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The promise of putting into place patterns for paying attention

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Serendipity in research and development: The promise of putting into place patterns for paying attention

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The concept of serendipity or accidental discovery is typically discussed in the context of organizational research and development (RnD) through narratives involving 'renegade iconoclasts' laboring at the periphery. Recently, robust academic literature has emerged that grounds serendipity epistemologically. In the current work, this literature is introduced in the context of the typical activities of contemporary life science-focused RnD organizations. Practical patterns are described that can increase the likelihood of realizing accidental (serendipitous) RnD discoveries.

Keywords: serendipity; research and development; innovation; organizational theory; accidental discovery

Introduction

Since the emergence and rapid global transmission of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), nearly every facet of the human experience has been affected.[1] The tragic loss of life and unprecedented strain on health systems, economies, supply chains, and individual mental health are just a few aspects of our lives that have been affected[2] and will continue to be affected well into the foreseeable future.

The novelty of the coronavirus necessitated an initial nonpharmaceutical public health response that included, but was not limited to travel restrictions, municipal lockdowns, mask wearing, and school closures.[3]

In parallel with this broad-spectrum public health response was an unprecedented (in its speed and outcome) attack on the virus through vaccine development. The viral genome was made public on January 11, 2020, just 1 month after the first report of a novel respiratory virus in Wuhan, China. Just days later, on January 15, Moderna (a US-based biotechnology company), in collaboration with the US National Institutes of Health, finalized its design of the prototype mRNA molecule that would constitute its vaccine. A mere 62 days later, clinical trials in humans began and the first dose of the vaccine developed by Pfizer was administered to a British nonagenarian in early December 2020. In stark contrast to this development story, for the polio vaccine in the United States, there was a 20-year span between the clinical trials and licensing.[4]

Concomitantly, during this time in the UK, a partnership between Oxford University and AstraZeneca (the Anglo-Swedish pharmaceutical company) emerged. AstraZeneca's involvement followed the estab-

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lishment of early clinical trials by the university. During the production of vaccines for clinical studies, a contractor accidentally provided doses at half strength. Following disclosure to the appropriate regulatory bodies, exploration of the effects of two dosing strengths were approved. Upon analyses of the trials, it was discovered that volunteers given a half dose, followed by a full dose, were conferred more protection from the disease (≤90% vs. 62%). The Head of Research at AstraZeneca dubbed this outcome 'serendipitous'.[5]

This is hardly the only example of unexpected side effects becoming the primary use for a drug; contextual observations of the psychological side effects of imipramine and chlorpromazine and of their respective impact on mood and anxiety, for instance, heralded the current era of psychopharmacology.[6,7] Recently, an exploration of the use of thalidomide-like molecules as molecule glue degraders was published. The authors discuss these molecules exploring both intentional and accidental methods of discovery.[8] This has particular importance given the growing role of alternative modes of target inhibition within the field of drug discovery.

The previous response to recognizing the significance of accidental drug discovery was to take a 'trial and error' approach to discovery by testing compounds similar to those already found.[9] However, more recent work suggests intentionally incorporating accidental discoveries into research processes.[10]

While innovative outcomes can be sought and planned for by organizations (i.e., through intentional acts of 'research'), there are always opportunities for accidental discovery. In contrast to planned approaches – which require specific focus, resource allocation, and coordination – the potential for accidental discovery is significant and yet remains underappreciated in organizational strategies.

Given this observation, anything that might make the realization of accidental discovery more likely should be considered of high importance. While there is robust literature regarding the realization of research, it is only recently that a formal language and epistemology have been developed regarding accidental discovery.

The following contribution, set against the backdrop of an almost existential need to innovate for survival, seeks to describe how life science-oriented research organizations can structure themselves to maximize the likelihood of chance situations giving rise to valuable outcomes. The principal message of this work is simple – there frequently exists significant unrealized 'excess value' resulting from normative research activities and there are some already well described patterns that can be used to realize this value.

Because strategy is involved, we employed the concept of 'serendipity' to characterize the kind of accidental discovery referred to in this study (explored further in a later section). This word, infamously invented by Horace Walpole in 1754 and gaining ground in popular usage worldwide ever since, captures those discoveries that happen 'by accident and sagacity'. What Walpole meant by sagacity, a word for a kind of perceptual wisdom, remains a point of debate. For our purposes, it suffices to state that it calls attention to the intentions involved in these discoveries, which differ from mere luck; these accidental discoveries need a 'prepared mind' or 'prepared organization' to make happen. By using this concept, we highlight the active role that RnD institutions can take when it comes to making room for accidental, valuable discoveries to take shape.[11]

This work is organized as follows. In the next section, we briefly describe how contemporary research activities are typically organized. The concept of accidental discovery is then more fully described and oriented with respect to the emerging literature. Several patterns are introduced, which describe a variety of scenarios for use within a research context such that acts of accidental discovery are both acknowledged, encouraged, and realized. Finally, concluding remarks are offered.

The role of research

In the following description, for foundational purposes, we take an abstract view of the role of research and the organization of actors who engage in it.

We consider organizations to be composed of coordinated individuals engaging in a variety of activities that contribute to the delivery of a service(s) and/or product(s). These activities are performed within a complex context consisting of tangible and intangible elements. These include, for example, a variety of physical spaces and surroundings, normative expectations (both documented and otherwise), and a complex adaptive culture.[12]

The actors themselves are unique, each with their own background and blend of intrinsic and extrinsic motivations. Engagement of the actor, in their work and toward the efficacy of the organization's mission in delivering service(s) and/or product(s), is a dynamic function of time and context, and is malleable in its nature.[13]

The service(s) and/or product(s) are consumed in a marketplace by customers.

To remain competitive, in a crowded marketplace, organizations are required to constantly revisit their offerings – by increasing their novelty (with respect to prior or competitor offerings), improving their value proposition (providing same or similar offerings for less, or more efficiently), or including some other differentiated quality (e.g., reduced environmental impact, greater sustainability, or availability).

As a result of its abstract framing, the above describes academic, governmental, and both for- and not-for-profit organizations situated within a democratically capitalistic system.

In short, the long-term viability of any such organization is dependent on growth, adaptation, and renewal. Accordingly, organizations have a vested interest in deploying their finite resources to establish systems, structures, and processes to systematically ask and subsequently answer questions that can make sense of their unknown, but developing context.

We consider research to be the act of asking and answering questions. Within the above framing, research has expected utility or value. This notion of value is contextual. For example, for a for-profit organization, the value may lie in the future commercial prospects of the research; while for an academic institution, the value may be derived from awards, grants, or enhanced standing.

Ultimately, value is expected to contribute to the continuity and viability of the organization. However, given the importance of organizational growth and renewal, it is important to recognize that while some actors may have formal roles

in engaging in research, all actors are nonetheless motivated (at least in principle) to identify and engage in 'research' opportunities.

To be clear, within this description, the 'orientation' of the research ('applied' vs 'basic' – or any other such framing of 'activities'[14]) is of limited importance to us. It is assumed that research is enabled and executed, and that outputs are realized.

Accidental discovery

In general, organizations have strived to control or contain uncertainty via methods such as risk assessment or targeted research, and through streamlining and the use of theory to avoid wastage by trial and error.[15,16]

Increasingly, however, organizational and business theory has recognized the benefit of unexpected opportunities, which have been historically described through stories, wherein the canonical narrative involves the lone rogue inventor developing a unique (and ultimately successful) product that was previously dismissed, marginalized, or unsupported. A classic example is the accidental discovery of vulcanization after Goodyear's long and arduous search for a way to make rubber more durable. Or the dogged promotion of the theory of the bacterial pathogenesis of stomach ulcers by Barry Marshall, who had first to change scientific theory to convince others that ulcers could be medically treated, as he had surprisingly learned. Stories such as these and of Fleming's accidental observation of penicillin, the development of the Post-It Note,[17] and the identification of Viagra[18] fill blogs online and popular books about the serendipitous discoveries that have shaped the world.[19,20]

While anecdotes abound, theory and practice have developed in parallel. In business, the role of serendipity in entrepreneurial success has been examined[21,22]; in information and collaborative sciences, the fortuitous discovery of resources and links between realms of expertise have become an increasingly hot topic[23–26]; in psychology, the problems of personal development, creativity, and insight have tapped into serendipity as something that plays a role among successful problem solvers and resilient individuals.[27–29] Recently, popular concepts such as antifragility and resilience illustrate this turn toward incorporating uncertainty and the unexpected into strategic approaches to everything from start-ups to libraries; this includes scientific research and technology development (e.g., the Crick Institute).[30,31] More generally, taxonomies and frameworks are beginning to emerge that support a rigorous epistemological foundation for this emerging field.[11,32]

While many approaches have been explored to enrich for unexpected discovery, many have focused on increasing the number of chances ('shots on goal'), the creation of specific focal groups wherein 'innovation' exists, or providing dedicated time for experimentation (20% time). While these efforts may enable accidental discovery, they curiously sit outside of the main body of research activities in which an organization is engaged.

In the following section, we describe the general features that occur regularly in research contexts, but that present ready opportunities for increasing the 'serendipity' of research overall. Discoveries made in these ways are considered rare and serendipitous, but we suggest that this is because these are methods not yet part of regular practice. Once they become common means for making new discoveries, the discoveries and innovations thereby made can be expected and even encouraged.

The promise: The realization of excess value

The last several decades have given rise to an increasingly complex field of regulations and restrictions on research, particularly in the development of medical interventions. These increased constraints also place restrictions on the opportunities that would otherwise arise by chance. Similar to the arguments from Vannevar Bush in the 1940s,[33] freedom of practice is frequently correlated with the capacity of scientists to make unpredicted discoveries (and thus to bring about great innovations and progress). However, there is little reason to presume that the directed research will produce fewer opportunities for discovery than curiosity-led research. If there is a difference, it is in the ability of the individual to take the time and leisure to pursue a new direction, despite being involved in other research.[34] For example, emphasis on clinical trial transparency and ethical design constrains a researcher's ability to embark on a new research program without careful consideration, but do not impede the opportunities presented. Rather, what is needed are procedures intended to ensure that the 'excess value' of the designed research is taken up along with the expected and predicted results and data produced.

This idea of excess value is drawn from work by Jonathan Kimmelman on the epistemology of translational clinical research, to capture the value that research into stem cell interventions might have in terms of new knowledge about safety and basic biology that such research produces.[35] Kimmelman identified this potential new knowledge as 'collateral value'. To push this metaphor further, we see that serendipitous discoveries are often generated along with this collateral value; when observations or results are not valuable in relation to the original research program, but instead contribute needed knowledge to another project or inspires the generation of a new research direction altogether.

A secondary source of excess value that exists in normal research practice is error reconstrued as opportunity. Dealing with error and unexpected results is a regular part of normal scientific practice.[36] For Thomas Kuhn, anomalies found their way into 'problem-solving' in science on a regular basis; it is only when the number and degree of anomalous findings overwhelm a paradigm's capacity for explicating or coping with them that the paradigm itself shifts. That is, the unexpected is expected within science.[37] Error, and dealing with potential error when unexpected results are observed, are ways that scientists regularly employ causal reasoning in their cognitive practice.[38]

There are a variety of organizational factors at play that seek to work against the realization of excess value. For instance, in high pressure environments, where the reduction of time from discovery to distribution is minimized wherever possible, taking time to pursue outliers and errors may not fit into routine laboratory practice.

As will be explored below, to enrich for the likelihood of the realization of excess value resulting from accidental discovery, the use of organizational support systems and structures, layered on top of the way in which the research is performed, is critical.[39]

Before proceeding, it is worthwhile to summarize some of the key points discussed above, as they have considerable practical considerations for a modern life science-focused research and development (RnD) organization. Specifically:

- Nothing about how an organization is structured necessarily prohibits the realization of accidental discovery.
- Normal research practices generate outputs that most certainly contain unrealized 'excess value'.
- This excess value is most likely realized not through the localization of specific and focused 'innovation efforts' but instead through work practices that attend to the creation and support of networks that allow researchers to explore, in the service of long-term stewardship.

Below, the literature describing the patterns that enable the realization of excess value are presented in more detail.

Patterns to enable accidental discovery

Two patterns emerge from the literature that, when employed, enrich for the likelihood of realizing serendipitous outcomes.

Hoarding the haystacks

The above argumentation suggests that through the normal act of research, an organization will generate outputs that may have excess (collateral) value. The easiest way to *not* realize this value is to discard the output (discarding the proverbial needle-containing haystack). Accordingly, the easiest way is to simply keep every output (i.e., to hoard the haystacks). Indeed, long forgotten files kept in drawers have a storied place in the literature of accidental discovery; the Grasberg mines in Papua New Guinea, for instance, were (re)discovered when someone found an old drawing in an office drawer of a mountain peak seen on a long-ago expedition.[40] The mines have been the subject of considerable conflict between local Papuans and foreign investors. This raises an important consideration, that not all discoveries are serendipitous from all perspectives, and ethical considerations should come along with any new research direction, even when generated by a seemingly positive chance discovery.

Of course, the difficulty with excess (collateral) value lies in the uncertainty of whether the output finding, data, or substance discovered has any value. Enterprises cannot be expected to continue building 'drawers' to keep old files in, nor are they able to easily access what is in them once filled.

Physical file cabinets are perhaps less of a worry for the contemporary firm as most outputs are stored digitally. The cost of archiving every experimental consideration (input and output) is comparatively negligible; thus, the 'surface area' for accidental discovery has increased immeasurably, the scale of the subsequent search and scoring problem has also increased. The proponents of supercomputer-powered discovery have explored this very problem, beginning with IBM and their WATSON initiative, using high-powered processing to make connections within a vast hoard of data and information. Even these 'wise' machines require humans to evaluate those connections and to see their value in terms of practicality and worth. Thus, while this seems an issue of excess value, it is also a problem of archival utility.

Because of these storage and access issues, keeping all potentially useful information cannot be the sole key to increasing serendipity within research institutions. Nor is relying on institutional memory or familiarity adequate, although that is another frequently cited source of serendipity.[41]

The who and the how

The active exploration of 'excess value' requires that both the individual and the organization within which the individual is working are supportive of such activities. This second pattern describes the enablement of an organizational context that both attends to support networks that allow researchers to take greater risks in pursuing the potentially valuable, and prioritizes flexibility and long-term benefits over quick, guaranteed returns.

Approaches advised in the serendipity literature to foster a sense of organizational flexibility include the cultivation of a culture of 'generative doubt', so that errors and failures are expected in progress, to the point where institutions look for opportunities to change themselves and adapt (the doubt, then, is toward their own expertise and assumptions about the path to success).[15,16] Another strategy is enabling a circular approach to development and hypothesis testing; the expectation of generating collateral value will open opportunities to branch out and reuse efforts in one area to support new research in another. Ensuring regular and engaged communication between diverse teams and universal, easy access to resources and results are other ways to create opportunities for sharing and reevaluating the potential value of unexpected (or interesting but so far not valuable) results.

In turn, organizational cultures must not only cultivate generative doubt and adaptive approaches toward their goals but also encourage this behavior among individual members by supporting their potentially fruitful suggestions. For interdisciplinary encounters to generate serendipity will require the collaboration of multiple researchers who are prepared to share and engage with the unexpected when it is offered. Notably, the exact combination of perspectives cannot be determined before the unexpected encounter or observation occurs, and maybe not even directly thereafter. Despite the widely acknowledged challenge of integrating disciplinary perspectives and local knowledge, cross-domain exchanges often lead to serendipity.

More than a simple combination of disciplines is necessary for this to work. For new ideas to arise and generate engaged debate over how to bring them to fruition, the members of a team must be not only willing to take the risk of making their unique contributions, they must be received as equal and worthy contributors by other group members.[23] Furthermore, time and resources are an important part of such support. In addition to 'flexibility' in promoting cross-disciplinary exchanges, it is advised that administrators of research funding 'should allow both a natural, unforced pace of work and a degree of self-direction that allows researchers to draw on the personal sources of inspiration' (p. 375).[34]

Finally, hiring practices within firms could acknowledge that curiosity, much like serendipity, has a robust epistemological foundation. Curiosity is formally described as a motivational state that is observed to drive information seeking

and exploration.[42–45] While some people are, by nature, more curious than others,[46] anyone's curiosity can be triggered at any time, and in this sense, curiosity is malleable. There are validated assessments for these traits, and attempts to enable a culture of 'generative doubt' might be well served by understanding the organizational composition through this lens.[47,48]

Putting in place patterns for paying attention

The literature suggests that a way to enrich for the likelihood of an accidental discovery is to recognize previously unrealized value that is already embedded in the outputs of usual research practices. This is most readily accomplished in the context of supportive networks, within an organization flexibly focused on the pursuit of long-term goals.

While compelling from an abstract academic review of the literature what, practically, does this mean for the modern RnD organization? How would one go about putting into place those critical patterns for paying attention?

This concern is decomposed into three domains of consideration: organization, function, and individual. This reflects a multiscale view of the modern firm, with coarse but illustrative boundaries. Specific 'tactics' are not described; instead, the focus is on broad characteristics of concerns to be addressed.

If work is a complex social problem, we do not 'solve for work'; instead, we institute strategies to cope with current contextual challenges, and do so with a sense of urgency. This does not require a 'laundry' list of possible interventions to be tried, but rather, the elucidation of general patterns of considerations to which attention should be paid. As a result, Table 1 is as informative as it is useless. It provides an overview of three patterns under the broad categories of 'goal' or setting a direction; 'culture' or promoting both attitudes and practices; and 'networks' of support and integration. These patterns are to be attended to at multiple scales, and not always in a way that is supportive or complementary – this is the complex 'mess'[49] that results from an attempt to organize actors in the service of something bigger than any individual.

Concluding remarks

Instead of focusing on 'engineering serendipity',[50] the very language of which suggests a deterministic realization of previously unrealized value, this work describes patterns that enrich for the likelihood of accidental discovery. This is an important distinction as it frames the act of the realization of previously unrealized value as a function of probabilities, which is more appropriate for describing this process.

Within this probabilistic view, and through a review of the emerging literature and epistemology around accidental discovery, patterns have been identified that, when paid attention to, will increase the likelihood of the emergence of serendipitous outcomes.

As the pandemic-oriented introduction to the current work alludes, this is a problem of almost existential importance. One of the aims of the current contribution is to highlight that it is increasingly possible to think deeply about how our life science-oriented organizations are structured in the hope that excess value is realized. Leave 'no stone unturned' in the search for novel therapeutic agents. That funding agencies themselves are recognizing this[51] is a crucial step and will further support and encourage the realization of 'excess value' from publicly funded research.[52]

A consequence of the nature of for-profit life science exploration is the 'selective reveal', in that it may not be in an organization's interest to fully share internal processes and learning. This is discussed in the context of open innovation in the following references[53,54] and naturally hampers our ability to fully describe and explore the realization of excess value as a community. It is likely that elements of the patterns described above might already be used. For example, the Design–Make–Test–Analyze approach is often discussed in the context of the deployment of artificial intelligence in drug discovery[55] and is a circular approach to development and hypothesis testing. We caution that this is routinely deployed as a 'workflow' and may need modification (i.e., project team intervention) to enable the realization of 'excess value'. Accordingly, frameworks for discussing and describing the role of humans as partners to machines is emerging and will serve as a boon to the field.[56]

These are important considerations for the modern RnD organization. There is nothing about a firm's current structure that would prohibit the realization of accidental discovery. Planning for the

TABLE 1

Broad patterns of intervention (goal, culture, networks) to enable 'paying attention' at different organizational levels (organization, function, individual).

	Organization	Function	Individual
Goal	A clearly articulated goal or north star that serves to orient actors even during times of ambiguity or uncertainty; it is in service of this goal that the organization exists.	A clearly articulated functional goal that appropriately orients functional efforts for the realization of organizational goal(s).	An understanding, firmly held at the individual level, regarding how the individual contribution connects to the functional and organizational goals.
Culture	Organizational adoption and practice for the establishment of normative behavior, grounded in, for example, generative doubt. Execution of determined practices at the highest organizational levels in service of the goal(s).	Adoption and localization of the philosophy and practices associated with, for example, generative doubt. Execution of practices at the functional level in service of functional and organizational goal(s).	Practice at the individual level of generative doubt as a part of individual contribution to traditional research practice.
Networks	Encourage and enable cross functional network participation. Understand and orchestrate.	Active participation in cross functional activities.	

unplanned requires organizations to move beyond marshaling organizational resources towards discrete action, and to instead think about outcome measurement and observation, capacity maintenance, and potentiality enablement. Accordingly, there exists the possibility of significant 'unrealized' excess value that could be realized were it simply 'paid attention to'.

Declarations of interest

No interests are declared.

Data availability

No data was used for the research described in the article.

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