamics that philosophers and sociologists have read into Kuhn's ideas of paradigm changes, an interpretation he himself felt forced to object in the remainder of his life (Kuhn, 1977). To be sure, all of this is not to deny the importance of situating science as a social enterprise, but it may really be necessary to refocus our efforts on the epistemic and

<sup>5</sup> It is worth pointing out that the issue here is not whether cold fusion itself is possible, or whether Aubrey de Grey's theory of longevity may not have its merits, but – rather – what characterizes the official narratives in introducing these ideas as controversies.

<sup>6</sup> In fact, there are several issues with regard to the social narrative of the quantum nose. Prior to the olfactory receptor discovery, there was hardly a homogeneous or powerfully organized community working on the biology of the olfactory system. Salient exceptions like Gordon Shepherd and Randy Reed, pioneered the field, but their interest in olfaction was not considered part of mainstream research. Before their breakthrough, Buck nor Axel weren't even on the map of olfaction research. Buck had been a senior postdoctoral researcher in Axel's lab, and while the latter was highly regarded in molecular biology he did not have ties to research on smell at the time. Additionally, the popularized portrayal of the olfactory community as consisting of conservative molecular biologists, who oppose any notion of quantum physics, does not account for the changing nature of the field that has also started to attract other physicists, such as Andreas Mershin and Dima Rinberg, who do not necessarily agree with Turin's model either. Neither is it fitting to brand Turin, having worked at prestigious institutions like UCL and MIT, as an academic outsider. And in this correction of social vectors, it is somewhat problematic that Solomon (2006a, 2008) anticipated gender biases to be in place when she questioned whether the shape theory might have been the dominant theory for implementing a "penetration metaphor." Yet, at the same time her account neglects to acknowledge the contribution of the only female scientist in this story, Linda Buck.



empirical dimensions of research practices. What can go wrong in our public science narratives such that specialist and non-practitioner views on evidence differ so fundamentally, as they do in the olfactory case, and yet are placed on a somewhat equal empirical and epistemic footing?

In light of this challenge, we must be aware of our own *narrative constraints* or biases in rational reconstructions of scientific developments. The identification of observational relevance in an open-ended scientific investigation is not determined exhaustively by the published and publically available data, as any scientific community operates by a form of “silent knowledge” that structures the internal dynamics of a field. This silent knowledge comes in several shapes and forms, such as negative results, replication failures, scientists holding off the publication of data to use in grant applications, informal exchanges between colleagues about their current work, gossip between labs, and so on (Firestein, 2012).

It is important to point out that these factors are more than merely social but inherently epistemic; they embody strategies to communicate and distribute information and research tendencies in a way that is closely correlated with the objectives of ongoing inquiry, which is advancing far too fast to be waiting for everything to appear delayed in an official publication. The rise of pre-print archives and the increased call for an outlet of negative results are interesting developments in this context (Berg et al., 2016).

So how should we think about philosophical expertise and situate it in relation to science in practice? Naturally such “silent knowledge” seems to lack transparency from an outsider's perspective, and so it enforces philosophical analysis of modern science to become more closely embedded in scientific practice by what Harry Collins calls *interactional expertise* (Collins & Evans, 2009). Interactional expertise is complementary to the specialist expertise of the scientist. Collins identified scientific expertise as distinct from other kinds of practice, viewing it primarily as a matter of experience and exchange with other practitioners. In this context, interactional expertise involves the conceptual understanding of a science “from within” by participant observation, without necessarily having the skills of its practitioners. A scientist without hands so to speak.<sup>7</sup> Many philosophers of science have engaged with science to a higher degree from the critical distance, so much so that one could consider this a form of *referred expertise*, the application of know-how from one domain to another one (Collins & Evans, 2009). Nonetheless, Collins (2012) also emphasizes that this kind of skill is often insufficient for judging scientific *developments*.<sup>8</sup> And the case at hand has further demonstrated the philosophical significance of this insufficiency.

It is important to understand that the special nature of interactional expertise is not limited to a linguistic capacity to “walk the talk,” and to adopt the lingo of an expert discourse. Crucial to the acquisition of interactional expertise is a form of epistemic fluency, meaning to be-

come able to adequately *situate the scientific content in a debate*. And key to an adequate understanding of empirical success in the olfactory debate was indeed the qualification of said content alongside with the disciplinary and experimental progression of specialist science. Non-trivially, scientifically relevant content can involve more than what is being published in journals. In effect, a correct assessment of scientific developments and choices also requires a sufficient understanding of what is not known, sometimes only anticipated, but not yet published at a certain time. Such “silent knowledge,” as we called it above, is integral to the dynamics of a scientific field. Not everything driving a scientific debate is published, or will ever end up being published, but it can fundamentally influence ongoing decision-making. Scientists themselves are increasingly aware of the impact these hidden dynamics can have on their research. Recent debates about topics such as reproducibility and negative results bear testimony to this trend. Philosophical work as interactional expertise can play a complementary role in this context (Chang 2006). More than observation, such complementary performance requires active participation in order to explicate, situate and analyze the dynamics that instruct the epistemic landscape of a field. In light of this, a rethinking of philosophical narratives in relation to scientific practice is important both for descriptive and normative purposes.<sup>9</sup>

What are the concrete epistemic implications of such philosophical “explication work” (a term adopted from Schickore 2018)? Notably it already indicates an broader understanding of successful scientific observation. Constitutive of its advancement, science does not just collect knowledge in the form of facts, data, instrumental expertise, etc. It uses these facts to develop more sophisticated questions about the things that we do not know – a kind of higher form of ignorance, if you will (for a scientist's view on the positive heuristics of “ignorance” see Firestein, 2012). Empirical success in an ongoing scientific debate is not only defined by a collection of experimental proofs and facts in favor of a model or hypothesis, as is suggested in rational reconstructions of theory-choice. Moving beyond the context of justification, empirical success in scientific practice is characterized by what certain experiments indicate and promise as potential avenues for further work.

In effect, empirical success in science is always also interactional success. It is about opening up empirical findings to be integrated with other experimental studies, and to allow for further engagement with their associated theoretical implications.<sup>10</sup> Case in point, Turin's lack of engagement with the current systems of practice in olfaction adds to his studies not being taken up by other researchers. (This might of course change with future studies that would integrate vibrational approaches alongside ongoing research in olfaction, thereby opening up further avenues for experimental engagement.) Conversely, the receptor discovery by Buck and Axel (1991) is a prime example of the notion of empirical success advanced here. This dis-

<sup>7</sup> Collins convincingly demonstrated that such interactive engagement leads to the acquisition of a special proficiency of being able to “walk the talk.” In an experiment, Collins and a scientific practitioner were asked technical questions (designed by scientists) about gravitational waves, a domain Collins has studied “on site” for several years. The answers were anonymized and given to other specialists, who had to decide which one of the answers is from the *real* scientific professional. Collins made an intellectual bet, and he won; he passed as a scientist in the eyes of other experts (Collins, 2012; Collins & Evans, 2009).

<sup>8</sup> Collins' criticism relates the lack of in-depth engagement with the special character of science in science studies to the disciplinary trajectory of the latter: while the first half of the 20th century adhered to an inadequate ideal of the rationalist scientists in logical positivism, “[s]ince the 1960s, certain academic groups have been effectively trying to turn us all into default experts by showing that there is nothing special about science” (Collins & Evans, 2009, 19).

<sup>9</sup> This consideration might also prove useful for currently growing philosophical interest in the use of case studies in the history and philosophy of science (in particular, see Kinzel, 2015 paper “Narrative and evidence. How can case studies from the history of science support claims in the philosophy of science?”) as well as recent interest in the construction of narratives in science (see the special issue by Morgan & Wise, 2017).

<sup>10</sup> Moreover, if we apply this definition to historical examples we can see this revised understanding of empirical success playing out as well. Chang's analysis of the chemical revolution as a plea for pluralism (2012) was conditional upon showing that research on phlogiston did not stop engaging with ongoing systems of practice, and therefore did not lose empirical significance. Proponents of phlogiston continued to produce ideas and observations that were taken up by proponents of Lavoisier's system, often to enhance their own understanding and open up new questions about ambiguous phenomena.

covery embedded olfaction into the wider experimental context of neurobiology by establishing its molecular ties with other cell membrane proteins.

Therefore, the real question we must ask is: Why has so little attention been paid to the impact of the receptors in this popularized narrative of the olfactory controversy? Given that the receptor discovery got awarded the 2004 Nobel Prize (thirteen years after the original breakthrough), it was not a lack of visibility of this key event that may have distorted epistemic access to the underlying dynamics of the olfactory community. And the receptor discovery is indeed the first thing olfactory scientists mention when questioned about the lack of reception regarding the Turin model today. Upon meeting the olfactory neuroscientist Stuart Firestein in January 2014 I had asked him: "What if Turin had made his prediction *before* the discovery of the olfactory receptors? Would it have changed the evaluation of his model?" I remember him thinking about my question, and then saying: "It would have given his model a little more time, perhaps. But I cannot see how it could have survived for too long after the receptor discovery and its implications in any case."<sup>11</sup>

So what constituted the deep impact of this receptor discovery, and why had it been missed in public and philosophical assessments of the quantum nose narrative? Fundamentally, the chief mistake in these discussions of an olfactory pseudo-controversy was to construct the two experimental contexts, traditional research on smell in analytic chemistry and new insights from molecular biology, as taking part of the same historical trajectory of experimental research. However, the hereby insinuated continuity in theorizing never existed. Instead, it constituted an artifact of a post hoc reconstruction from the philosophical narrative of confrontational model-choice.

Without doubt the receptor discovery transformed the field of olfaction by modifying scientific explanations of structure-odor relations in fragrance chemistry. But it would be misleading to reduce this shift to a mere change regarding the accommodation of chemical data in the trajectory of smell research. The significance of the receptor discovery was its interactional success in terms of its prospective value. It essentially opened up research in olfaction to a variety of *new* experimental possibilities and embedded it within broader advances in neurobiology (Buck 2005).

For this, we must revisit the receptor discovery in its full context: Buck and Axel's (1991) findings were constitutive of olfaction as a modern molecular site because they occurred at a time when GPCRs were just turning into a major topic in biology. For example, the sequences of another family of GPCRs, the  $\beta$ -adrenergic receptors, had just been isolated and established after being a subject of heavy debate and doubted in their existence deep into the 1970s and even 1980s (Barwich & Bschor, 2017; Lefkowitz, 2013). So instead of reinforcing a conservative paradigm that had been in place for 30 years or more – as it was presented in the narratives of Turin, Burr, and Solomon – the receptor discovery embodied a new scientific outlook for research on olfaction with little experimental ties to the context of SORs in analytic chemistry (from which the vibration theorists were drawing support). Moreover, the sheer force with which this discovery arrived on the scene was rendered visible far beyond the hitherto small olfactory research community. Notably GPCRs were a considerably young entry in the molecular inventory of biochemistry, with only the family ties between rhodopsin and the adrenergic receptors having been published in the late 1980s. Insights into the olfactory receptors, revealing themselves to be the largest protein gene family in the mammalian genome, thus also changed the experimental as well as theoretical outlook of general studies on GPCR, catapulting

the olfactory pathway into core neurobiology and marking its proactive value.

By now it should be clear that there never was a genuine scientific controversy in olfaction as painted in public and philosophical discourse. Thus, let us conclude with the roots of such dissonance between the public perception and the practitioners' discourse. Overall the misrepresentation of the scientific context, as unraveled in this article, rests on a very general programmatic commitment that also brings us back to our central concern about a reevaluation of empirical success in ongoing science; the commitment to confrontational models in theoretical comparisons. Philosophical reconstructions of rational choice scenarios in science has had a long tradition; consider Kuhnian paradigm changes, competition between progressive and degenerating research programmes in Lakatos, or Laudan's idea of scientific advancement by successive theories as better puzzle solvers than previous ones. Solomon (2001) explicitly situated herself in this tradition of modeling rational choices between competing research programs; and her outline of the olfactory controversy in particular rested on a comparison between the conservative or paradigmatic model and its rival contender.

But if we want to account for developments in ongoing science, we are strongly cautioned to abandon this persistent confrontational narrative of Kuhnian paradigms and its philosophical successors in dissent analysis.<sup>12</sup> The problem with paradigms and comparative notions is that they were developed as primarily historical tools for the post hoc organization of research developments, positioning alternative ideas as being in competition. However, when dealing with the changeable dynamics in current science, such tools can fail considerably to account for important *discontinuities* and the *occasional absence of a strictly programmatic model* that frequently mark significant changes in how to position and assess empirical successes in an experimental system. For example, contemporary receptor studies do not rely on a univocal paradigm, as the whole straw-man narrative of shape versus vibration suggests. Rather, inquiry into the ligand binding behavior of the olfactory receptors oscillates between assumptions of induced fit, selected fit, or flexible combinations of both (for a detailed review of these mechanisms see Barwich, 2015b). Further, the details of receptor-ligand binding in olfaction invite new insights to this day (Poivet et al. 2018). One should not take such open-endedness of current inquiry into odorant binding for a lack of modeling success. Having no fixed or stable model is the very characteristic of unresolved and forward moving inquiry, not its flaw. Moreover, this instability and ambiguity of contemporary developments does not make assessments of current experimental data arbitrary or lacking a guideline to evaluate their success.

Without this organizational narrative of model competition in ongoing science and its flexible modeling perspective, where does this leave us for our philosophical understanding of the criteria for empirical success? As we saw with our analysis of the olfactory controversy, the general *categories* of empirical success we applied earlier – data accommodation, instrumental reliability, and predictive power – do provide useful tools by which to analyze scientific trends and developments. Still, it is important that their particular instantiations are judged and constantly reevaluated against the requirements of the empirical context in question. Central to the misrepresentation of the olfactory debate was a lacking measure concerning the *qualification* of empirical data and its relevance in light of changing disciplinary objectives in ongoing science. Empirical success has traditionally

<sup>11</sup> Firestein, personal communication 2014.

<sup>12</sup> Even for historical cases it is not uncontested whether Kuhnian paradigms provide us with an accurate account of events, as Hasok Chang (2010) demonstrated with the example of the Chemical Revolution.

been framed as being a measure for or against a theory. But without such fixed theoretical anchor, or an unambiguous theoretical framework, we must conceive of the measures for empirical success differently.

In summary, such measures of qualification, as we have seen, involved: (1) the changing evidential status of data production methods (e.g., psychophysical studies had greater impact at the time of Amoore compared to today); (2) the historically changing relations of data sets to theoretical explanations (irregular SORs); (3) the network strength of data sets (the vibrational model only presents successes in relation to its own framework but does not carry strong impact for general research about receptor behavior); and (4) the temporary fit of an explanation with insights into the empirical characteristics of a target system (e.g., lack of protein data in the vibration theory).

## 5. Conclusion

How must we situate the observational relevance of empirical success in terms of changeable decision vectors? We suggest approaching the dynamics in ongoing science similar to how the practitioners deal with it; namely, by identifying the open empirical questions and prospective value of available experimental implementations to see how they shape current developments. In particular, this can be achieved by combining two factors. The first factor concerns the context of *epistemic appraisal*. We saw that observational relevance is determined by an interactional network of methods. Instead of accounting for individual experiments via categorical pros and cons as accumulative vectors in a competitive decision-vector framing, we may want to reconsider empirical evidence as weighted by its inherent network character. For example, to what extent does an observational result strengthen or weaken the current connections between two or more other models and experimental contexts at a certain time (and under which disciplinary premise)? Or to what degree does an observation integrate previously neutral evidence? Here, we need to be sensitive to the temporal dynamics, in particular, when these interactions shift focus from one group of problem explanations to another.

This way of framing offers a multi-dimensional grid in which empirical evidence is scaled in parallel with other developments. Instead of stipulating scientific rationality to designate a somewhat ahistorical calculation of evidence in relation to competing models, empirical success becomes a moving target that is defined by an inherent network that ties various strands of research to an empirical problem. What determines the dynamics of this network model of scientific decision-making in ongoing science? In this context, the second factor we suggest considering involves *heuristic appraisal*. Heuristic appraisal outlines the potential fertility of future work on a scientific problem and thus concerns the assessment of the *prospective* values in experimental strategies (Nickles, 2006, 2009). In the case of the olfactory controversy we saw indeed that observations count as empirically successful when they are “proactive” in the sense that they open up further avenues of inquiry instead of merely being supportive of a past or current framework (the success of the receptor discovery was not a confirmation of a modeling hypothesis regarding the mechanism of odor detection; rather, it opened new doors about what odor detection actually is and, most importantly, integrated olfaction into the broader context of sensory neuroscience).

Thus, when engaging with current science, philosophical analysis needs to be sensitive to the origins of the objectives in ongoing science before aiming to provide a critical understanding of scientific decision-making. Current science advances fast. It is in a state of constant flux and development, resulting in changeable conceptual narra-

tives. It matters that philosophers of science disentangle the different threads of modeling, and identify the context of the historically substantiated explanations. Only then can we analyze whether scientific hypotheses have remained stable over time or entailed a new modeling approach instead, and invest greater care in understanding the reasons for their respective successes. Science, in this sense, acts not only as the subject of science studies but also their corrective.

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