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► **To cite this version:**

Pierpaolo Andriani, Renata Kaminska. Exploring the dynamics of novelty production through exaptation: a historical analysis of coal tar-based innovations. *Research Policy*, 2020, 50 (2), pp.104171. 10.1016/j.respol.2020.104171 . halshs-03070325

**HAL Id: halshs-03070325**

**<https://shs.hal.science/halshs-03070325>**

Submitted on 2 Jan 2023

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# **Exploring the dynamics of novelty production through exaptation: a historical analysis of coal tar-based innovations**

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## **Abstract**

Theories of technological change fail to account for innovation stemming from affordances of previously developed artefacts. The literature has highlighted that novelty can originate from market needs, from inferences made from scientific theories or be the object of deliberate technology projects in technology-push models. More recently, scholars have suggested that exaptation, defined as the co-option of artefacts for new functions, may constitute a different path to novelty production. However, the link between the existing artefact and the genesis of new functions driving exaptation is underexplored. Through a longitudinal case study of instances of emergence of new technologies stemming from a single compound, coal tar, we show that exaptation plays a role in all novelty production and, in some cases, it is its main determinant. We build a model of exaptive novelty production that captures the interactions between secondary effects of existing technology, affordances, functionalities, and the emergence of new functions. Our model enriches the theory of innovation by integrating both serendipitous and planned processes as well as both artefactual characteristics and human intentionality.

**Keywords:** exaptation, innovation, affordances, serendipity, function

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## 1. Introduction

Schumpeter's distinction between invention and innovation constitutes one of the foundations of innovation and technology studies. The distinction articulates a view of technological change based on the separation between the production of novelty (referred to as invention - be it an idea, a prototype, a technique, or all of them) and the impact of novelty on society (referred to as adoption or diffusion).

In this article we focus on novelty production and particularly on its antecedents. The literature highlights that novelty emerges via two different processes, namely, market-pull and technology-push. Market-pull models (Golder et al., 2009; Hauser et al., 2006; Maggitti et al., 2013), propose that novelty production starts with the identification of a market need that then informs the design of technology to deliver a pre-identified function. Technology-push models, on the other hand, are based on the idea that science and technology advancements are the main source of innovation (Di Stefano et al., 2012; Nemet, 2009). This literature focuses mostly on deliberate science/technology programs and the translation of scientific/technological advancements into new products.

Historian of technology, Arthur (2009), proposes a model of novelty production that partly echoes the market-pull/technology-push distinction. According to Arthur (2009), new technologies can emerge either from the recognition of new market needs (the 'need' channel) or through the discovery of previously unknown effects of natural phenomena (the 'phenomena' channel). A closer look at Arthur's phenomena channel allows to make a more fine-grained distinction between: (1) theory-based mode of novelty production, where novelty derives from the application of scientific theories to solve specific problems and (2) effect-based mode of novelty production, where novelty derives from the serendipitous observation of previously unknown effects of existing artefacts (technologies and materials) that, absent any causally explanatory theory, are directly turned into novelty. While Arthur (2009) pays much attention to the theory-based mode of novelty production, the effect-based mode receives only a brief mention.

We propose a third, exaptive, mode of discovery. Convincing empirical evidence in the serendipity (Merton and Barber, 2004; Yaqub, 2018), exaptation (Dew, Sarasvathy, and Venkataraman 2004; Andriani and Cattani 2016; Garud, Gehman, and Giuliani 2018) and history of technology (Mokyr, 1990)—literatures point out that in addition to market and

science/technology factors, the source of novelty is often found in secondary effects of technologies, artefacts and materials, already deployed in the economy. We argue that the observation of these effects may trigger a discovery process based on the co-option of the underlying technology for a new function. Such secondary effects of existing technologies, however, are ignored in the market-pull and technology-push literature and conflated with science-push factors in Arthur's analysis.

Given this research gap, we raise two questions: first, what is the relative importance of the *exaptive* mode vis-à-vis the other novelty production modes? Second, how is the serendipitous observation of a secondary effect of artefacts turned into novelty? To answer our research questions, we analysed the instances of emergence of major technological discontinuities deriving from one artefact, coal tar. We show that about half of the new radical technologies stemming from coal tar emerged via the *exaptive* mode of novelty production, whereby an unexpected artefactual effect triggered a process giving rise to new-to-the-world functions. The emergence of new-to-the-world functions is accompanied by the co-option of the existing technology into a new domain of applications. This process is blind in the sense that the new function and the domain were unanticipated at the beginning of the novelty emergence process. We also show that, while in the production of novelty based on a deliberate search for functions that satisfy pre-existing needs, *exaptive* processes coexist alongside market-pull and science/technology push modes of novelty production, in instances of *exaptive* novelty production, market and science/theory factors are present, but play an important role in the final phase of the process. Finally, we build a model of *exaptive* novelty production, which illustrates how this mode is more likely than market, science, and technology factors to explore the unknown unknowns leading to radical innovation.

This paper is structured as follows. First, we review the literature on novelty production and exaptation. Second, based on the longitudinal study of over 100 years of coal tar history, we generate new theoretical insights into novelty production. More specifically, we study eight instances of coal tar-based scientific discoveries and build a model of *exaptive* novelty production. Third, we discuss our findings and highlight our contributions. Finally, we describe the implications and limitations of our research.

## 2. Literature review

Market-pull and technology-push have for a long time been two dominant alternative perspectives on novelty production (Di Stefano et al., 2012). Market-based models of new product development (Golder et al., 2009; Hauser et al., 2006; Maggitti et al., 2013) privilege the identification of customer needs as the novelty production starting point. Novelty here concerns the design of an artefact that performs a desired function. However, Reid and de Brentani (2004, p. 170) point out that market-driven novelty production is “*relevant for incremental new product situations*”. They insist that in the case of discontinuous innovation ideas are generated before market needs are identified. Such models are broadly classified as technology-push models (Roberts, 2007; Takey and Carvalho, 2016).

Technology-push models are based on the idea that science and technology advancements are the main source of innovation (Di Stefano et al., 2012; Nemet, 2009). The technology-push literature focuses on deliberate, planned science/technology programs and the translation of scientific/technological advancements into new artefacts, even though their final application may be unknown. In the most influential version of the technology-push argument, i.e. the ‘linear model of innovation’ (Di Stefano et al., 2012; Stokes, 1997), applied science and technology depend on basic science (Stokes, 1997), thus subordinating technology to science and practice to theory (Schatzberg, 2018). Even if the linear model of innovation has for a long time been paradigmatic and continues to influence the way production of novelty is viewed (Balconi et al., 2010; Godin, 2006), it has become subject to growing criticism (Rosenberg, 1994).

Some economists and historians of technology have offered a more nuanced viewpoint on novelty production. For example, according to Arthur (2009), novelty emerges either from the recognition of new needs (the need channel) or through the discovery of unknown effects of natural phenomena (the phenomena channel). However, in his 2009 book, Arthur devotes only a short section to the phenomena channel, which he describes in the following manner: “*typically someone notices an effect, or posits it theoretically, and this suggests an idea of use—a principle*” (Arthur, 2009, p. 119). A closer look at Arthur’s phenomena channel points to the existence of two distinct modes of novelty production: 1) theory-based and 2) effect-based. In the first mode, which echoes the linear model of innovation (Stokes, 1997), novelty emerges from the search for applications of scientific theories (e.g., the observation of atomic fission

contributed to a more refined understanding of atomic structure, which was then used to develop military and civilian applications for atomic energy).

In the second mode, which received relatively little scholarly attention, novelty comes from serendipitous observations of secondary effects of existing technologies and practices, absent explanatory theory. For example, Edward Jenner's (1798) serendipitous observation that people infected with cowpox never contracted the deadly smallpox (Kinch, 2018) led him to the idea of vaccination without any understanding of its underlying causes and dynamics. Roentgen X-ray discovery fits the pattern above. Two serendipitous observations (distant luminescence and differential organic tissue absorption) gave rise in a few months to a technology based on a radiation so mysterious that was called X. The serendipitous observations of secondary effects absent explanatory theory echoes the concepts of exaptation (a) and affordances (b), which we discuss next.

### ***Exaptation***

The concept of exaptation is rooted in Darwin's evolutionary theory. The term *exaptation* was coined by Gould and Vrba (1982). It designates a character, which is fit for its current role (hence *aptus*) but for which it was not designed. It owes its fitness to features present for other reasons, and is therefore *fit (aptus) by reason of (ex) its form, or ex aptus*" (Gould and Vrba, 1982). Based on this idea, Gould and Vrba (1982) developed a new taxonomy of evolutionary change, which can be either *adaptive* or *exaptive* and stressed the paramount importance of exaptation in evolution.

Exaptation defined as the process through which "*characters, evolved for other usages (or for no function at all), later "coopted" for their current role*" (Gould and Vrba 1982), has been used to explore the evolution of technology (Andriani and Cattani, 2016; Cattani, 2006; Dew et al., 2004). In the artificial world, exaptation stands for a process whereby technological modules and/or technological knowledge (Cattani, 2006), developed for one purpose, get co-opted to carry out a different function in a different domain (Andriani and Carignani, 2014; Mokyr, 1998). Exaptation inverts the typical design process by which artefacts are designed to perform a pre-existing function (Alexander, 1964). Instead, a function (often unknown) emerges often serendipitously from an existing artefact.

The new *exapted* function may be new-to-the-artefact or, more rarely, new-to-the-world. In the second case, exaptation may lead to the emergence of a new market via a niche construction process (Beltagui et al., 2020; Dew and Sarasvathy, 2016; Odling-Smee et al., 2003). Indeed, “occasionally, exaptations...open new evolutionary trajectories in complex systems [which] require the co-construction of specialized adaptations and further exaptations, culminating ultimately in the emergence of a new niche (Andriani and Cohen, 2013, p. 7).

Exaptation differs from the process of invention and discovery but shares with them some common features. It differs from invention in the sense that an exaptation is ‘found’ not ‘made’. It is also different from discovery because exaptation concerns the *co-option* of an existing artefact for a new function (although the new function could be discovered). The co-opted technology is often improved or recombined with other technologies to optimally perform the new function. In this case we have a new function and a new technology.

The literature on exaptation in management studies and economics is relatively recent. Several aspects of exaptation are still underexplored.

Functionality, function, and mechanism of action. Artefact co-option across functional domains constitutes the core mechanism of exaptation. However, a function is an ambiguous concept (De Winter, 2010; Lloyd and Gould, 2017; Vermaas and Houkes, 2006). A function may be defined with reference to a market. In this case an artefact designed for market A and co-opted in market B is said to be *exapted*. The definition of a function may also hinge on what the artefact does and how it performs its task. In this case, a market transfer does not automatically confer functional novelty. To clarify the ambiguity inherent in the concept of function, we propose to use Arthur’s (2007, 2009) hierarchy of concepts, which links a function to natural phenomena and his definition of function as a purposeful use of a functionality.

Arthur (2009, 2007) based his analysis of technology on a hierarchy of concepts, linking the natural world with human needs. First, phenomena are natural regularities (e.g., gravity, wind, electricity). They exist independent of observers. Second, a principle of use captures the way phenomena can be harnessed: “*that air pressure falls with altitude is a physical phenomenon; the idea of using this effect to measure altitude constitutes a principle*” (Arthur, 2007, p.277). Third, a functionality expresses the generic effect of harnessing natural phenomena (e.g., the functionality of a GPS is geolocation; the functionality of an altimeter is the measurement of

altitude). Fourth, a function is a purposeful use of functionality. Thus, functions fulfil needs (e.g., geolocation is used to navigate from point A to point B; altimeters to aide assisted landing).

The distinction between function, functionality, and principle of use (in the following we will refer to it as the *mechanism of action*) introduces some nuances in exaptation. Following Kauffman (2000), Andriani, Ali & Mastrogiorgio (2017) and adhering closely to the original meaning in the evolutionary biology (Gould and Vrba, 1982), we refer to exaptation as implying a functional change in what the artefact does, not only in the way it is used. Thus, on the one hand, in some exaptations the co-option is based on the same functionality, as in the example of a GPS system, which was originally used to guide smart bombs from point A to point B and which was later co-opted to guide cars from location A to location B. On the other hand, other exaptations are based on functionality change (in addition to co-option across different markets). One such example is the same GPS system, which is used to measure the presence of volcanic ashes in the sky and it also used as a high precision clocks in ultrafast financial trading. In these cases, exaptations are based on different functionalities. In the volcanic ashes detection case, the new functionality is the change in the transmissivity of the GPS signal caused by volcanic ashes and in the trading case, it is the extreme, space-independent, synchrony of the GPS' atomic clocks.

Historians of technology (Arthur, 2009; Mokyr, 1990) pointed out that innovations that harness newly discovered natural phenomena are likely to be more radical. Likewise, as suggested in Andriani, Ali & Mastrogiorgio (2017), it is plausible that exaptations based on the newly discovered functionalities are also likely to be more radical. The distinction between new-to-the-world and new-to-the-artefact matters because the latter can be the object of intentional search via analogy or other search mechanisms, whereby the former cannot (Felin et al., 2016).

Frequency and importance in innovation. Despite the growing interest in exaptation, there is little quantitative evidence of its importance in innovation. A measure based on potential functions indicates that about a third of innovations is exaptive in nature (Andriani et al., 2017) and that about 10% of exaptations are radical. However, this measure refers to potential and not market-implemented functions. Moreover, the percentage of exaptation that is based on new-to-the-world functionalities and their impact on the economy remains unknown.

Foresight. Exaptation is at least partly an emergent, nondeliberate process (Dew, 2007; Gould, 1991; Kauffman, 2000). However, the probability of exaptive events (what the Nobel Prize for

Chemistry Langmuir defined the "*calculations upon the unforeseen*" (Merton and Barber, 2004, p. 192)) can be *engineered* via *serendipity arrangements* (Garud et al., 2016), i.e. appropriate organizational practices that favour serendipitous discoveries (Cattani, 2008). Exaptive pools (Garud et al., 2016) that capture and systematize organizational memory (Cattani, 2006), including scientific discoveries, provide the elements that may "*become coupled during staged exaptive events designed to increase and harness complexity. The possibilities that emerge from such events can be contextualized within exaptive forums where actors and discoveries become entangled*" (Garud et al., 2018, p. 15).

Process or discovery. There is no consensus in the literature whether exaptation is a protracted process or an instantaneous recognition of a hidden opportunity in an existing technology. On the one hand, the 'need-solution pair' perspective (von Hippel and von Krogh, 2016)<sup>1</sup>, implies the latter. Agents may suddenly perceive that an existing artefact provides a solution to a problem of which they have not previously been aware. The opportunity discovery view in entrepreneurship literature confirms this view. For example, Shane<sup>2</sup> (2000, p. 451) argued that "*people do not search for entrepreneurial opportunities because "opportunity, by definition, is unknown until discovered"; and one cannot search for something that one does not know exists*" (Shane, 2000, p. 451). Moreover, it "*involves the surprise that accompanies the realization that one had overlooked something in fact readily available*" (Kirzner, 1997, p. 72). The effectuation (Read et al., 2010), creation (Chiles et al., 2010) and narrative views (Garud et al., 2016) take a different stance and see the construction of opportunities (including exaptive ones) as a complex process in which distributed agency elements co-evolve within a changing context. Exaptation becomes a time-based process, which depends on technological, human and organizational contexts, including artefactual modularity, affordances (discussed below), and narrative properties, such as temporality, relationality and performativity (Garud et al., 2018).

Exaptation models. If exaptation is a protracted process, how does it unfold? The design-exaptation feedback cycle (Andriani and Carignani, 2014) is rooted in the form-function cycle and focuses on modular systems. The cycle starts from functionality emergence (mostly serendipitous) followed by functionality deliberate selection and terminates with the adaptation of the co-opted artefact. The integrated exaptation model (Andriani and Cattani, 2016) is centred

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<sup>1</sup> The authors do not use the word exaptation.

<sup>2</sup> Interestingly all the cases discussed by Shane in his 2000 papers are exaptive, although Shane does not use the term.

on artefact-agent-context interactions and on affordances leading to functional shifts. Both models are function-centric, that is, both assume artefacts with defined functions at each stage of the model, including the functional shift stage.

### *Affordances*

Arguing that cognition is a relational property, Gibson coined the word affordance to bypass the subjective-objective dichotomy in perception (Gibson, 1977). Affordances are defined as “*the perceived or actual properties of the thing, primarily those fundamental properties that determine just how the thing could possibly be used*” (Norman, 1988, p. 9). Thus, individuals do not perceive qualities residing in the object but merely the object’s *affordances*. The recognition of affordances rests on a non-cognitive process, indicating “*action that is not motivated by conscious thought or that involves information processing and abstract analysis*” Nayak *et al.* (2019, p. 15). Affordances are *opportunities for action* (Stoffregen, 2003, p. 124) that link the artefact and the observer (Glaveanu, 2012). They express the potential to perform a known function more efficiently or a new, previously unknown function (Autio *et al.*, 2018). In the former case the perceiver gives meaning to an artefact through an already known function, as in *a ladder affords climbing and a chair affords sitting*. In the latter, the affordance is *hidden* (Gaver, 1991) and must be discovered. Its related function needs to be articulated in a process that requires exploration, learning and patience.

From its origin in visual perception, the theory of affordances has been applied to explain the dynamics of design (Kaptelinin, 2014). Affordances are defined as: “*what one system (say, an artefact) provides to another system (say, a user)*” (Maier and Fadel, 2009, p. 19). This interaction-based definition splits affordances in two general types: artefact-artefact affordances (AAAs) and artefact-user affordances (AUAs). In the first type affordances determine the behaviour of two artefacts, or modules, acting together. In a design context, AAAs are deliberately designed to satisfy a user’s need, therefore, effectively making artefact-artefact affordances the enablers of artefact-user affordances. In an emergent setting, however, AAAs occur independently from users’ deliberate design and may then spontaneously manifest themselves as unexpected technological effects that a perceptive agent may harness for an existing or emergent need.

The interaction between AAAs and AUAs points to a general property of affordances, namely, sequentiality. The latter refers to “*situations in which acting on a perceptible affordance leads to information indicating new affordances*”(Gaver, 1991, p. 4).

The theory of affordances has recently been used to explain novelty production in the domains of entrepreneurship and innovation (Nayak et al., 2019). For example, scholars have argued that affordances constitute the initial step of the exaptation process (Autio et al., 2018; Felin et al., 2016; Nayak et al., 2019). The theory of affordances constitutes a promising avenue for exaptation theory and shows the potential to clarify several problems of exaptation theory. First, exaptation theory rests entirely on the concept of function in its relationship with an underlying form. Function however is form independent (Maier and Fadel, 2009) whereas exaptation is strictly form dependent (different forms would give rise to different exaptations). The misalignment between form and function in relation to exaptation has generated ambiguity that has plagued the concept of exaptation in the artificial domain since the beginning. This issue is non problematic for known function but becomes critical for functions that are discovered through exaptation. Linking exaptation to affordances promises to strengthen both the theory and practice of exaptation, because it anchors functional change and consequently exaptation in affordances, which are strictly form dependent. Second, such approach has the potential to shed light on the initial phases of exaptation.

In general, the review of the literature on exaptation uncovers several unexplored aspects of the dynamics of exaptation, in particular, the initial phase of exaptation, the relationship between exaptation and affordance, the role of function and functionality, and the modalities of exaptive innovation triggered by secondary effects of technologies. To elucidate these points, we focus on two research questions: first, what is the relative importance of the exaptive mode vis-à-vis the other novelty production modes? Second, how is the serendipitous observation of a secondary effect of artefacts turned into novelty via exaptation?

### **3. Methods**

The objective of this research is to enrich our understanding of the innovation process and, more specifically, its initial stage. The nature of the research defined in terms of ‘how’ (novelty emerges) and the exploratory nature of this work pointed to the use of a qualitative case study method (Yin, 1994) with the focus on past rather than contemporary events (Kipping et al.,

2014). This methodological choice is in line with a growing consensus that history and social theory need to be more often brought together (Kipping and Üsdiken, 2014; Weatherbee et al., 2012).

The literature highlights the differences in epistemological positions of historians and qualitative case study social scientists, mainly in relation to evidence, explanation, and temporality. While in general social scientists prefer self-generated data, analysis and chronology, historical research privileges archival sources, narration and periodization (MacLean et al., 2016). The historical method uses a retrospective point of view to establish significance (i.e., causes, consequences, and meanings) of events in light of antecedent or subsequent developments. In other terms, “*historical reasoning emphasizes temporally contextualized explanations*” (Bucheli and Wadhvani, 2014, p. 4). Moreover, whereas social scientists privilege explicit articulation of theoretical constructs and detailed explanation of methodologies used, historians tend not to articulate their methods, suggesting implicit embedding of theory within analysis (MacLean et al., 2016). This last point has recently resulted in calls for more disclosure relative to the methodology used to analyse historical sources (Kipping and Üsdiken, 2014).

Notwithstanding some of the above mentioned differences and debates, scholars have highlighted similarities between qualitative case studies and historical methods with the most important one being the fact that their purpose is to discover (or verify the existence of) general patterns, rather than to discover laws or test hypotheses (Gottschalk, 1951). Also, both navigate between induction and deduction<sup>3</sup> in the theory building process (Yates, 2014). As a result, researchers have pointed to reasons why historical methods are compatible with and enrich qualitative case studies of innovation. First, historical methods allow to explore the temporal order of roles played by the different agents (inventors, users, technologies, needs, etc.) involved in the innovation process and provide a longitudinal perspective on how these roles change over time (Page and Schirr, 2008; Rosenzweig et al., 2015). Second, historical method involves collecting data from a variety of independent sources that describe the sequence of events close to the time of their occurrence, providing the necessary detail and, above all, a distance allowing to interpret the way innovation emerged from its technological, social and institutional context (Hargadon and Douglas, 2001).

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<sup>3</sup> The words induction-deduction hides a complex dynamic, which tend to oversimplify the reality of theory development.

Because of the similarities and the potential of mutual enrichment, many authors suggest a possibility of creative synthesis and building of conceptual and methodological bridges between the two camps, predicated on the idea that history can enrich theorization on innovation through its power to “stretch the scope of explanations” (Lippmann and Aldrich, 2014, p. 128). Kipping and Üsdiken (2014) propose that the historical approach to innovation studies is a means of incorporating historical complexity within the theorization process and call it *historical cognizance*. Going a step further, Stinchcombe (2005) puts forth that historical methods can greatly contribute to addressing causal questions in social science. Consequently, along with Üsdiken and Kieser (2004) and Maclean, Harvey and Clegg (2016), we adopted an ‘integrationist’, ‘history to theory’ (Kipping and Üsdiken, 2014) approach to qualitative case studies and historical analysis with the objective to generate historically-informed new theoretical insights into the novelty production process.

### ***3.1 Selecting the Coal Tar Case***

Observation of phenomena may constitute a starting point for both historical researchers and qualitative case study scholars. Both use theoretical rather than statistical sampling (Graebner and Eisenhardt, 2004). In contrast to random sampling from populations used in theory testing studies, theoretical sampling emphasizes selecting cases based on their likely contribution to improved theory about the focal phenomenon. Theoretical sampling involves focus on one or a small number of cases (Eisenhardt and Graebner, 2007), which can be, for example, organizations, projects or processes with multiple temporal phases.

Theory building case-based research is particularly useful when existing theories are inadequate to explain the focal phenomenon (Volmar and Eisenhardt, 2020). The researcher must, however, make sure that the selected case provides all the categories relevant to the theory, which is in the process of elaboration (Eisenhardt, 1989; Glaser and Strauss, 1967; Miles and Huberman, 1994).

Several cases of serendipitous technological discoveries of coal tar related technologies and applications, which could not be explained by the existing theory dominated by the need-based and theory-based models, suggested that some other mechanisms must have been at play in the emergence of novelty. Therefore, in order to better understand the different mechanisms involved in novelty production, we decided to reach beyond the anecdotal evidence and dig into

the entire century of the coal tar history, starting from Thomas Perkin's discovery of artificial dye in 1856 and ending, in the 1950s, with the emergence of psychopharmacology. Coal tar fits the criteria of a multiple historical case study analysis because a century-long history of highly diverse innovations allowed the researchers to spot patterns without the risk of anecdotal selection bias. Data sources are public, removing the risk of researchers' bias in the production of data. For parsimony and clarity, we restricted the analysis of coal tar innovations to the pharmaceutical and medical industries, excluding from scrutiny other industries in which coal tar played a significant role such as for example, explosives, photography, or perfume.

### ***3.2 Data Collection and Analysis***

Scholars using qualitative case studies and historical methods differ the most in the type of data they collect. While qualitative case-based research in innovation studies is concerned with the modern-day phenomena and privileges ethnography, interviews and observation as primary sources of data, historical research involves "collecting, verifying, interpreting and presenting evidence from the past" (Golder, 2000, p. 157). Yates (2014) notes a certain distrust in the other camp's data preference and highlights that both would benefit from broadening their spectrum of acceptable data. Since our objective was to better understand how novelty production happened in specific instances in the past, we collected historical data reporting on the different cases of coal tar related discoveries.

Coal tar records are available since its synthesis at the end of the 18th century. We collected evidence on the cases of coal-tar derived technology emergence from primary sources, through publicly available repositories of historical archives. To better understand the scientific aspects of new technologies, we explored academic databases (e.g., PubMed) for medical and pharmaceutical articles. When possible, we privileged technical sources such as medical manuals, chemistry books or scientific papers published as close as possible to the event. Additional primary evidence came from public libraries and exhibitions. To avoid ex post interpretation bias by the authors of the evidence, we prioritised sources written as close to the events as possible. For example, Lister's papers, medical manuals, and Lister's hospital Ward Day Books. Writings on the past from a later date (historical books, memoirs, biographies, papers, etc.) constituted the secondary sources we used for the purpose of triangulation.

Data collection and interpretation was a long and iterative process, which evolved alongside our theory building. To overcome a certain number of issues relative to the nature of historical data (e.g. incomplete, temporally remote records, created in specific historical contexts by different authors for a diversity of reasons rather than by the researcher to answer a specific research question), we followed a set of analytical and interpretative processes drawing on “*both the historiographical tradition and qualitative methods in organization studies*” (Kipping et al., 2014, p. 312). This methodology involved three main elements: (1) a critical evaluation of the sources of evidence to determine its internal and external validity; (2) triangulation of various sources to reduce bias and increase the robustness of the results; and (3) an iterative process of situating the texts within their historical context. It is important to note that the above processes were not necessarily performed one after another, in a linear manner. Rather, they often co-occurred.

After each round of data collection, we proceeded with the critical evaluation of the sources to establish their validity and credibility (Berg and Lune, 2004). Source validity was established through external source criticism, which involved a careful examination of the authors (their legitimacy, professional background, etc.) and the time/place/context of the text production. Source credibility was established through internal source criticism involving selection of texts written as close as possible to each instance of idea generation. We privileged accounts by people who were directly involved in these instances. We made sure that the authors of our primary sources were trustworthy. This involved verifying that they had the necessary competency to report on the circumstances surrounding the emergence of new ideas and no apparent reason to hide any facts.

Our research was a multiple-case study (Eisenhardt, 1989) based on historical data. We started by the within-case study analysis before proceeding with the inter-case analysis. The within-case study analysis involved organizing a large quantity of data and writing detailed case descriptions allowing for unique patterns of each case to emerge. To understand how new ideas emerged in each case, we first identified the new coal tar-based discoveries in our sources and then, organized the instances of their emergence chronologically and constructed chrono-stories relative to their discoveries. We focused on the main actors involved in the generation of new ideas and on the context of idea emergence. The objective of the inter-case study analysis was to generalize patterns across cases (Eisenhardt, 1989).

As highlighted by Maclean, Harvey and Clegg (2016), the validity of research using historical data derives from historical veracity and conceptual rigor, the former depending on the faithfulness to and reliability of available evidence and the latter on the quality of theoretical contributions. Our critical evaluation of the sources of evidence contributed to historical veracity. We also elaborated a specific analytical protocol to assure the quality of our theoretical contributions. Independent analysis of evidence by the two authors constituted an important element of this protocol. Differences in the interpretations were discussed and confronted with further evidence allowing to reach an agreement on the final interpretation of events leading to idea emergence. For example, in the Lister's case, virtually all the sources reported that Lister generated his antiseptic surgery idea after reading Pasteur's papers in 1865. The exception is Wootton (2006), who argued the contrary<sup>4</sup>, albeit without supporting evidence. To verify this, we searched for additional publications<sup>5</sup> by and on Lister. This brought us to identify a particularly rich primary source of evidence, Lister's Ward Day Books, where he reported his medical notes after visiting patients. The literature claimed that the Ward Day Books for the year 1865 had gone missing (Fisher, 1977, p. 135). But they exist at the Glasgow City Archives. We were granted special permission to access the documents and found evidence that Lister started experimenting with antiseptic surgery in 1864, not 1865 as all the historical sources claimed.

We also engaged in extensive triangulation of sources while interpreting another complex case of Laborit's discovery of the first antipsychotic drug, where there was no consensus on Laborit's role. We found two different views. Some authors (e.g. Caldwell, 1978) believed that from the beginning Laborit was looking for an antipsychotic drug. Most of the scholars (López-Muñoz et al., 2005; Raviña, 2011) instead argued that the emergence of the antipsychotic drug was a serendipitous discovery in the quest for something else. The analysis of the internal notes of Rhone Poulenc, the pharmaceutical company that provided Laborit with chlorpromazine, shows no mention of psychiatric usages, proving the unintentional nature of the discovery. This interpretation was further corroborated by Laborit's autobiography (Rouleau and Laborit, 1982) and by Swazey (1974), who was tasked by the National Institute of Mental Health to determine the truth in the 'antipsychotic saga'.

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<sup>4</sup> According to Wootton, Lister learnt about the germ theory of disease not from Pasteur but from one of the papers by Schwann published in 1830s.

<sup>5</sup> About 31 books and more than 50 papers, after excluding hagiographic or unreliable material. List of publications is available upon request.

Our analysis involved frequent moving back and forth between the historical sources and our research questions in developing interpretations that best fit the progressively increasing amount of collected data. Theory was confronted with detailed historical evidence to test its explanatory power and identify explanatory limitations. The value of our research lies in confronting the existing theory on the generation of new ideas with the empirical evidence and enriching the theory. Figure 1 illustrates the links among the original compound, coal tar, its derivatives, and the related innovations.

## 4. Results

Our first result consists in identifying instances of the emergence of radical innovations stemming from one compound, coal tar. The gas extracted from coal became popular in the first part of the 19<sup>th</sup> century as illumination by gas substituted oil and candles. Gasification left residues such as light oil and coal tar.

Figure 1 represents the genealogical tree of the major innovations between 1834 and 1952 rooted in coal tar and its derivatives. We identified eight major cases of radical innovation, four of which are detailed in this section while the other four are described in appendix 1. The four cases we present below capture the most salient aspects of novelty production related to exaptation.

< <please insert figure 1 about here>>

Friedlieb Runge was the first chemist to analyse coal tar and extract aniline and phenol (Ihde, 1984). Coal tar-based radical innovations started in 1856 with Thomas Perkin's discovery of artificial dyes. Section 4.1 presents the analysis of the transformation of coal tar from a noxious by-product to the "queen of the by-products of many manufactures" ("Utilization of Coal Waste," 1876, p.159).

### ***4.1. The discovery of artificial dyes and the emergence of the modern chemical industry***

Perkin's discovery of aniline purple, the first industrially produced artificial dye, set in motion the progression of the genealogical tree displayed in Fig. 1. In 1856, Perkin, an 18-year-old university student, was tasked with synthesising artificial quinine from coal tar. Quinine was the only effective remedy for malaria. It was scarce, expensive, and crucial to supporting colonial

expansion. Perkin started from a component of coal tar, that is, aniline. He failed to synthesize quinine but, instead, obtained a substance with a strong purple colour, which he called mauveine. While “chemists came across new colours at random almost every week, and just as easily dismissed them as being an undesirable or irrelevant side-effect of their missions” (Garfield, 2002, p.35), Perkin paid attention, probably because he was an amateur photographer and painter. A test on silk (probably accidental) revealed mauve's remarkable resistance to light and washing. Probably because of the silk test, Perkin conceived the idea of using mauve as an artificial dye. We know that the discovery was unintended (Perkin wrote: *this discovery did not in any way originate from a desire to produce a colouring matter, as is sometimes stated, but in experiments of a purely theoretical nature* (Perkins, 1915, p. 5) and that it wasn't derivative from a theory (*at the date of its introduction very little was known of the chemistry of colouring matters* (Perkin, 1915, p. 76)). Perkin abandoned his academic career and, with family money, launched Perkin & Sons, the first industrial dyes manufacturing company.

The consequences of Perkin's discovery and the commercial success of mauve were unprecedented in scale. Coal tar dyes triggered the emergence of the modern synthetic chemical industry, which became one of the pillars of the second industrial revolution (Chandler, 2005). In the space of two decades, more than 2000 dyes were synthesized by hundreds of companies (Murmah, 2003), making Perkin “*the creator of the modern chemical industry*” (Johnston, 2008, p.84). Thus, an exaptation of a coal tar component (i.e. aniline) was instrumental in the emergence of a new industry. The discovery of mauve was not the result of purposeful research work meant to discover artificial colours, nor did it evolve out of a robust knowledge base or clearly articulated need.

#### ***4.2. Emergence of antiseptic surgery***

Carbolic acid (hereafter CA), a component of coal tar, originally isolated by Runge in 1834, played a central role in the emergence of modern medicine. CA provided the seeds of the idea of antiseptic surgery that Joseph Lister developed and diffused between 1865 and 1885. As a result of his advancements, and despite strong initial resistance by his contemporaries, Lister is considered the ‘father’ of modern surgery (Fisher, 1977) and modern medicine (Wootton, 2006). In fact, “*No breakthrough before Lister's, except perhaps the discovery of anaesthesia, had*

*contributed to such an incredible advancement in relationship to the surgical arena”* (Toledo-Pereyra, 2010, p. 241).

The dominant interpretation of Lister’s contribution links to his unique background in microscopy and chemistry, which prepared him to understand the value of microbiology (an emergent science) developed by Louis Pasteur. According to such view, Lister applied Pasteur’s work on the germ theory of disease to surgery. Lister seems to have recognized that Pasteur’s work on fermentation explained infection and consequent suppuration in post-surgery patients. A selective reading of Lister confirms this view: *“a flood of light has been thrown upon this most important subject by the philosophic researches of M. Pasteur, who has demonstrated ... that ... the germs of various low forms of life ... now shown by Pasteur to be its essential cause”* (Lister, 1867, p.2). Having recognized in Pasteur’s work a causal theory of post-infection surgery, Lister sought a substance that killed germs (but not the patient) and found carbolic acid. The process appeared to start with a need (i.e., to overcome the high mortality rate in surgery), followed by the development of a theory (i.e., Lister applied and extended Pasteur’s theory to understand the cause of infection in surgery), which ultimately led to the search for technology to prevent and eliminate infection.

For a long time, historians believed this sequence of events leading to Lister’s innovation. This view came from two main sources written long after the events: the introduction to Lister ‘Collected Papers’ written by a group of close Lister collaborators in 1909 and Lister biography written by John Godlee<sup>6</sup> (1918). The former unambiguously attributes to the reading of Pasteur the origin of the antiseptic surgery idea. The latter reports the seminal event that led Lister to discover Pasteur. Godlee reported that in 1865, Thomas Anderson, a professor of chemistry and Lister’s colleague at the University of Glasgow, drew Lister’s attention to Pasteur’s work. No prior evidence of this conversation exists elsewhere.

More recently, a historian of science, David Wootton (2006), suggested that the dominant interpretation was wrong. Wootton (2006) suggests (but without new evidence) that, rather than learning the germ theory from Pasteur, Lister learned an earlier version of the germ theory from the 1830s papers published by Schwan. However, Wootton’s interpretation concurs in that theory preceded practice in the development of the antiseptic method.

The dominant interpretation fails to explain the following:

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<sup>6</sup> Godlee was Lister’s nephew, disciple, colleague, and biographer.

First, it contradicts Lister's clear statement that "*This mode of experimenting, as described by Pasteur, besides charming me by its simplicity and conclusiveness, had a further special interest for myself, because, before knowing of it, I had explained to my own mind on the same principle [our emphasis] the remarkable fact, previously quite inexplicable*" that infection does not follow when a fractured rib punctures a lung" (Lister, 1868, p. 60). In other words, Lister states that he developed his germ theory of diseases independently of Pasteur. Moreover, "*In a letter to his father written in 1866, however, he said that he had made one of the ten greatest discoveries in world history*" (Wootton, 2006, p. 226). Lister needed the authority of Pasteur to convince his critics and hence downplayed his own role in the genesis of antiseptic surgery (Wootton, 2006).

Second, the known chronology of events does not fit the dominant interpretation. Lister's discovery of CA preceded his reading of Pasteur: "*In the course of the year 1864 I was much struck with an account of the remarkable effects produced by CA upon the sewage of the town of Carlisle, the admixture of a very small proportion not only preventing all odour ..., but ... destroying the entozoa which usually infest cattle fed upon such pastures*" (Lister, 1867, p.326). Lister's experimentation with CA started toward the end of 1864<sup>7</sup>, whereas the dominant interpretation, in a classic linear fashion, states that Lister looked for a suitable antiseptic after learning about Pasteur's theory.

Third, in Lister's own account there is no evidence of Pasteur. In fact, Lister wrote that "*the applicability of carbolic acid for the treatment of compound fracture naturally occurred to me*" (Lister, 1867, p.326).

An analysis of historical evidence and Lister's writings suggests that the route to the genesis of antiseptic surgery was exaptive. We argue Lister's accidental discovery of the properties of CA started the process that led to the development of antiseptic surgery. A careful reading of Lister's Ward Day Books<sup>8</sup> shows the following. Lister used CA for the first time on December 8, 1864, not March 1865 (as universally stated in the literature)<sup>9</sup>. Lister used CA first to combat suppuration and later on to prevent infection. The former point was not revolutionary whereas

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<sup>7</sup> In a letter to his father dated 28 January 1866, Lister wrote: "I am trying some more experiments with carbolic acid, etc., upon healing sores and wounds." Godlee later reported: "It is known that these experiments had been in progress for more than a year" (Godlee, 1918, p.162).

<sup>8</sup> The authors took pain to trace Lister's Ward Day Books, which are consultable upon permission at the City of Glasgow Archives. Lister's Ward Day Books starts in 1861. Lister's main biographer (Fisher, 1977) reports that Lister's 1865 Ward books went missing. This is inexact. Only the period April-September 1865 is missing.

<sup>9</sup> With one exception: BBC journalist Martin Goldman who reported the same information in 1987 (Goldman, 1987).

the latter was. At this point Lister had clearly introduced in the practice of surgery the antiseptic/aseptic method of surgery, almost certainly before reading Pasteur. Lister was clear about the genesis of the antiseptic idea: “*My attention for several years having been much directed to the subject of suppuration ..., I saw that such a powerful antiseptic was peculiarly adapted for experiments with a view to elucidating that subject, and while I was engaged in the investigation, the applicability of carbolic acid for the treatment of compound fracture naturally occurred to me*” (Lister, 1867, p.326).

Lister’s idea matured in two stages. First, Lister - the scientist - co-opted CA to test his hypothesis that suppuration was caused by decomposition (“*powerful antiseptic was peculiarly adapted for experiments*”). Lister’s thinking was that if CA killed micro-organisms in sewages, it could do the same in wounds. He noticed that one of the symptoms of decomposition, the putrid odour, was the same. Second, Lister- the scientist and the doctor - conceived the idea (‘*naturally occurred to me*’) to co-opt CA for an additional function of preventing suppuration during his experiments and surgical practice to control suppuration (“*while I was engaged in the investigation*”). Lister’s idea linked his decade-long rumination on the causes of infections with the property of CA of killing germs in the sewage of Carlisle. Lister’s choice of words indicates the lack of systematic search for materials that served a pre-defined use. Most importantly, Lister makes no reference to inference from Pasteurian theory.

Consequently, the idea of experimenting with the CA, we suggest, came from an analogy, and emerged as a result of a successful practice in an unrelated field. In this case, doing precedes knowing. This evidence indicates that one of the most important 19<sup>th</sup> century medical innovations was a result of the exaptation of CA, a component of coal tar.

### ***4.3. The emergence of pharmacological psychiatry***

The development, in 1952, of the first antidepressant, iproniazid, and the first antipsychotic drug, chlorpromazine, seemed to have followed the same path. These discoveries represented epochal events that contributed to the creation of the pharmacological psychiatry, a new scientific and therapeutic sector of pharmacology creating a new pharmaceutical market.

#### *From aniline to the first antidepressant*

Iproniazid originated in a class of molecules called hydrazine, synthesized from aniline in 1876 (Mendola, 1890). For a long time, no one paid attention to the biological activity of

hydrazine, which incidentally became infamous for powering the V2 missiles that bombed London in World War 2. After the war, several pharmaceutical companies experimented with the large left over cache of hydrazine (Shorter, 2009) and observed hydrazine antituberculous activity (Madkour, 2004). In 1951, three groups<sup>10</sup> independently synthesized two antituberculous molecules: isoniazid<sup>11</sup> and iproniazid. During clinical trials in 1952, the two molecules (especially iproniazid) showed an exceptional activity against tuberculosis but caused a curious and unexpected side effect of euphoria. Euphoric patients were “*dancing in the halls tho’ there were holes in their lungs*” (Sandler, 1990, p.136). Although other substances were previously used<sup>12</sup> (Shorter, 2009), iproniazid became the first antidepressant representing a radical discontinuity in psychiatry (Raviña, 2011). Three aspects are particularly important:

1. The discovery of iproniazid’s effect led to research that culminated in the formulation of “*a radical new hypothesis about the cause and treatment of depression. Depression ... was a result of a ‘chemical imbalance’ of neurotransmitters in the brain*” (Mukhurjee, 2012, p.2). Iproniazid’s case is therefore an example of how practice anticipates and stimulates the emergence of theory.
2. The discovery of an antidepressant drug helped define the underlying condition: “*not only were there no antidepressants ... but depression as it is now understood did not exist either*” (Healy, 2000, p.394). The iproniazid effect on depression was so unexpected that one of the discoverers, Kline, failed to convince Hoffman Roche that it “*had a valuable opportunity rather than the other way around*” (Li, 2006, p.142).
3. Linguistic innovation also highlights the originality of the discovery. The term ‘antidepressant’ was coined to describe the effects of these new drugs (Ramachandrai et al., 2011). Its diffusion, together with the word psychopharmacology, follows the term iproniazid (Fig. 2).

<<please insert figure 2 about here>>

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<sup>10</sup> Hoffman-La Roche and Squibb in the United States and Domagk’s group in Germany.

<sup>11</sup> Isoniazid was synthesized from hydrazine in 1912, called synthesized isonicotinic acid hydrazide.

<sup>12</sup> Namely, amphetamine and barbiturates to treat depression symptoms.

### *From methylene blue to the first antipsychotic*

The discovery of the first antipsychotic derived from the methylene blue, and indirectly from coal tar, is another radical innovation of exaptive nature. Methylene blue belongs to a class of molecules called phenothiazine and was the first phenothiazine ever discovered. The basic nucleus of phenothiazine was synthesized in 1883 in the textile industry by modification of methylene blue (Ban et al., 2004). While searching for antimalarial effects of phenothiazine, the French laboratory Rhone Poulenc discovered its antihistaminic (anti-allergic) properties, leading to the development, in 1947, of a drug called Fenegan (López-Muñoz et al., 2005).

This discovery intersected the work of a French military surgeon, Henry Laborit, a very creative, controversial, and eclectic surgeon, who, after World War 2 noticed that the organism's self-defence against stressful events may become self-destructive. In contrast with mainstream medical theory and practice, Laborit prolonged the vegetative state that accompanied anaesthesia to reduce surgical shock, thereby controlling patient reactions to surgical traumas. Laborit observed that after the administration of Fenegan, *“our patients are calm, relaxed and euphoric even after major operations; they appear to really suffer less”* (Rouleau and Laborit, 1982, p.267). Contrary to current belief, Laborit reasoned that fear and anguish might have a chemical basis and be part of the body's reaction to aggression. It followed then, that chemicals might affect the mood. As a result, Laborit asked Rhone Poulenc to find, in the family of Fenegan, *“a lytic agent that would prevent surgical shock, through depressant actions on the central nervous system”* (López-Muñoz et al., 2005, p.117). In other words, Laborit aimed to find a potentiator of anaesthetic. Rhone Poulenc looked through its previous research on phenothiazines and found one molecule (later called chlorpromazine) that one of their chemists, Charpentier, prepared in 1944 and then ignored. Rhone Poulenc sent chlorpromazine to several doctors for testing, accompanying the drug with a note stating that Laborit had tested chlorpromazine as a potentiator of anaesthesia and that it exhibited collateral effects when used with anaesthetics, analgesics, and hypnotics (Rouleau and Laborit, 1982, p.70). There was no reference to psychiatric use (Swazey, 1974).<sup>13</sup>

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<sup>13</sup> Rhone Poulenc mentioned potential psychiatric uses of chlorpromazine in its internal notes in 1951–1952 (Swazey, 1974, pp.92–100). However, it failed to appreciate the importance of this finding and mentioned specific applications for schizophrenia and manic states (in March, 1952) only after Laborit's paper anticipated such uses as a sleep potentiator (Laborit et al., 1952).

In 1952, Laborit published a paper suggesting the use of chlorpromazine in psychiatry to improve sleep and avoid the use of barbiturates. He persuaded some psychiatrists to try chlorpromazine as an alternative to electroshock (López-Muñoz et al., 2005, p.118), which was then the only remedy against severe psychoses. The results were astonishing: the first patient, Jacques Lh, an extremely agitated and manic case, left the hospital after three weeks of treatment and resumed a normal life (López-Muñoz et al., 2005). Chlorpromazine was called “*the aspirin of psychiatric hospitals*” and became the leading treatment of schizophrenia (Rouleau and Laborit, 1982, p.71).

This discovery brought about profound changes in psychiatric institutions. “*By May 1953, the atmosphere in the disturbed wards of mental hospitals in Paris was transformed: straitjackets, psychohydraulic packs and noise were things of the past! Once more, Paris psychiatrists ... became pioneers in liberating their patients, this time from inner torments, and with a drug: chlorpromazine. They accomplished the pharmacologic revolution of psychiatry*” (Caldwell, 1978, p.30). Another significant change was that the number of mentally ill patients at psychiatric hospitals decreased rapidly: “*in the US, from about 5.5 million patients in 1950 to about 400,000*” (Raviña, 2011, p.59). By legitimizing the idea that “*a drug could influence the course of a major psychosis*” (Maxwell and Eckardt, 1990, p.119) and that the cause of psychosis was a chemical malfunctioning of the brain (Tone, 2008), chlorpromazine contributed to the emergence of a new field (but also new words, such as, antipsychotic, psychopharmacology and biological psychiatry).

## **5. Discussion**

Theory highlights that novelty may derive from needs (market-pull processes), from science/technology (theory-driven or technology-push) or from exaptive (secondary effects of artefacts turned into affordances) processes. In Table 1 a and b, we map the presence or absence of these three modes in radical innovations stemming from coal tar to evaluate the frequency of their occurrence. Their presence (or absence) is determined in the following way: need is a factor if the main result of the research (or part of) is arrived at in the quest to satisfy the original need. Theory is a factor if the main result of the research (or part of) is arrived at by inference from

theory<sup>14</sup>. Affordance is a factor if the main result of research (or part of) is a direct consequence of the serendipitous emergence of a technology affordance. Whereas Table 1 a synthesizes innovation cases where all three innovation modes are present.

<<please insert table 1a about here>>

Table 1b presents cases reported above, where exaptation via artefact affordances played the most important role in novelty production.

<<please insert table 1b about here>>

Based on the analysis of events of radical innovation, we built a model of exaptive novelty production (Figure 2). We found that the exaptive novelty production process was composed of three stages: 1) emergence of unusual effect, 2) emergence of affordances, 3) discovery of a new function. These stages are separated by two gates: 1) the ignorance gate and 2) the usefulness gate.

<<please insert figure 3 about here>>

The first stage of the exaptive process starts from the emergence of an unusual effect of an artefact during a purposeful research in domain A. Gate crossing demands two capabilities: signal detection and reality/novelty establishment for the new effect. Following Firestein (2012), we call such filter the ‘ignorance gate’ (see Figure 3) because gate crossing signifies the discovery of previously unknown areas of ignorance. The newly discovered ignorance also discloses potential new research areas.

The effect can be observed or not and its detection depends on ‘mind preparedness’. The latter is a non-cognitive process which depends on “*empirical sensitivities*” defined as a tacitly transmitted or developed “*finely-honed attunement to environmental solicitations and the*

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<sup>14</sup> By absence of theory we do not mean that anyone could have arrived at the discovery, implying that specialism does not matter; nor we mean that the discoveries were time-independent implying that they could have happened at any point in time and in presence of very different theoretical bases. We mean that the available theory was not instrumental in the discovery dynamics.

*discernment of affordances*” (Nayak et al., 2019, p. 283). The attunement is a key characteristic of the ‘prepared mind’. Any researcher involved in a deliberate search is potentially exposed to two types of signals: the expected ones, to which the researcher is sensitized, and the unexpected ones, to which the researcher may not be predisposed. For example, in the antidepressant case, the expected signal concerned the organismal reaction to the antibacterial drug. The unexpected one concerned a psychological signal (euphoria) to which the pathologists were not predisposed. A finely-honed attunement enables a researcher to discriminate between the two signals.

Signal detection triggers the exaptive process if it elicits the questions: is the effect real and novel? Does the observation carry information about an unknown phenomenon or is experimental error<sup>15</sup> or noise? If not, is it something previously known and thus not worth of further inquiry? Signal detection failure is frequent when the effect conflicts with a dominant paradigm<sup>16</sup>. Reality/novelty attribution depends on what Shane (2000) calls *prior knowledge*, which creates a ‘knowledge corridor’ (Shane, 2000, p. 452) between the domain of observation and the emergent domain. As knowledge concerning the observation domain is taken for granted, the prior knowledge that is necessary to create a corridor between the domain of observation and the emergent domain concerns the emergent domain. Therefore, if the two domains coincide, that is when the emergent effect is rooted in the science and technology of the observation domain<sup>17</sup>, then prior knowledge exists automatically. If they diverge, like in the case of pathologists observing a psychological effect in the antidepressant case, then lack of prior knowledge regarding psychiatry may impede the reality and novelty attribution by the agents. The presence or absence of prior knowledge overlap introduces a stochastic element in the ignorance gate.

The reality/novelty attribution creates a new research context potentially leading to a new research program. Before, researchers work with an artefact A, afterward, with a new artefact  $\bar{A}$ , which exhibits a new effect.

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<sup>15</sup> The effect of penicillin on bacterial growth was noticed several times before Fleming (Brown, 2013) but often discarded without understanding the importance or novelty of the observation.

<sup>16</sup> The bacterial cause of ulcer is a paradigmatic case. Several gastroenterologists had noticed the presence of bacteria in the stomach of ulcerous patients only to dismiss the observation as an experimental error. Stomach was too acidic to permit bacterial life. In 1982 Warren and Marshall published on the causative role of stomach bacteria in ulcer, because they decided that their experimental observation of bacteria in ulcerous stomachs was not an error. They were awarded the Nobel Prize for Medicine in 2005.

<sup>17</sup> In the Post-it and Teflon cases, the unexpected effect concerned the domain of chemistry of competency of the researchers.

The second stage of the exaptive innovation process involves the uncovering of affordances. The acceptance of the reality/novelty attribution raises two general questions related to artefact-user and artefact-artefact affordances. The first is prospective: does the new behaviour afford new functionalities and functions that users can exploit to solve problems and satisfy their needs? In other words, does the new behaviour cause the emergence of new artefact-user affordances for artefact  $\bar{A}$ ? The second is retrospective: what unknown complementarities regulating the interaction within the components of artefact A and/or between A and its context (artefact-artefact affordances) enabled the emergence of the new effect? In other words, new effects push researchers to understand two sets of affordances: affordances of the new artefact  $\bar{A}$  and affordances enabling the emergence of  $\bar{A}$  itself. The distinction between effect emergence and affordances generated implies that affordances can be deliberately and cognitively sought for once a new effect has been detected (rather than perceptually and non-cognitively noticed during the process of emergence of a new use).

The transition between affordances and functionality/function stage is conditional on crossing the 'usefulness gate'. Usefulness gate crossing implies overcoming "*the boundary that emerges between the domain of science and the domain of use*" (Garud et al., 2018, p. 10), in other words, turning an affordance into a function. Two factors help crossing the 'usefulness gate' (Figure 3): insight and affordance-functionality distance.

An act of insight (Usher, 1954) is a cognitive process that links in a new synthesis two or more fields that were held in the inventor's mind at different levels of consciousness. As Usher put it, insight is to '*bring the two premises under one roof*' (Usher, 1954, p. 64). An act of insight is part of a multistep cumulative synthesis process of invention. Insight is a local process enabled by the specific stage in which the actor is situated. There are two aspects to stage setting: 1) *the field of direct perception* and 2) *the field of imaginative construction* (Usher, 1954, p. 74). The former leads to emergence of creative dissonance and corresponds to the first part of our model. The second is the linking of the dissonant aspects in a new synthesis. In our model an act of insight concerns the translation of an affordance into a functionality, that is, the process of abstracting from a specific occurrence of an effect to a general functionality, which links the generic affordance with a specific use. In Perkin's case, for example, this involved the transformation of the serendipitous appearance of aniline purple into the idea that chemistry could create new artificial colours on demand usable in industry. In the antidepressant case, this

involved going from the observation of induced euphoria to the idea of using synthetic drugs to alter patients' mood and control symptoms. In the antipsychotic case, this involved moving from the observation of induced quietude to the idea of inducing quietude to control symptoms.

Framed this way, the transition from affordance to functionality is a process of abstraction from the context of the original observation to the domain of use. Such transition may rely on several mental processes including analogy (Gavetti et al., 2005), metaphor (Cornelissen, 2005), pattern making (Loasby, 2007) and narratives (Garud et al., 2016).

Insight is constrained by the affordance-functionality distance. We define the affordance-functionality distance as the cognitive distance between the original observation and the development of a new functionality idea. The distance depends on the overlap between the knowledge underlying the original domain and the knowledge underlying the new functionality. The overlap may be wide, thus not requiring specialized knowledge of the new domain of functionality. The example of the X-ray discovery is instructive. It was common knowledge among scientists and laypersons that a non-invasive way of peering inside the human body did not exist. Therefore, when Roentgen saw the skeletal structure of his hand holding a photographic plate during a cathodic ray experiment, he immediately conceived a new functionality: using a cathodic ray apparatus for peering inside the human body (Kevles, 1998). In this case the distance affordance-functionality was small and turning the effect into a new functionality did not require specialized knowledge of the target domain (besides the capability of operating a redesigned cathodic ray tube). In the antidepressant case, although lacking specialized knowledge in psychiatry, the doctors involved in the antituberculous trial did not know of any chemical substances that reliably and safely altered people's mood. In the antipsychotic case the overlap existed because of Laborit's suspicion (unusual for a surgeon) that mind states were influenced (or determined) by biological parameters. This pushed him to explore the use of psychological states as an adjuvant to surgery. The artificial dye case is more difficult to explain. It is unclear how Perkin thought of the artificial dye functionality and its use in the textile industry. We could suppose that because Perkin was an amateur painter and photographer, he was probably sensitized to colour perception and use.

Crossing both gates results in the generation of an embodied functionality. Functionality refers to a generic technological capability without any apparent market use. This implies a wide search for an existing or latent need that links what a technology does with how the technology is

effectively employed by a user to solve his/her problems. The researchers in the coal tar case had little or no knowledge of the sectors that the development of the initial effect would ultimately impact. In other words, a functionality represents a ‘solution looking for a problem’. Perkin knew how to produce artificial colour but to serve what function? Substitution of natural colours in painting? Colorant for textiles? As an adjuvant in microscopy? Likewise, Roentgen’s X-ray apparatus constituted a revolutionary functionality, but its function was not immediately known: scientific study for better anatomy tables? Diagnostic tool in orthopaedic cases? Entertainment device? Roentgen had no idea that X-ray’s first use would be in a tribunal to solve a court case (Kevles, 1998).

An exaptive functionality is embedded in a technology. Embeddedness constitutes the most distinctive feature of the exaptive process and sets it apart from other channels. When form-follows-function (need and technology/science-push channels), the innovative solution (that represents the way to fulfil the function) needs verification and demands the design of an appropriate technology to deliver its associated function. In the exaptive mode the functionality (and function) comes embedded in an artefact. Consequently, the stage of verification and design of an artefact can be omitted because the solution itself constitutes the generalization of an existing technological effect embedded in an existing technology.

In addition, embeddedness implies that the functionality is also intrinsically associated with a technique<sup>18</sup>. Mokyr (2002) defines a technique as a set of executable instructions that instruct an agent about how to deliver a function. For instance, the doctors who discovered the antidepressant effect of iproniazid knew approximately how to administer it to fight depression. They simply had to repeat the steps that were followed to fight tuberculosis. The existence of the technique precedes idea generation, as the technique emerges in the original research in domain A. This implies that the definition of exaptation in the artificial world may need to be expanded: exaptation consists in the functional shift of an artefact **and** the technique that enables the

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<sup>18</sup> Mokyr (2002) makes a distinction between propositional ( $\Omega$ -knowledge or *episteme*) and technical knowledge ( $\lambda$ -knowledge or *techne*). The former is about the “know what” and “why,” and it relates to beliefs about natural phenomena and regularities. Propositional,  $\Omega$ -knowledge is concerned with the justification about how and why natural phenomena arise and how useful knowledge (i.e. technical) work and is controlled and exploited. According to Mokyr, techniques are rooted in propositional knowledge. However, their discovery does not necessarily need or follow propositional knowledge. Techniques may emerge in absence of propositional knowledge. Mokyr states that such emergence is the exceptions not the rule. In rare cases, techniques may arise without any epistemic base. These are singleton techniques that usually result from serendipitous discoveries.

delivery of the original and the exapted function. The technique provides materiality to the functionality. Finally, the identification of a function leads to the necessity to optimize the original underlying technology for the new task. This last step terminates the entire exaptation process.

In Table 1 a, we find the presence and co-existence of the three novelty production factors: need, theory, and affordances. There are three main differences between the cases in the two tables. First, the presence of a compelling need works as a focusing device that restricts and directs the agents' actions within the sector defined by the need and forms an envelope within which the agents' actions acquire sense. Second, the need helps define a problem to be solved: consequently, contrarily to the first set, the sequence goes from problem to solution rather the other way around. Both problem and solution pertain to the same sector, although, the creative solution may come from the outside, as in the Lister case. Third, the functionality is not embedded in a technology and therefore the idea generated by the exaptation needs verification and the related technique needs to be developed. Interestingly, as illustrated by the Lister case, exaptive events may play a role in generating the solution to the original need.

As an overarching need drives the agents' action and the sequence goes from problem to solution, in this type of novelty production the exaptive process points toward the domain defined by the need and not away from it as in the previous case.

## **6. Contributions and Implications**

Through the longitudinal case study of the history of coal tar, we showed that exaptation plays an unsuspectedly significant role in the production of novelty. We estimated that about half of the innovation events were predominantly of exaptive nature. The other half resulted from the coexistence of the three innovation modes, market-pull, science/technology push and exaptive.

The model we elaborated (Figure 3) shows that the exaptive process is composed of three stages with the transition between the stages conditional on crossing two *gates*. The first stage corresponds to the appearance of an unusual effect of an existing artefact. The transition to the second stage requires crossing the *ignorance gate*, which involves the recognition, by a 'prepared mind', that the unusual artefactual effect is real and novel. After crossing the ignorance gate, the exaptive process enters the second stage, involving the discovery of artefact artefact-artefact and artefact-user affordances. Advancing to the third and last stage of the exaptive

process, namely the discovery of new functionalities and functions of an artefact, is conditional on crossing what we termed the *usefulness gate*, which depends on insight and the affordance-functionality distance. In the exaptive process, a new function emerges when a ‘solution finds its problem’ which results in the original artefact and the corresponding technique being coopted and modified for the new function. In this sense, in comparison to the need and theory/technology channels, exaptation is an inside-out model of innovation whereby an affordance generates a solution to a problem to be found outside the original area of research.

We emphasise that our model describes cases in which exaptations are ‘pushed’ by the emergence of an unsuspected secondary effect of technology. They are therefore not the result of an explicit search process.

Our research makes several theoretical contributions. First, it highlights the role of an unexpected artefactual effect as an antecedent of the exaptive process. Second, it identifies the gates that can potentially impede the progression of the innovation process and points to factors facilitating (or not) gate crossing. Third, the model helps to disentangle functions from functionalities and highlights the interdependences between effects, affordances, functionalities, and functions. Fourth, it suggests that the defining trait of exaptation, namely the co-option of an existing technology for new purposes, extends to the technique that delivers a given function<sup>19</sup>.

Our research contributes to several ongoing scholarly debates, for example, on the opportunity ‘creation versus discovery’ in entrepreneurship (Shane, 2000), on foresight Garud, Gehman and Giuliani (2018, 2016) and on blind search (Campbell, 2005; Kantorovich and Ne’eman, 1989; Van Andel, 1994) and serendipity (Merton and Barber, 2004).

Shane (2000) posits that opportunities are discovered by alert entrepreneurs. He presents empirical evidence for the instantaneity and completeness of opportunity discovery, i.e. entrepreneurs conceive a complete idea immediately after learning about the capabilities of a new technology. Although Shane (2000) does not use the term exaptation, his entrepreneurs co-

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<sup>19</sup> In addition to the points mentioned above, our model differs from other exaptation models because it is less function centric. The design-exaptation feedback cycle (Andriani and Carignani, 2014) and the integrated exaptation model (Andriani and Cattani, 2016) are function-centric, that is, both assumes well-defined functions at each stage of the model, including the functional shift stage. This is not always true for two reasons: first, as Garud et al (2016) notice, building on the classic works of Gould and colleagues (Gould and Lewontin, 1979; Gould and Vrba, 1982; Lloyd and Gould, 2017), ‘junk’ and spandrels are often precursors of major innovations and exaptations. Junk and spandrels are devoid of current function and consequently function-centric models fail to appropriately account for them. More importantly, function-centric models neglect unexpected technological effects that cannot be associated with functions, because of their transient and uncertain nature and their associated affordances.

opt 3D printing machines for new purposes, effectively *exapting* them. The coal tar cases are starkly different because the emergence of new functions is neither instantaneous nor complete, insofar considerable time passes between the initial observation and the gradual emergence of a new function. We argue that the two cases are complementary. In relation to our model, Shane's opportunity discovery corresponds to the transition from functionality to function, which is in several cases relatively straightforward, especially in the case of the general-purpose aspect of 3D printing technology. Shane's entrepreneurs are presented with a new functionality (3D printing) and, in a process resembling the emergence of the *need-solution* pair (von Hippel and von Krogh, 2016), they imagine a function that fulfils an underlying need. In the coal tar cases instead, new functions emerge at the end of a process that includes various stages and gate-crossing. Opportunities are in this case constructed because at the beginning researchers and/or entrepreneurs do not have a clear vision of the end result. In other words, the discovery of an opportunity is unlikely if all one has is an unusual technological effect, which does not point to any practical application. Instead, opportunity discovery is possible and likely if one starts from a functionality that can be connected to an existing (but not necessarily conscious) need. Therefore, we suggest that in the case of *exaptive* innovation, the creation versus discovery argument depends, among other things, also on the level of advancement in the exaptation process.

Furthermore, our model's attention to the early phases of the exaptation process contributes to the foresight discussion. Garud, Gehman and Giuliani (2018, 2016) introduced the idea of *exaptive pools*, which constitute the exaptation reservoir that can be deliberately managed to 'engineer' *serendipitous exaptive events* (Garud et al., 2016). This raises the question of what feeds exaptive pools? Our model suggests that in addition to 'scientific discoveries' (Garud et al., 2018) exaptive pools should also include proto-discoveries in the form of unexpected technological effects from which the exaptive process starts.

Evolutionary epistemology frames the problem of radical advancement in science and technology (ST) in terms of blind-variation-and-selective-retention. The term blind indicates that ideas that open new trajectories in ST are "*generated independently of the problems they eventually solve*" (Kantorovich and Ne'eman, 1989, p. 508), in other words, they are generated as by-products ("*innocent problem solving*" (Kantorovich and Ne'eman, 1989, p. 512)) of more linear and incremental Kuhnian 'normal' science. As Kantorovich and Ne'eman (1989, p. 514)

describe it: “*since he tries to solve problem A, being aware of problem A, while accidentally solving (another) problem B, the solution of problem B is, indeed, generated blindly with respect to B.*” Campbell sees a ‘blind search’ as an effective strategy for ST advancement because in any sector in which a developed body of knowledge (traditions, heuristics, theories and models) exists, there must be areas that are blind to such body; “*In going beyond what is already known, one cannot but go blindly. If one can go wisely, this indicates already achieved wisdom of some general sort, which limits the range of trials*” (Campbell, 2005, p. 422). The artificial dye, antidepressant and antipsychotic cases fall squarely within the ‘blind search’ framework.

The literature on blind search (Campbell, 2005; Kantorovich and Ne’eman, 1989; Van Andel, 1994) advocates serendipity (Merton and Barber, 2004) as a key element of ST advancement: “*in view of the basic assumptions of our theory, science can make significant progress only by serendipity*” (Kantorovich and Ne’eman, 1989, p. 516). The coal tar case shows that serendipity (finding-B-whilst-looking-for-A) is the result of multiple stochastic elements that intervenes at different points of our model: a) emergence and observation (or not) of unexpected effect; b) availability of prior knowledge enabling gate crossing; c) conversion of affordances into functionality; d) existence or not of need satisfiable by emergent functionality, none of which can be fully anticipated, therefore explaining the blindness of serendipity. Serendipity, however, is a catch-all term and does not provide a full description of the coal tar case because it lacks a functional analysis, which is instead provided by the exaptive model. We argue that Campbellian ‘blindness’ applies to our exaptive model in the sense that the result was unknown at the beginning of the process. However, blindness applies to the variation side and not to the selective retention side of our evolutionary model. Selective retention instead operates through gate-crossing, which determines the emergence of new elements (affordances, functionalities, etc.) that can be deliberately retained, thereby moderating the blindness of the process.

Blindness also implies that exaptive mode is more likely than other modes to explore unknown unknowns, significantly expanding the limits of our ignorance. In the coal tar case, the actors involved in *exaptive* innovations were involved in routine, within-paradigm science and technology (ST) activities, Yet, they ended up generating new fields of knowledge and technology, which were unknown at the beginning of the research process. The set of potential innovations that can be achieved given the complete stock of knowledge available at time *t* is known as the *adjacent possible* (Kauffman, 1995). The coal-tar case shows that the adjacent

possible can be divided into two areas. The first area falls within the accepted paradigms and is reputed to be achievable within reasonable time and available resources. The second area either lies outside accepted paradigms and thus effectively invisible or deemed to be unachievable within reasonable time and available resources. The first area contains the known unknowns, whereas the second includes (but is not limited to) the unknown unknowns, the ideas “lying out of the path of the imagination” (Francis Bacon cited in Taleb (2008, p. 167). Whereas, the discovery of the artificial dye, the antidepressant and the anti-psychotic drugs falls in the second area, Lister’s systematic efforts, though partly outside the dominant paradigm of their time, fall in the first. This tendency of the exaptive channel to explore the unknown unknowns should be explicitly factored in the choice of the balance of a portfolio of projects in organizations and research policy.

## 7. Policy implications

Considering the fact that from the 1970s research productivity has declined about 7% a year, both in public institutions and private organizations (Bloom et al., 2020)<sup>20</sup> and that one of the reasons evoked to explain the decline in innovation productivity (Funk, 2019; Knott, 2017; Ness, 2015) is the marginalization of serendipity<sup>21</sup>, our research offers several significant policy implications for enhancing innovation. Our model implies that the potential of exaptive innovation to address unknown unknowns leading to radical innovation can be realised only when researchers are free to follow unexpected leads, often arising outside their own field of specialization. Such flexibility, both at the individual and team level, has been limited by the recent increasing dominance of target-driven innovation programs, in which research goals must be identified ex-ante, researchers are selected on the basis of their professional expertise in the

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<sup>20</sup> In pharma the productivity crisis goes under the name of the inverse Moore’s law: the number of approved drugs is roughly constant but their cost of development doubles every decade (Meyers, 2007; Scannell et al., 2012).

<sup>21</sup> Apart from our results and anecdotal evidence about the importance of unexpected discoveries (Ban, 2006; Merton and Barber, 2004; Meyers, 2007; Van Andel, 1994; Yaqub, 2018), Dunbar’s empirical observation that about 50% of findings in science are unexpected (Dunbar, 2001) let one foresee that a large fraction of funded project should apply for supplementary grants to follow unexpected leads. The National Institute of Health (NIH) allows such request for unanticipated events but only if they fall within the scope of the original grant. Even in such restrictive context, the NIH statistics for supplementary grants are the following: in the period 1997-2018 the number of supplementary research award decreased from 35 to 25 (average 31) against an increase of funded project from 7338 to 11071 (average 9467) (*NIH Research Portfolio Online Reporting Tools (RePORT)*, 2005). Supplement grants account for 0.34% of the total. There is little room even for deviation within the scope of the project, let alone breakthrough discoveries!

target area, timing/resources must be declared *ex ante* and deviations from set targets are often discouraged.

In our view, several changes to the research funding and evaluation processes could enhance serendipitous discoveries. The first involves relaxing the tight matching between deliverables and targets in funded proposals, which discourages deviation from the set targets.<sup>22</sup> The second involves introducing a mix between recurrent and competitive research funding. The replacement of the recurrent funding system (Laudel, 2006), in which researchers were allocated a constant stream of funding, by the competitive funding system seems to have led to a situation where researchers predefine research objectives they are more confident to reach, diminishing their overall potential of producing risky radical novelty. The third involves changing the peer-review mechanism for grants, which according to (Horrobin, 2001; Nicholson and Ioannidis, 2012), has generated a culture of conformity. The current peer-review process is known for discarding both the low-quality and the high-risk projects that break away from the dominant paradigm, as reflected in the title “Conform and be funded” of Nicholson and Ioannidis’ (2012) article published in *Nature*. In fact, Boudreau et al. (2012) found an inverse correlation between the novelty of a proposal and the probability of its funding success. More generally, we advocate for a greater diversity of research methods in funded research projects. Indeed, we believe that the difficulty for serendipitous, exaptive discoveries is compounded by the increasing dominance of hypothesis-driven research<sup>23</sup>. Inductive research, for example, is often discounted as second-rate science and rejected at the funding stage. But hypotheses are often the results of previous, fuzzy research and not always its driver (Kell and Oliver, 2004).

Finally, our research suggests that the recent call for more interdisciplinary research projects should be upheld. The trend toward hyper-specialization generates an objective obstacle to explore the interfaces between disciplines, often sources of exaptation. The structure of training and the system of professional incentives tend to accelerate specialization, resulting in a constellation of intellectual archipelagos (Epstein, 2019). The consequence is that as immunologist Casadavell puts it: “*Everyone acknowledges that great progress is made at the*

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<sup>22</sup> Gillies reports the case of the AHRB (Arts and Humanities Research Board), one of the UK leading funding bodies, that explicitly states that ‘*one of the criteria for getting an unsatisfactory assessment is explicitly stated to be failure “to conduct the research as agreed at the time of the award”*’ (Gillies, 2015, p. 6). There is no surprise that unexpected data are likely to be ignored.

<sup>23</sup> A google ngram research shows that the term hypothesis-driven starts appearing in the 1980s. Leaf (2013, p. 205) reports that the term was absent in *Nature* papers until 1994 and then it has quickly become ubiquitous.

*interface, but who is there to defend the interface?”* (cited in Epstein (2019, p. 279). The result is that true uncertainty and exaptive innovation end up being ruled out (Leaf, 2013; Meyers, 2007; Scannell et al., 2012). The Nobel Prize winner Joshua Lederberg summarized it well: *“the implication that an investigator should ‘know what he is doing’ before being worthy of a grant flies in the face of the actual history of the most creative discovery. ... About the most important matters, we are always too ignorant in advance to spell out the discoveries we might make”* (Lederberg, 1989, p. 6).

## **8. Limitations and avenues for future research**

This research suffers from several limitations that suggest additional paths for future research. First, the generalizability of the findings is limited because of the size and scope of the sample used in the coal tar case. Although we focus on over hundred years of coal tar-based radical innovations, larger-scale empirical efforts are necessary to statistically assess the relationships among factors involved in each stage and gate of the exaptive innovation model, and to help define the conditions according to which these relationships vary. The second limitation relates to the use of historical sources of evidence. The latter are usually incomplete and have not been created by the researchers to answer a specific research question, but rather constitute *‘traces of the past found ex-post’* (Kipping et al., 2014). Moreover, the contexts in which sources of evidence were produced may be vastly different from the one in which the research is conducted, questioning the applicability of findings to the present day. Some historians (Mokyr, 2002) argue, for example, that the dominant role of science increasingly drives the generation of new insights, leaving a smaller space for serendipitous exaptive discoveries. However, there is a reason for scepticism. In pharma research, for instance, there is little evidence that the recent massive increase in scientific knowledge has led to increased productivity. If anything, the opposite seems to be true (Scannell et al., 2012; Swinney and Anthony, 2011).

We suggest numerous paths for future research. We believe that turning to psychology and organization theory literature would allow to explore in more detail the psychological and organizational aspects of *exaptive* innovation. More precisely, further research is required to better understand the dynamics of crossing the ignorance and the usefulness gates. Foresight constitutes another promising research direction. Foresight relates to the relationship between the probability of occurrences of exaptive events and the organization, cultural and psychological

conditions that facilitate or hinder their occurrences. We think that the exaptation model may offer a fine-grained platform to anchor foresight studies. Furthermore, more research is required to better understand the agency of technology. Material agency has been proposed in Actor-Network Theory (ANT). It focuses on ‘*a semiotics of materiality that is symmetrical with respect to human and non-human agency*’ (Knappett and Malafouris, 2008, p. 4). However, rather than focusing on how networks of agents (human and non-human) create possibilities for innovation, we suggest looking at the effect of embeddedness on the generation of ideas and technologies. Embeddedness influences exaptation in two ways: first, material affordances act as leading indicators of technological possibilities inherent in the interactions between artefacts and their environment and, second, the embeddedness of ideas (expressed both as functionality and function) and techniques into artefacts confer a degree of agentic materiality (Leonardi et al., 2019) to the exaptive process that determines a preferential direction of development.

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## Appendix

### *Discovery of the first symptomatic drugs*

In addition to aniline and phenol, Runge extracted a substance from coal tar called leukol (white oil). Given its chemical similarity to quinine, it was later renamed quinoline (Mendola, 1890, p.61). The similarity between quinoline and quinine prompted several chemists to study the properties of quinoline, hoping to duplicate quinine's antimalarial properties (Findlay, 1917).

While studying the effect of quinoline on the central nervous systems in 1874, MacKendrick and Dewar observed a strong antipyretic effects" (MacKendrick and Dewar, 1874). This finding was surprising and important, and suggested the idea that synthetic chemical substances (i.e., artificial drugs) could control disease symptoms. The quest for a coal-tar based antipyretic yielded in 1881 at Erlangen University the first coal tar-based drug with the synthesis of Kairin, a derivative of quinoline that exhibited marked antipyretic activity. *Kairin was the first medicinal compound any dyestuff company had ever manufactured. A new era had dawned* (Sneader, 2005). A similar quinoline-based drug, called antipyrine, was introduced in 1884 and became "the most widely used drug in the world until aspirin" (Sneader, 2005, p.126). The powerful analgesic effects of antipyrine were discovered a year after its introduction (Kebler et al., 1909). It became the first synthetic analgesic widely used for rheumatoid arthritis pain and headache.

### *From methylene blue to the emergence of modern medicine*

The development of thousands of new dyes followed Perkin's discovery of the first artificial dye. Many of these dyes ended up playing an unintended but important role in the history of medicine and pharmaceuticals. Methylene blue (MB), synthesized by Caro in 1876, and quickly adopted by the textile industry (Findlay, 1917), was key for the emergence of chemotherapy

Coal tar-based dyes were widely adopted in microscopy, which had been using natural dyes to increase contrast and reveal otherwise invisible structures (Krafts et al., 2011).

Paul Ehrlich, a physician passionate about dye chemistry and a recipient of the Nobel Prize for Medicine, 1908, was the first to use MB to experiment with staining. He observed an unusual effect, that is, that MB selectively stained pathogens, such as bacteria and parasites. This observation led to several revolutionary implications (Schirmer et al., 2011). As a dye chemist, Ehrlich knew that dye molecules performed a double function in textiles: one part of the molecule adheres to the textile fibre, and the other imparts colour. Dye chemists focused on the

dye-fibre colour aspect and did not pay attention to the dye-fibre adhesion. Ehrlich, however, observed that the latter modified cellular behaviour and interfered with metabolic functions. His observation that micro-organisms preferentially absorb methylene blue led to the ideation of the “magic bullet” concept, which states that selective absorption of synthetic chemicals (i.e., dyes) may kill pathogens (the “bullet” function) without affecting the host (the “magic” aspect). Though not easily accepted<sup>24</sup> (Ryan, 1992, p.89), the magic bullet idea became the foundation of synthetic pharmacology and therapy (Raviña, 2011).

Developing the implications further, Ehrlich repositioned MB as a drug and prescribed it against malaria, making it the first synthetic drug ever used to fight a disease (Schirmer et al., 2011). Ehrlich called this approach chromotherapy, which literally means treatment with dyes, later renamed chemotherapy. Ehrlich further speculated that a chemical affinity causes the effect of dyes on pathogens through surface receptors. Thus, useful drugs could be identified through a process of systematic screening of available dyes until the right match dye-receptor was detected (Ryan, 1992, p.89). In other words, Ehrlich developed a pharmacological research program based on the systematic attempt to co-opt textile dyes as drugs.

Since Ehrlich’s first use in medicine and histology, MB has been utilized in a wide variety of applications, ranging from research to therapy, many of which discovered via the emergence of unexpected affordances (Oz et al., 2011; Schirmer et al., 2011).

### ***From azo dye to the first antibiotic***

Azo dyes, a successful class of dyes synthesized in the 1860s from aniline (Yates and Yates, 2016), led to the emergence of antibiotics. Ehrlich’s magic bullet approach to fighting infectious diseases raised expectations that there would soon be cures for major diseases. However, no new drugs were developed by Ehrlich’s method for about two decades, and considerable scepticism emerged about the chemotherapy approach (Lesch, 2007).

Bayer was an exception. Bayer decided to pursue Ehrlich’s chemotherapy approach and formed an interdisciplinary research laboratory with dye chemists and medical doctors, who either studied under Ehrlich or subscribed to his general approach. They developed two main lines of research. The first built directly on Ehrlich’s discovery of the antimalarial property of

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<sup>24</sup> Even his mentor, Robert Koch (Nobel Prize for Medicine and together with Luis Pasteur the father of microbiology) *found the notion of swallowing or injecting chemicals totally repugnant* (Ryan, 1992, p. 89).

methylene blue. Bayer continued Perkin's earlier attempts to synthesize better quinine, with researchers exploiting the similarity between quinine and methylene blue and using Ehrlich's systematic screening approach. The result was two (methylene blue derivatives) successful antimalarial drugs: Plasmoquine in 1924, Atabrine in 1930 (Raviña, 2011), which became, alongside quinine, the main antimalarial drugs until World War 2 (Maj, 1998). Bayer also synthesized Chloroquine from MB (Lowe, 2020)

The second research line, led by Gerhard Domagk, also used Ehrlich systematic screening but started from the red-azo dye family. To strengthen earlier reported red-azo antibacterial activity, Bayer chemists used an old trick from the textile dye industry. They added a sulphonamide side-chain on the dye molecule to make dyes bind better to the textile fibre (Raviña, 2011), thus increasing washing resistance.<sup>25</sup> The Bayer team synthesized a molecule in 1932, Prontosil Rubrum<sup>26</sup> (Meyers, 2007), characterized by unprecedented, broad antibacterial activity against streptococci *in vivo*, but ineffective *in vitro*. Prontosil was revolutionary in the therapeutics of bacterial diseases (Finch and Roger, 2011; Lesch, 2007; Raviña, 2011). It was the first widely used, wide-spectrum antibiotic resulting in Domagk's Nobel Prize for Medicine in 1939.

In 1935, scientists at the Pasteur Institute in Paris serendipitously discovered that body metabolism splits Prontosil Rubrum into its components—the red-azo dye and the sulphanilamide group—thus explaining the *in-vitro/in-vivo* difference in the effect of Prontosil. The antibacterial activity was due entirely to the colourless sulphanilamide (i.e., not a dye). Before suspecting its germicidal properties, sulphanilamide was patented by Bayer in 1908 as a dye intermediate. Paradoxically, the first antibiotic widely used before penicillin was produced in the textile industry for 30 years before a long chain of events led to the recognition of its therapeutic potential (Lesch, 2007).

The effect of Prontosil-sulphanilamide was discovered without any understanding of its mechanism of action. The discovery originated in dye chemistry from Ehrlich's magic bullet idea and by the systematic screening of red-azo-sulphonamide compounds *in vivo* and *in vitro*. The difference between *in vivo* and *in vitro* results led scientists to suspect that sulphanilamide did not directly kill bacteria but instead disrupted some metabolic functions necessary for their

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<sup>25</sup> The first sulphonamide-containing azo, Supramine, was introduced in the market in the early 1900s (Lesch, 2007).

<sup>26</sup> After the name of the sulphanilamide compound that the industry had been manufacturing for decades (Li, 2006; Meyers, 2007).

growth. In 1940, scientists discovered that sulphanilamide prevents a precursor of folic acid from linking to the bacterium, thus interfering with its nutrition (Sneader, 2005). This discovery led to the emergence of the drug metabolism field (Lednicer, 2007) and the anti-metabolite theory of competitive inhibition (Woolley, 1952). Based on Ehrlich's 'lock-and-key' idea of the magic bullet (Woolley, 1952), the anti-metabolite theory became the foundation of rational drug design: scientists could hone in on a pathogen, identify a molecule necessary for its metabolism, and design an anti-metabolite that would stick to the cell, thereby locking out the pathogen (Sneader, 2005).

The sulpha drugs were the culmination of medical research started by Ehrlich in the 19<sup>th</sup> century, resulting from the systematic screening of existing or modified dyes in search of new functions and exaptations.

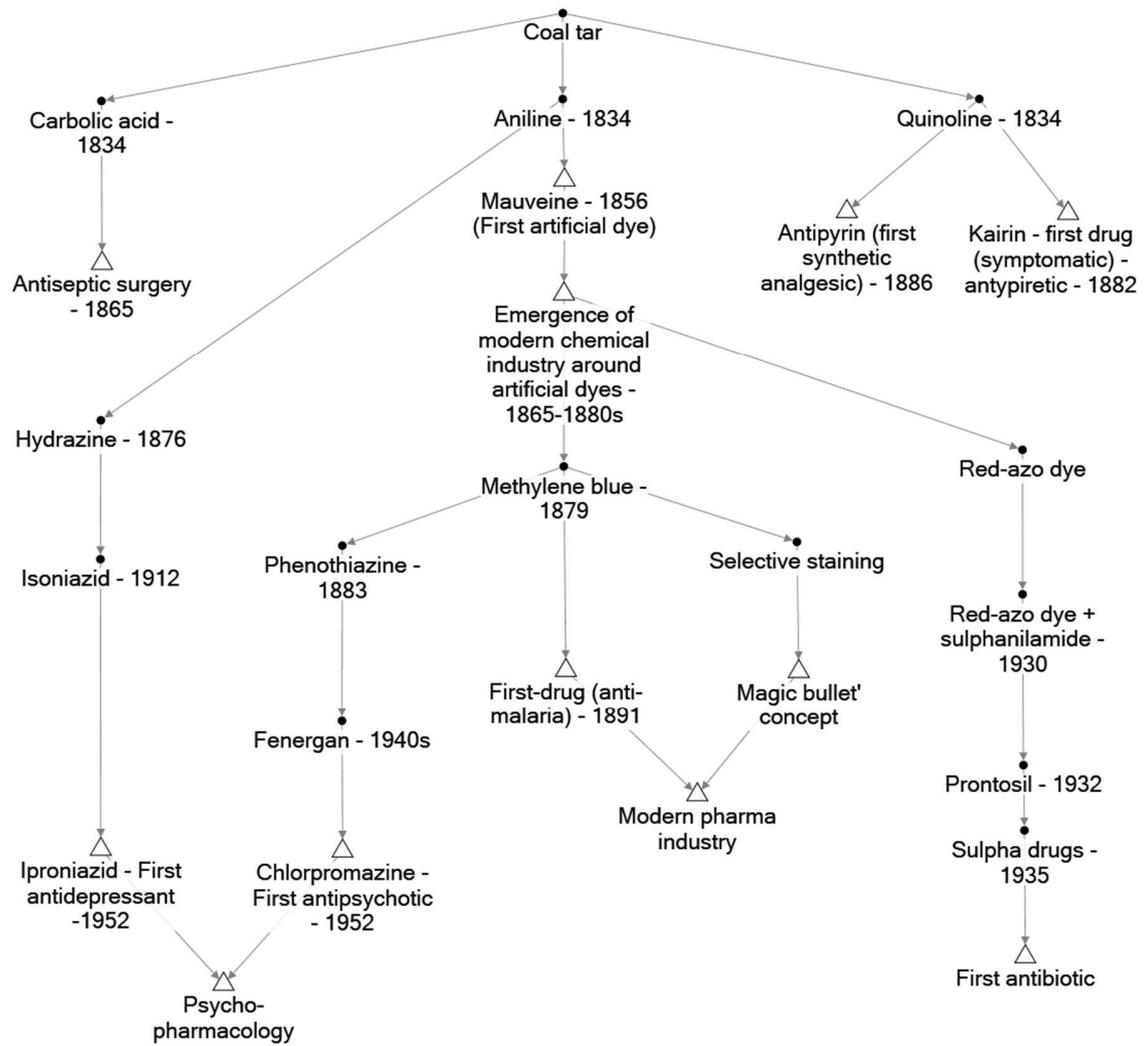


Figure 1. Genealogical tree of the major medical/pharmacological coal tar-based innovations. The vertical dimension axis indicates time.

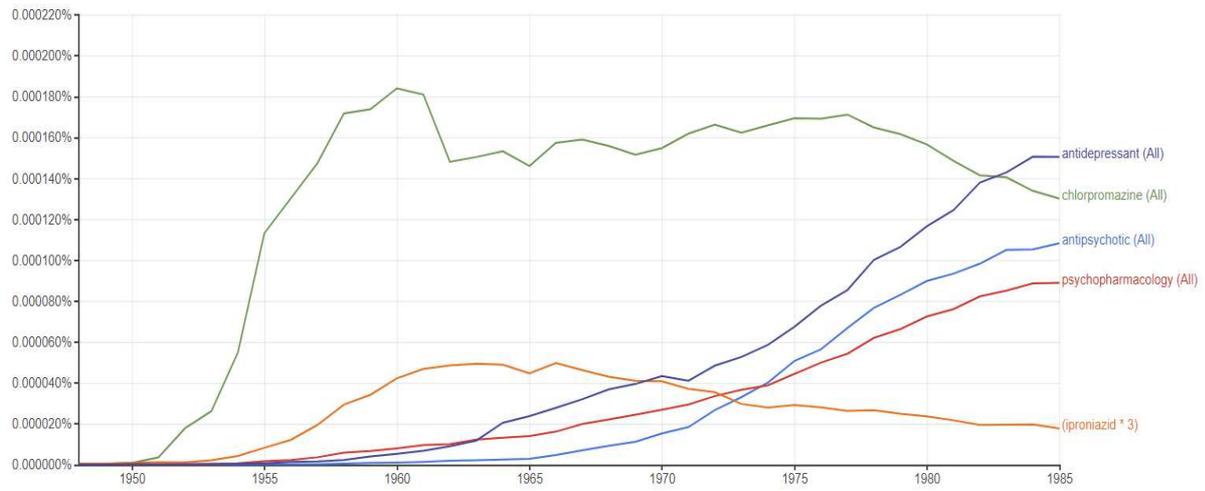


Figure 2. Google n-gram of diffusion of words. The vertical axis indicates the frequency of selected words. The horizontal axis indicates the time frame (1950 to 1985).

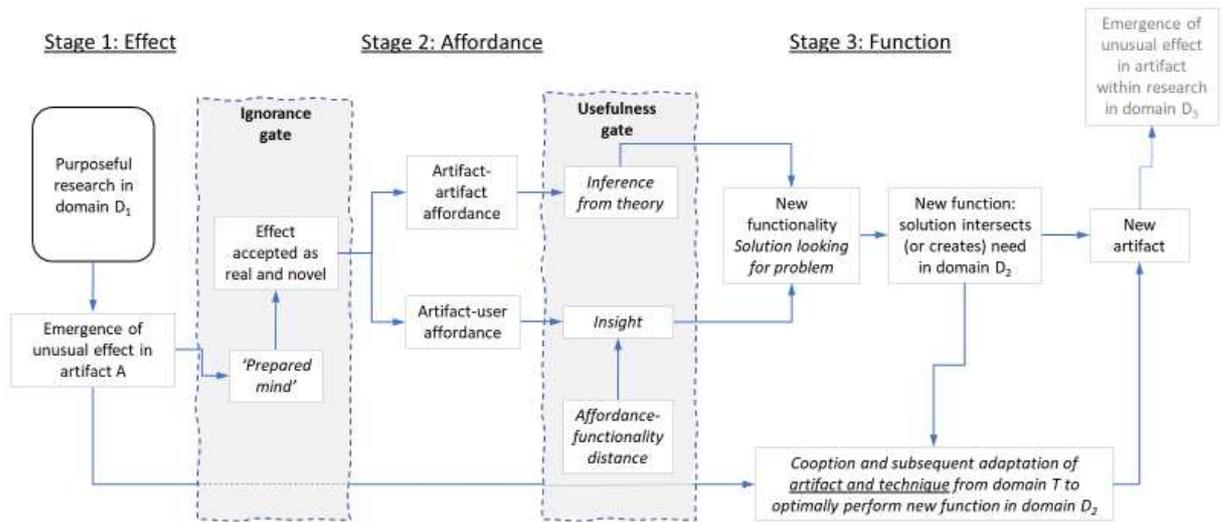


Figure 3. A three-stage and two-gate exaptive innovation model

<b>Discovery of:</b>	<b>Date</b>	<b>Need</b>	<b>Theory</b>	<b>Affordance</b>
<b>Antiseptic surgery</b>	1865	<b>Present</b> Lister looked for a way to reduce post-surgical mortality.	<b>Present</b> There were several theories about infections. Mainstream theory did not consider germs as causative.	<b>Present</b> Carbolic acid's antiseptic properties afforded the emergence of antiseptic surgery through the co-option of carbolic acid in surgery.
<b>Magic bullet idea (in appendix)</b>	1880s	<b>Present</b> Ehrlich's purpose was to understand the aetiology of infectious diseases.	<b>Present</b> Germ theory of disease and dye chemistry informed Ehrlich's research. However, the magic bullet idea was not directly derived from theory.	<b>Present</b> The interaction of methylene blue with pathogens revealed that methylene blue stained and altered pathogens' cellular metabolism. This effect suggested the <i>magic bullet</i> idea.
<b>First synthetic drug (in appendix)</b>	1880s	<b>Present</b> Ehrlich's looked for a cure for infectious diseases.	<b>Present</b> Germ theory of diseases, dye chemistry and magic bullet idea informed Ehrlich's discovery of first synthetic drug (against malaria).	<b>Present</b> The interaction of methylene blue with pathogens suggested the idea of using methylene blue (and by extension other dye-based synthetic chemicals) to fight diseases. Hence the affordance of methylene blue led to the emergence of the first synthetic drug.
<b>First antibiotic (in appendix)</b>	1932	<b>Present</b> Domagk's purpose was finding a cure for infective diseases.	<b>Present</b> Germ theory of disease, organic chemistry, and magic bullet approach informed Domagk's research	<b>Present</b> The unsuspected antibacterial effect of sulphanilamide property afforded the emergence of first wide spectrum antibiotic drug.

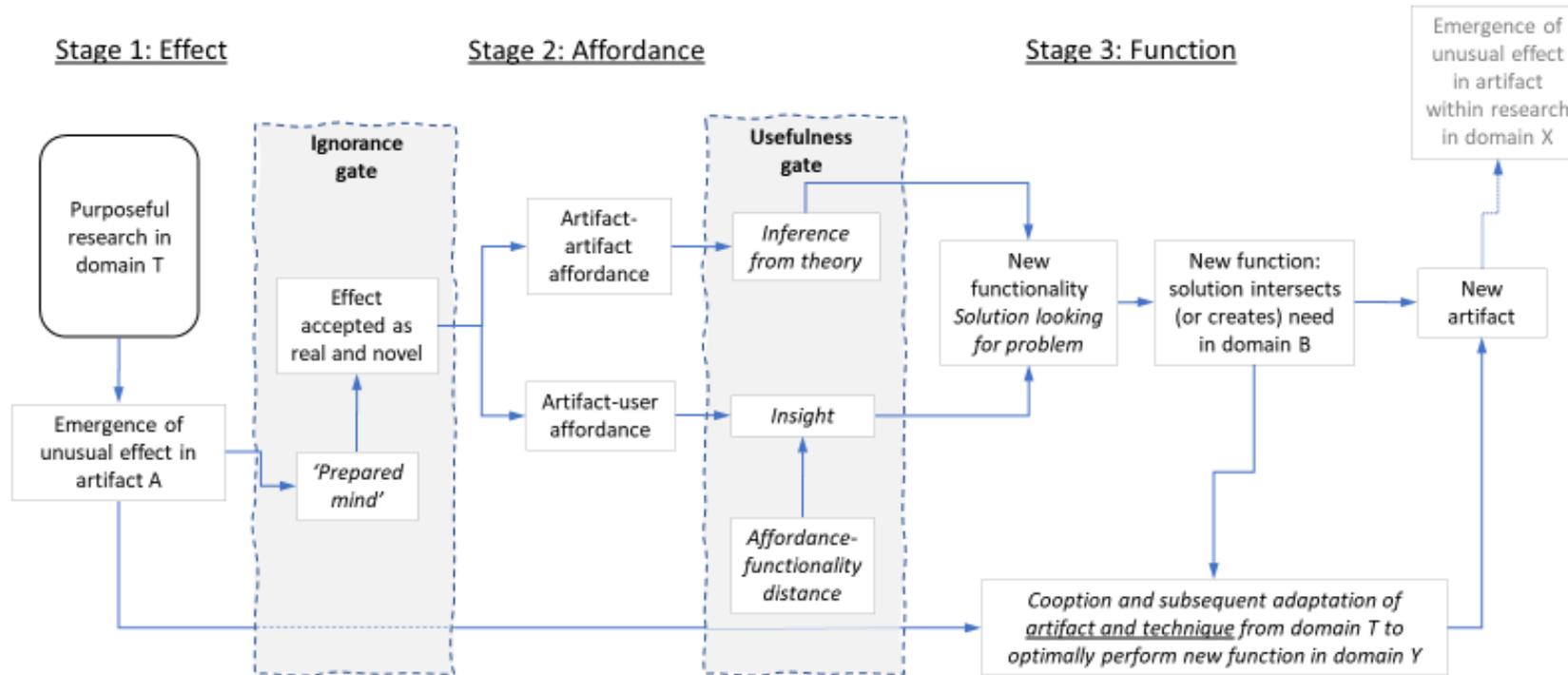
Table 1a. Innovation cases where all three novelty production modes played a role

<b>Discovery of:</b>	<b>Date</b>	<b>Need</b>	<b>Theory</b>	<b>Affordance</b>
<b>Artificial dye</b>	1856	<b>Absent</b> Perkin looked for artificial quinine not artificial dye.	<b>Absent</b> The field of artificial dye chemistry was non-existent.	<b>Present</b> The unexpected appearance of a strong purple colour in aniline suggested the idea of artificial colouring resulting in the co-option of aniline for dye colouring.
<b>First symptomatic drugs (in appendix)</b>	1883	<b>Absent</b> Pharmacists looked for better vermifuge not for analgesic and antipyretic drugs.	<b>Absent</b> There was no theory explaining why drugs could lower temperature and reduce pain.	<b>Present</b> The affordances of drugs' developed for other purposes revealed analgesic and antipyretic properties resulting in the emergence of the first symptomatic drugs.
<b>First anti-psychotic</b>	1952	<b>Absent</b> Laborit looked for a better anaesthetic.	<b>Absent</b> There was no theory explaining the effect of synthetic drugs on psychosis.	<b>Present</b> Chlorpromazine, a drug originally developed against malaria, revealed unexpected action on the central nervous systems (sedative effect) and later a second unexpected effect against psychotic and manic states. Chlorpromazine afforded the first systematic pharmacological treatment against psychosis and the emergence of pharmacological psychiatry.
<b>First anti-depressant</b>	1952	<b>Absent</b> Scientists' looked for treatment for tuberculosis.	<b>Absent</b> There was no theory explaining the effect of anti-depressant.	<b>Present</b> Iproniazid' unexpected property of making people euphoric afforded the first treatment for clinical depression.

*Table 1b. Exaptive innovation cases where affordances played a dominant role in novelty production.*

## A Model of Exaptive Novelty Production Process----- Graphical abstract

Based on the analysis of the history of coal tar, we build a model of exaptive novelty production process. It starts with the appearance of unexpected effect of an artifact designed to perform a function in the domain  $D_1$  and ends in the cooption of the artefact and its new function to the domain  $D_2$ . In this model, the need and the theory/technology drivers of innovation play a secondary role. The model captures the dynamics of the discovery of unknown unknowns, characteristic of radical innovation.



We highlight two implications:

1. Serendipity and the process 'blindness' help explore the unknown unknowns.
2. Radical innovation can be enhanced by reorganizing Science and Technology institutions in a way to allow for more research of exaptive nature.