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The Structure of Serendipity

Abstract

Serendipity is routinely but mistakenly used as synonymous with chance events, luck or providence. It is thus not surprising that serendipity remains comparatively underresearched. After all, how is one to unlock the 'black box' of chance? Rather than being synonymous with chance, serendipity results from identifying 'matching pairs' of events that are put to practical or strategic use. With this etymologically accurate definition in mind, serendipity thus describes a *capability*, not an event. It follows that human agency, and not probability, is properly the focus of attention. Drawing on its 16th century etymological origins, we 'unpack' four serendipitous innovations in science to illustrate the nature of serendipity. In developing this argument, we propose a novel typology. We conclude by exploring implications for research and practice.

Key words: serendipity, chance, innovation

"Discovery is seeing what everybody else has seen but thinking what nobody else has thought" – Albert Szent-Györgyi

Our principal thesis is that serendipity is typically incorrectly – and eventually unsuccessfully – used as synonymous with chance coincidence, luck or providence. This popular characterization obscures our appreciation of the structure of innovation. After all, how is one to unlock the 'black box' of chance, except to assign it a probability?

Rather than being tantamount to chance events, serendipity results from the ability to identify 'matching pairs' of events – events that are *meaningfully*, but not necessarily causally, related. In contrast with serendipity's popular application, this characterization is true to serendipity's etymological origins. For serendipity reflects a capability, not, as is routinely assumed, an event.

This paper proposes that serendipity, as capability, affords an opportunity to extend scholarly research into innovation processes. To unpack this theme is its first objective. But it also seeks conceptual clarity by proposing a typology of serendipity. This typology is induced from descriptions of four scientific discoveries. To outline the implications of this conceptualization for research and practice is its third objective.

Defining serendipity

Serendipity is commonly used in reference to 'the happy accident' (Ferguson, 1999: 194; Khan, 1999), the finding of things without seeking them (Austin, 2003), and as synonymous with 'any pleasant surprise' (Tolson, 2004: 51), fortuity, chance,

randomness, or luck. The New Oxford Dictionary of English defines it as "the occurrence and development of events by chance in a happy or beneficial way". This source also defines chance as *any* event happening in the absence of any obvious design (randomly or accidentally), one that is irrelevant to any present need, or one of which the cause is unknown (Mayr, 1998; NODE¹).

Regaining in popularity in the early 20th century, serendipity became particularly popular in signifying the role of chance in scientific and industrial innovation (Tolson, 2004). Nearly one in ten of the most-cited scientific papers of all time explicitly mention serendipity, as popularly defined, as a contributing factor (Campanario, 1996). Nobel laureate Francis Crick thought it to be the only source of true novelty (Kaplan, 2001: 224). Simonton (2004: 161) similarly thought it to be the principal basis for scientific creativity. As to serendipity's popularity, by 1958 the word had appeared in print only 135 times. During the 1990s, it was used roughly 13,000 times in newspapers alone. A straightforward Google search reveals nearly 3 million documents containing references to serendipity today.

Yet scholarly research on serendipity is "anecdotal, sometimes hagiographic and rarely systematic" (Campanario, 1996: 3; Bandura, 1982, 1998), typically in reference to chance events. Barney, for example, referred to serendipity as a manifestation of a firm's good luck (1986: 1234). Jacobson (1990) observed that the unobservable factors that help determine firm performance, including luck, can be so significant that they outstrip the effects of those more amenable to measurement. Mancke (1974), Rumelt and Wensley (1980), and Jacobson and Aaker (1985) likewise expressed concern at the degree to which market share effects (following PIMS) can be overstated if not allowing for unobservable factors, including luck. Denrell, Fang and Winter (2003) emphasized the role of serendipity in the discovery of new strategic opportunities through the acquisition and leveraging of complex (as opposed to commodity) resources. Bertrand and Mullainathan concluded that CEO pay corresponds as much "to a lucky dollar as to a general dollar" (2001: 902). Cattani's (2004) recent study of the fiber optics industry led

¹ New Oxford Dictionary of English

him to conclude that performance variations between firms are, in part, a consequence of luck, in the development of resource heterogeneity. Likewise, Mintzberg (1987) and Mintzberg and Hugh (1985) recognized the role of random events in strategy formation, as did Cohen, March and Olsen (1972).

Yet, to equate serendipity to chance is to tell but a small part of a more interesting plot. Serendipity entails the identification of meaningful combinations of two or more events. These combinations are meaningful insofar as they can be put to practical or strategic use. To paraphrase Burt, serendipity is "to see bridges where others see holes" (2004: 351, footnote 2)¹. The mathematician Poincaré's précis is instructive:

[The useful or interesting combinations] are those who reveal to us unsuspected kinship between other facts, long known, but wrongly believed to be strangers to one another...[Accordingly,] among chosen combinations the most fertile will often be those formed of elements drawn from domains which are far apart. Not that I mean as sufficing for invention the bringing together of objects as disparate as possible; most combinations so formed would be entirely sterile. But certain among them, very rare, are the most fruitful of all (as quoted in Simonton, 2004: 42).

This characterization of serendipity is a radical departure from its popular uses, yet both more accurate historically and more useful for innovation research. Horace Walpole in a letter sent to his friend and distant cousin Horace Mann on January 28, 1754, told of a critical discovery he had made, based on a 16th century tale of three princes of Serendip (Sri Lanca)². The narrative talks of three princes who, one day, were sauntering along a trail and happened upon a camel driver. Having lost a camel, he wondered whether the princes might have seen it. Though they never saw the lost animal, they were nonetheless able to accurate describe it: it was blind in one eye, lacking a tooth, and lame.

² "This discovery, indeed, is almost of that kind which I call *Serendipity*, a very expressive word, which, as I have nothing better to tell you, I shall endeavor to explain to you: you will understand it better by the derivation than by the definition. I once read a silly fairy tale, called *the three Princes of Serendip*: as their Highnesses traveled, they were always making discoveries, by accidents and sagacity, of things which they were not in quest of: for instance, one of them discovered that a mule blind to the right eye had traveled the

Furthermore, the camel was carrying butter on one side and honey on the other, and was being ridden by a pregnant woman. Their description was so accurate, in fact, that the camel owner accused the princes of having stolen his camel, and formally charged them in the emperor's court. However, in the presence of Emperor Behram, it became clear that the princes were entirely innocent, having merely pieced together various events. They explained that they thought the camel blind in the right eye because the grass had been cropped only on the left side of the road. They inferred that it was missing a tooth from the bits of chewed grass scattered across the road. Its footprints seemed to suggest that the animal was lame and dragging one foot. Also, finding ants on one side of the road and flies on the other, they concluded that the camel must have been carrying butter on the ant's side, and honey on other. Finally, as for the presence of a pregnant woman, a combination of carnal desires on the part of the princes, and imprints of hands on the ground sufficed to bring about this final conclusion (Merton and Barber, 2004: 4).

Obviously, the princes did more than observe a suite of chance events. The tale is instructive precisely because the princes relied on creativity in recombining events – what Einstein called the 'combinatorial play' – and also practical judgment to deduce 'correct pairs' of events so as to generate a surprisingly effective (and, as it happens, entirely accurate) plot. This 'combinatorial play' underscores a distinct and identifiable *capability*, namely to recombine any number of observations and deduce 'matching pairs' – or sets of events that appear to be meaningfully related. These events can be either causally related (causal), such as the unintended consequences of design, or causally unrelated (a-causal), such as mere random occurrences. We refer to these as *recombinational capabilities* – the ability to recombine events (rather than resources) in unusual, but meaningful, ways.

The prevalence of serendipity

As early as 1679, Robert Hooke alluded to the importance of serendipity in research, describing invention as 'being but a lucky bitt of chance'. "We shall quickly find that the

same road lately, because the grass was eaten only on the left side, where it was worse than on the right—now do you understand *Serendipity?*" (Quoted in Merton and Barber, 2004: 2).

number of considerable observations and Inventions this way collected will a hundred fold out-strip those that are found by Design" (as quoted in Merton and Barber, 2004: 161). Priestley, writing in 1775, corroborated Hooke's conclusion by stating that "more is owing to what we call chance, that is, philosophically speaking, to the observation of events arising from unknown causes, than to any proper design, or preconceived theory in this business" (ibid.: 162). Likewise, the physicist and Nobel laureate Bridgman commented: "...how seldom the course of scientific development has been the logical course...Much more often the course of development is determined by factors which are quite adventitious as far as any connection goes with immediate human purpose", as did the French biologist Richet: "It will be a rather humiliating profession of faith, since I attribute a considerable role to chance" (ibid: 164-5). Bernard noted that ideas are often born by chance; Root-Berstein (1989) thought invention to be guided by intention, but discovery by surprise; Harwick, upon examining 43 cosmic phenomena concluded that about half took place in a serendipitous manner, whilst Koestler described scientific discovery as full of arrivals at unexpected destinations, and arrivals at correct destinations but by the wrong boat (Campanario, 1996). Philosophers of science have been similarly critical of innovation as the consequence of careful design. "The history of science", Feyerabend concluded, is "as complex, chaotic, full of mistakes, and entertaining as the ideas it contains, and these ideas in turn will be as complex, chaotic, full of mistakes, and entertaining as are the minds of those who invented them (Feyerabend, 1993: 11).

Aside from product innovations, Portes (2000) provides illustrations of serendipity in public policy generation. Merton supplies examples of serendipity in social research, or "the fairly common experience of observing an unanticipated, anomalous and strategic datum which becomes the occasion for developing a new theory or for extending an existing theory" (Merton, 1948: 506). Indeed, he acknowledged serendipity as having contributed to his own work on its sociological semantics (Merton and Barber, 2004: 238). Govier (2003) too published a detailed account of serendipity in psychology research. Eco documented historical instances of serendipity in semiotics: "the best instances, false beliefs and discoveries totally without credibility have resulted in the discovery of something true (or at least something we consider true today)", via a

mechanism known as serendipity (Eco, 1999: ix). Van Andel and Bourcier, citing Plato's: "[a] man cannot inquire either about what he knows or about what he does not know[.] For he cannot inquire about what he knows, because he knows it, and in that case is in no need of inquiry; nor again can he inquire about what he does not know, since he does not know about what he is to inquire", conclude that serendipity may well be responsible for much progress (van Andel and Bourcier, 2001: 1606).

Kuhn suggested that the process of scientific discovery begins with the awareness of anomaly, or 'unsought factors': "the recognition that nature has somehow violated the paradigm-induced expectations that govern normal science" (Kuhn, 1970: 52-53). He acknowledged the role of serendipity in the development of his own theory on the structure of scientific revolutions. Struck by the stark contrast in social dynamics between the Center for Advanced Studies in the Behavioural Sciences (where he spent the 1958-9 year) and the scientific community in which he had been trained, he hit on the idea of scientific 'paradigms', or "scientific achievements that for a time provide model problems and solutions to a community of practitioners". As Kuhn admits: "Once that piece of my puzzle fell into place, a draft of this essay [The Structure of Scientific Revolutions] emerged rapidly" (Kuhn, 1970: viii).

Thus, it seems chance occurrences alone do not adequately explain new scientific discoveries. Consistent with Pasteur's oft-cited aphorism, Rossman, writing in the 1930s, suggested:

Chance or accident plays a very small part in inventing today. We have seen...that the inventors...employ deliberate and systematic methods in making their inventions in which chance has a very small part. Only 75 out of 259 inventors who were asked whether chance or accident played any part in their inventing replied in the affirmative...Many impressive and highly colored stories have been told of accidental discoveries and inventions. It is natural, of course, that such stories should appeal to the popular imagination. A careful study of these stories of accidental invention, however, will reveal the fact that lucky accidents only happen to those who deserve them. In nearly all cases we find that

the accident happens only after a persistent and carefully conducted search for what is wanted (quoted in Merton and Barber, p. 166-7).

Varieties of serendipity

The natural sciences are fertile sources of serendipity in innovation. Particularly wellknown examples include aspirin, penicillin, the smallpox vaccine, anesthetic (nitrous oxide), and insulin. Says Werth:

Scientists, curiously, talk a lot about luck. As murderously as they work, as dedicated as they are to rigor, as much as they may believe in their own perfection, they concede that great scientific careers are almost always favored by something else: great timing of an unseen hand connecting the observer and the observed. Pasteur's oft-used remark about fortune encapsulates the view, almost universally shared among scientists, especially in the drug industry, that *they'd rather be lucky than good* (1994: 210; italics added).

Following are detailed descriptions of serendipity in four scientific discoveries. Three of these were awarded a Nobel Prize. Our primary criterion for selecting these examples was that each had to be well documented, allowing us to draw on a variety of sources to afford triangulation. These sources would typically include biographical accounts of the discovery, as well as reflections by collaborators, peers, philosophers and historians of science, and journalists. In chronicling the elucidation of the DNA molecule, for instance, we used biographies of both Francis Crick and Jim Watson, as well as their original 1953 article in Nature, and a daunting stack of related articles and books.

We think these discoveries to be good illustrations of the *true* nature of serendipity as exploiting a particular capability, namely that of identifying 'matching pairs' of events – or events that are meaningfully rather than causally related – that permit applications which "quicken the practice of innovation, or bear upon generalized theory" (cf. Merton, 1948: 506). Serendipity features in each.

Serendipity by way of random variation: Penicillin

Alexander Fleming shared the 1945 Nobel Prize in physiology or medicine with Ernst Chain and Howard Florey for the discovery and isolation of penicillin. Their story is well documented. In September 1928, Fleming noticed a contaminated culture plate amongst various un-incubated petri dishes piled up in the sink of his laboratory. Sometime during that summer, a spore appears to have wafted in from the mycology labs one floor down, and landed on one of his Petri dishes, creating a circular mold colony. In conversation with D.M. Pryce, a former research student, Fleming happened to pick up this particular dish and noticed that the mold had killed off the staphylococcus colonies (bacteria, the properties of which he had been researching for some time) immediately surrounding it. He noted it was from the Penicillium notatum family, very much hoped it to be an alternative source of lysosome (which, based on his previous research, he knew to be responsible for destroying bacteria), yet failed to isolate it. He subsequently seems to have lost interest, publishing nothing on it after 1931 (Crease, 1989).

This historic event was anticipated by a similar chance discovery ten years earlier. Alexander Fleming was notoriously untidy and experimental. In January 1919, plagued by a bad cold, Fleming used his own mucus as a source of bacteria for his experiments. His subsequent observation that something in this mucus seemed to be inhibiting bacterial growth lead to his discovery of the enzyme lysosome (which prepared the way for his discovery of penicillin in 1928). His research assistant recorded the circumstances surrounding the discovery of lysosome:

Early on, Fleming began to tease me about my excessive tidiness in the laboratory. At the end of each day's work I cleaned my bench, put it in order for the next day and discarded all tubes and culture plates for which I had no further use...[Fleming], for his part, kept his cultures...for two or three weeks until his bench was overcrowded with 40 or 50 cultures. He would then discard them, first of all looking at them individually to see whether anything interesting or unusual had developed...if he had been as tidy as he thought I was, he would never have made his two great discoveries...Discarding his cultures one evening, he examined one for some time, showed it to me and said 'This is interesting'. The

plate was one on which he had cultured mucus from his nose some two weeks earlier, when suffering from a cold. The plate was covered with golden-yellow colonies of bacteria, obviously harmless contaminants deriving from the air or dust of the laboratory, or blown in through the window from the air in Praed Street (as quoted in Gratzer, 2002: 215-6).

Undoubtedly, Fleming was lucky in that the bacteria that had colonized his dish were of a kind uniquely susceptible to being eliminated by lysosome. Moreover, the penicillin mold that appeared in Fleming's dish in 1928 was exceptionally rare with unusually high antibacterial properties, and was able to incubate during an unusual cold weather spell followed by a warm period to grow the staphylococci. As Waller concludes, Fleming's discovery "was built on an impressive edifice of chance events, several of which had an exceptionally low likelihood of occurring even in isolation (Waller, 2002: 252).

Fleming's observations, while entirely unanticipated, were meaningful, not least because the effect of molds on bacterial growth had been fairly well established. At least seven scientists, including Pasteur, had confirmed this several decades earlier. According to Slowiczek and Peters (2004), written records dating back to 1500 BC describe how molds and fermented materials were used as therapeutic agents. Serious research on the contamination of laboratory-grown bacterial cultures in the late 1800s highlighted the impact of mold on bacterial growth. Specifically, in 1875, John Tyndall explained to the Royal Society how a type of penicillin had killed off bacteria. In 1874, William Roberts observed that penicillin cultures did not exhibit bacterial contamination. Only a few years later, Louis Pasteur and Jules Francois Joubert noticed that their anthrax bacterial culture failed to grow when contaminated with mold. Yet again, in 1871, Joseph Lister found that urine samples that were contaminated with mold did not allow for bacterial growth. And a dissertation written in 1897 by Ernest Duchesne, a French medical student, described the discovery, partial refinement and successful testing on animals of an antibiotic based on penicillin. Indeed, Waller (2002) notes that Fleming's personal contribution never advanced beyond that of Duchesne (who died of tuberculosis before bringing his project to fruition).

While Fleming had always claimed that penicillin would prove to be a wonder drug (Waller, 2002), he was never able to produce a purified form of it, and his discovery lay dormant for ten years. In 1938, two Oxford University scientists, having stumbled on Fleming's original article, purified and stabilized a form of penicillin so its therapeutic potential could be demonstrated. Quite by chance they ended up using mice that proved unaffected by the toxicity of penicillin (one of very few species that do not find penicillin toxic). Given the desperate need for treating wound infections sustained during WWII, Florey surrendered his patent rights to allow US pharmaceutical factories to produce large batches of the life-saving antibiotic (Bishop, 2003).

Given the crucial roles of Florey and Chain in isolating and purifying penicillin, it is perhaps little wonder that Fleming felt his Nobel Prize to have been undeserved. As a contemporary recalls: "he told me often that he didn't deserve the Nobel Prize, and I had to bit my teeth not to agree with him" (as quoted in Gratzer, 2002: 219). After all, Fleming's observations made perfect sense. He was sagacious in construct a meaningful 'bridge' between two random occurrences and observations made by others before him.

Serendipity as the unintended consequence of design: sildenafil citrate

Serendipity can also come about as the unintended consequence of innovation, where products are discovered to have uses other than those for which they were originally designed. Particularly well-known examples include *aspirin*, intended as an anti-inflammatory but widely used as a preventative measure against heart attacks, and *minoxidil*, developed to treat high-blood pressure but prescribed against hair loss. Even *Coca Cola* was originally patented (in 1886) as "Pemberton's French Wine Coca" for medicinal purposes, as a nerve and tonic stimulant, and a cure for headaches.

A particularly recent example entails Pfizer's discovery of a temporary cure for erectile dysfunction. In the mid-eighties, Pfizer began a research program into angina -a disabling heart condition that results from an insufficient supply of oxygen to the heart. When an active chemical compound had been isolated (*sildenafil citrate*), Pfizer

scientists took the customary route of commencing clinical trials. When safety trials suggested that the drug was relatively non-toxic, Pfizer ensued with second phase trails to test for efficacy using volunteers afflicted with the heart condition. To Pfizer's chagrin, the trial results proved disappointing.

However, clinicians running the ongoing safety studies had learned of some interesting side effects to the drug. As one of the original project team members recalled: "When the first observations of erections were reported, the investigator who was doing the study in Wales was a little bit embarrassed to mention it...When we explored the possibility of treating patients with erection problems...some of those patients said 'hey this is working', I need some more supplies..."²

Pfizer decided to commit another \$340 million to the project by repeating Phase II clinical trials using impotent men as a target group. The drug's effectiveness was, this time, beyond doubt. The Food and Drug Administration approved Viagra in March 1998. It had generated revenues of US \$300 million by early May 1998 in the US alone. Ranked as the third best-selling drug of the past ten years, Viagra's net present value is estimated at over US\$6 billion.

Clearly, Pfizer scientists were fortuitous in discovering its 'accidental' side effects in toxicity trials. Yet why is this so surprising? After all, the role of luck in scientific and technological advances is well recognized. At the same time, however, some scientists at Pfizer had become increasingly aware of the likely efficacy of their drug when used to treat erectile dysfunction, so much so that Pfizer was to loose its lucrative UK patent in November 2000 for reasons of 'obviousness'³.

Pseudo-serendipity by way of random variation: DNA

In other serendipitous discoveries, chance plays a much less significant role. For example, elucidating the 'double helix' structure for Deoxyribose Nucleic Acid (DNA) required a combination of unplanned events and a good deal of sagacity. James Watson and Francis Crick were awarded the Nobel Prize for this discovery in 1962. Both were

frank about the spirit of adventure, tenacity, and youthful arrogance – but also frustration, fear, mistakes, and serendipity - that marked this process of discovery. Having met at the Cavendish Laboratory of Cambridge University in 1951, Watson and Crick recognized a shared interest in the role of DNA in heredity. Neither had formally been assigned to DNA research; in fact, both creatively masked some of their DNA work by relating it to other in-house projects (e.g. the tobacco mosaic virus (TMV) and X-ray diffraction of polypeptides and proteins). They intuited that DNA contained the 'secret of life', and that its structure, "once found, would be simple as well as pretty" (Watson, 1999: 13). Aware of the elaborate crystallographic analysis of Wilkins and Franklin at King's College, London, and the little progress it had achieved, Crick and Watson decided to approach DNA elucidation instead through model building. In sharp contrast to Franklin's continued insistence that "there was not a shred of evidence that DNA was helical", they expected the molecule to contain two or three chains (Watson, 1999: 79). Watson's loosely related work on TMV seemed to support a helical structure. One night in June 1952, he was examining X-ray photographs of a new TMV sample and noticed its telltale helical markings. If this were true of the virus, then why not also of DNA?

Further serendipitous events followed to direct Watson and Crick's efforts. One entailed a discussion over beer with John Griffith, a theoretical chemist, after an evening talk by the astronomer Tommy Gold. Gold alluded to 'the perfect cosmological principle', to which Griffith responded by wondering whether an argument could be made for a 'perfect biological principle', according to which genes would self-replicate. While this hypothesis had been floating about for nearly three decades, most scientists assumed that gene duplication required the creation of a 'negative' template from which a copy could subsequently be crafted (Watson, 1999). Francis, by contrast, thought DNA replication to involve attractive forces between the flat surfaces of the bases with different structures. That evening they agreed that Griffith would try to calculate these attractive forces. Shortly afterwards, Griffith responded by hinting that adenine and thymine should stick to each other as, in principle, should guanine and cytosine (the four bases of DNA). Francis paired this observation with prior research by Chargaff, suggesting that these four bases seemed to occur in equal quantities. This suddenly made sense. As Crick commented:

The key discovery was Jim's determination of the exact nature of the two base pairs (A with T, G with C). He did this not by logic, but by serendipity...In a sense Jim's discovery was luck, but then most discoveries have an element of luck in them. The more important point is that Jim was looking for something significant and *immediately recognized the significance of the correct pairs when he hit upon them by chance* (Crick, 1988: 65-66; italics in original).

Some time later, yet another non-trivial idea surfaced. "It came while I was drawing fused rings of adenine on paper. Suddenly I realized the potentially profound implications of a DNA structure in which the adenine residue formed hydrogen bonds similar to those found in crystals of pure adenine" (Watson, 1999: 145). Thus, Watson concluded, DNA might consist of two chains with identical base sequences held together by hydrogen bonds between pairs of identical bases Even if this hypothesis subsequently proved to be false, it did point Watson towards the correct 'double helix' structure for DNA.

Perhaps the most significant serendipitous event was the sharing of an office with Jerry Donohue, a crystallographer who, when confronted with Crick and Watson's semideveloped model, claimed that most textbooks representations of tautomeric forms of guanine and thymine were highly improbable. This proved to be a terrible disappointment, as they relied on these forms in building their model. As Watson recollects: "Thoroughly worried, I went back to my desk hoping that some gimmick might emerge to salvage the like-with-like idea. But it was obvious that the new assignments were its death blow" (Watson, 1999: 151). Only the next morning, when clearing his desk of papers, did Watson conceive of a sequence of adenine-thymine pairs, held together by two hydrogen bonds, as being identical in shape to a guanine-cytosine pair, held together by at least two hydrogen bonds. When verifying this possibility, Donohue raised no objections. Thus, the double-helix structure was conceived.

The unforeseen dividend of having Jerry [Donohue] share an office with Francis, Peter and me, though obvious to all, was not spoken about. If he had not been with us in Cambridge, I might still have been pumping for a like-with-like structure. Maurice [Wilkins], in a lab devoid of structural chemists, did not have anyone about to tell him that all the textbook pictures were wrong (Watson, 1999: 163).

The first in a series of four articles announcing the discovery was published Nature in 1953. The only allusion to its considerable implications for heredity was famously entailed in its final sentence: "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material" (Watson and Crick, 1953: 737). The article was just over a page in length.

Pseudo-serendipity as the unintended consequence of design: PCR

Kary Mullis was awarded the 1993 Nobel Prize in chemistry for his discovery of a DNA amplification method called polymerase chain reaction (PCR), a molecular biological method for creating multiple copies of a specific stretch of DNA (e.g. a single gene or part of a gene) without using a living organism. By taking DNA polymerase from heat-loving (thermophylic) bacteria, Mullis was able to separate DNA in two strands by heating it to 96°C, but without also destroying the DNA polymerase used to duplicate DNA when cells divide. Thus it was no longer necessary to manually add DNA polymerase after each DNA strand separation. Instead, the process could be simplified and automated to copy as many DNA strands as required. This ingenious method is used today in diagnosing infectious and hereditary diseases, and in DNA fingerprinting.

Mullis came to this discovery one night while driving his car along California's Highway 128. At the time (in 1983), he was employed at the Cetus Corporation, who was to sell the rights to Mullis' PCR method to Hoffmann-La Roche for US\$300 million. With time on his hands, he had started to think about an improvement in DNA sequences, a thought-puzzle that ultimately lead him to PCR. Mullis recognized the importance of his discovery immediately: "This simple technique would make as many copies as I wanted of any DNA sequence I chose, and everybody on Earth who cared about DNA would

want to use it. It would spread into every biology lab in the world. I would be famous. I would get the Nobel Prize" (Mullis, 2000: 6-7).

Despite the significance of Mullis' discovery, it was not entirely unexpected given that PCR relies on a reconfiguration of well-known, existing technologies. As Fields (2001: 10052) points out, "PCR arose from dideoxy sequencing, developed in Frederick Sanger's laboratory about 6 years earlier". In turn, dideoxy sequencing was based on the 'plus and minus' system, another of Sanger's techniques. The 'plus and minus' system itself was enabled by various pre-existing technologies, including radioactive precursors to follow DNA molecules, other methods for separating DNA fragments, the isolation and characterization of DNA polymerase, and various other techniques (Fields, 2000).

So by the early 1980s, all of reagents and procedures were in place for PCR to come about. Many molecular biologists other than Kary Mullis could have invented PCR, making its eventual introduction *inevitable*. All that was needed was the inspiration of one individual with the willingness to putter about with enzymes and primers (Fields, 2001: 10052; italics added).

Indeed, in his autobiographical account Mullis acknowledged that "there was not a single unknown in the scheme. Every step involved had been done already" (Mullis, 2000: 9). Mullis' sagacity resided not in seeing what no one had seen before, but in thinking what no one had yet thought of.

Serendipity revisited

Despite individual differences, these four innovations share at least one important feature: they were made by individuals able to 'see bridges where others saw holes'. To see bridges, or 'matching pairs', is to creatively recombine events based on the appearance of a meaningful rather than causal link. Both Fleming and Pfizer's scientists applied creativity and practical judgment in matching observations of unforeseen events with findings reported by others, and in selecting which of these combinations might be fruitful. They rightly interpreted coincidences as meaningful in the context of the knowledge available to them at the time. However, the particle from the mycology labs

wafting through Alexander's Fleming's open window to contaminate a bacterial culture is a random variation, as were the unusual changes in temperature. By contrast, the unanticipated side effects of sildenafil citrate surfaced in part as a result of research design; after all, toxicity trials tend to use men between the ages of 18 and 30, as did Pfizer's clinical trials.

Crick and Watson's discovery of the 'double helix' structure of DNA was marked by various unplanned events such as Watson's loosely related work on TMV (corroborating their suspicions of a helical structure), and exchanges with Griffith and Donohue (in directing them towards the specific, but unorthodox, pairing of bases). Yet they always knew they were after the structure of DNA, believing it to contain the secret of life. Thus, DNA illustrates pseudo-serendipity, insofar as chance events enabled the unraveling of the molecule, yet these events never caused them to deviate from this original target. Similarly, Mullis had been searching for a method that would improve the replication of DNA fragments. His PCR method relied entirely on existing technologies. Eccentricity, rather than chance, may have played a role in Mullis' discovery. A product of 1960s Berkeley, he confessed to far-reaching experiments involving LSD, antihistamines, and various home-made psychoactive drugs, using himself as the principal subject. Based on his autobiographical account, Mullis' innovation rather seems to have been a consequence of sloppy research and naivety ("in truth, I was terribly naïve...if I had had more knowledge about what I was doing, PCR would never have been invented", p. 24), a refusal to be bound by prevailing scientific paradigms, and a keen eye for matching pairs of technological developments, able to select what seemed like effective technological combinations; a feat accomplished by leveraging his powers of observation, combination, adjudication, and application.

While the 'unplanned' or 'random' element retains a role in serendipitous innovation, it appears to be more peripheral than typically assumed. For it is but one of several raw materials – albeit an important one – on which serendipity relies but is not, strictly speaking, tantamount to. Chance is an event, serendipity a capability. Chance has no bite but for creativity in brokering random events meaningfully with other events.

"Significant inventions are not mere accidents", suggested Nobel laureate Paul Flory (Roberts, 1989: x). "Many a man floated in water before Archimedes; apples fell from trees as long ago as the Garden of Eden [...] chance discovery involves both the phenomenon to be observed and the appropriate, intelligent observer" (Walter Cannon, as quoted in Merton & Barber, 2004: 171-2). As Jung (1973) points out, the process of recognizing a-causal events is subjective. It is intrinsic to the observer. As aptly put by Willis Whitney, formerly a director of research for General Electric:

In every individual's stock of knowledge (his conscious and subconscious assets) there lie the peculiar items or records of his former thoughts. Some of them may 'pop out' or 'come to mind' when a novel or unexpected event crosses his mental threshold. Some sort of catalysis has taken place. This all indicates dependence of the gift of serendipity upon the total (even forgotten) knowledge and training of the individual (quoted in Merton and Barber, 2004: 173).

A typology of serendipity

By exploiting the similarities and differences across these case histories, we are able to arrive at a typology of serendipity. When it came to the discovery of PCR and DNA, those involved found what it was they were looking for but by way of chance. By contrast, in the discoveries of sildenafil citrate and penicillin, scientists discovered something different from what they were looking for. The former can be labeled 'pseudo-serendipity' (Roberts, 1989), also known as 'serendipity analogues' (de Chumaceiro & Yaber, 1995). Here the objective remained unchanged, but the route towards achieving this objective proved unusual and surprising. By contrast, the latter is 'true serendipity', or 'serendipity proper' (de Chumaceiro & Yaber, 1995), so as to emphasize a change in objective as a result of the discovery process.

A further distinction can be made between chance as the unintended consequence of research design, and chance as pure random variation. So, for instance, in the sildenafil citrate and PCR examples, opportunities arose as a direct consequence of the way the study was designed: the unintended side-effects of sildenafil citrate appeared precisely because Phase 1 clinical trials generally use healthy male volunteers (rather than

females); the idea of PCR relied entirely on Mullis' imaginative efforts at recombining a set of existing technologies. In the cases of sildenafil citrate and PCR, the unintended consequence is *causally related* to a design process. By contrast, the discoveries of penicillin and DNA benefited from random chance occurrences: the spore in Fleming's dish had most likely wafted in from the mycology labs located one floor down; Crick was fortunate to share his office with a crystallographer (an advantage not shared by Wilkins and Franklin). Either event was *causally unrelated* to any research design – or a-causal. The resulting typology can be represented by means of a simple matrix (Figure 1).

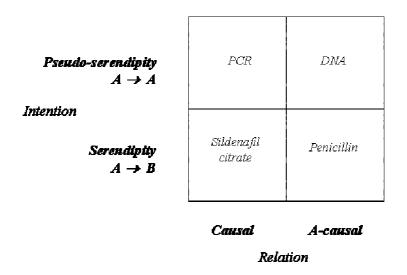


Figure 1: A typology of serendipity

Conclusions and implications

This paper addressed the context of scientific innovation, rather than its context of justification (or validation) or commercialization. Specifically, it attended to innovation through what is popularly called serendipity. In so doing, the papers aimed at three objectives: (a) to respond to a paucity of research on serendipity; (b) to provide conceptual clarity in defining serendipity; and (c) to propose a means of operationalizing serendipity for research purposes. As for the first of these, the paucity of empirical research may be explained, at least partly, by an incorrect use of serendipity as synonymous with chance, luck or providence. Thus defined it remains difficult to operationalize. This paper sought conceptual clarity in proposing four types of

serendipity, exemplified by four examples. Each illustrated serendipity as the identification of 'correct pairs' of events, where 'correct' means 'meaningful', not causal. After all, the princes of Serendip were sagacious, inasmuch as they made unplanned observations.

Serendipity, the examples suggest, may benefit from a degree of sloppiness, inefficiency, dissent, failure, and tenacity – on "loafing and savoring the moment, of wandering and loitering and directionless activity of all sorts" (Ferguson, 1999: 194), or those things organizational research seeks to minimize in its emphasis on efficiency. "It often pays to do somewhat untidy experiments, provided one is aware of the element of untidiness" (Merton and Barber, 2004: 192-3). Clearly, as Merton and Barber (2004: 201) note, too much dictatorship over research is clearly as stifling and impractical as it is morally repugnant.

Research on innovation entrepreneurship by Burgelman (1983) and Bygrave (1989) emphasized the importance of "controlled sloppiness" in highly innovative organizations. Furthermore, Weick (1977) and March (1981) suggest that activities not directly related to the organization mission improve the capacity of response to changing conditions. This sloppiness-by-design can help organizations in responding to serendipity.

This 'controlled sloppiness' is also consistent with those who have emphasized the necessity to sustain a balance between freedom and constraint, emergence and planning. Mirvis (1998), adopting jazz improvisation as a metaphor, suggested creating situations where unplanned interactions are directed by an ex-ante preparation. The purpose is that of providing an environment where unintentional events can occur and be noted. By tolerating a measure of 'sloppiness' through structural diversity, organizations can prepare themselves for serendipity. Similarly, relationships that span groups of individuals that would not normally interact may increase an organization's propensity to access, absorb, and exploit diverse sets of ideas. Geletkanycz and Hambrick (1997) observed that managers, whose relationships span organizational and industry boundaries, tend to attain a higher level of performance. Similarly, McEvily and Zaheer

(1999) found that manufacturers with more non-redundant sources of advice beyond the organization seemed to have greater access to competitive ideas. Koput and Powell (2003) concluded that biotechnology firms with mores types of activities involving more types of partner organizations had higher chances of survival and earnings potential (cf. Burt, 2004: 358). Likewise, Pennings and Harianto (1992: 365) in their study of the US banking industry found that the more a firm "accumulated networking skills, as inferred from the magnitude of strategic alliances, the higher the probability of innovation". Furthermore, Bundy (2002), based on his experience of R&D management, stressed the importance of diversity and connecting apparently unrelated bits of know-how to foster innovation.

Likewise, the safeguarding of the freedom of dissent is a requisite for organizations in search of innovative solutions (Nemeth, 1997). Also, freedom to act independently in the initial stages of an innovation process, or to be able to reconfigure existing problems into new lines of research, tends to facilitate the emergence of unexpected discoveries. Furthermore, a risk-taking and entrepreneurial ambiance, reinforced by symbols and incentives, may encourage the development and dissemination of novel ideas. Finally, the active search for diversity and heterogeneity in profiles, specialties, and disciplinary backgrounds may supply the right blend of talents necessary for innovation. It can also be enhanced through managerial techniques such as brainstorming of open-ended discussion groups. Intuition plays a critical role to the extent that it can help synthesize disparate ideas, and thus achieve serendipity (Isaack, 1978). In the same spirit, Swedberg (1990: 3) and Burt (2004: 350) quoted John Stuart Mill ([1848] 1987: 581) as suggesting that "it is hardly possible to overrate the value...of placing human beings in contact with persons dissimilar to themselves, and with modes of thought and action unlike those with which they are familiar...Such communication has always been, and is peculiarly in the present age, one of the primary sources of progress".⁴

Serendipity, properly understood, also accentuates the importance of the historical and social features of the innovation process. Insofar as serendipity relies on scientists 'matching' events meaningfully with their knowledge of the past, to understand this past

is as vital as to anticipate the future. By the same token, the myth of the 'lone scientist' sits uncomfortably alongside the definition of serendipity. It is unlikely that Fleming, Watson, Crick, and Mullis could have achieved their breakthrough innovations without the benefit of those around them. The elucidation of DNA is particularly relevant in this respect. These conclusions are consistent with Hargadon's (2003) detailed study of breakthrough innovations.

To understand serendipity as a capability, rather than as tantamount to a chance event, opens a Pandora's box of questions for future research: Are some organizations 'luckier' than others, and if so why? If chance favors the 'prepared mind', what does preparedness mean in the context of organizations? Is there such a thing as 'organizational serendipity'? Or is serendipity invariably embedded in individual people, leaving innovation in the hands of recruiters? How differently do organizations respond to accidental discoveries? Is there an optimal degree of inefficiency or wastefulness to be tolerated (even planned for) in innovative organizations? What organizational processes allow for one research trajectory to be pursued (even if triggered by coincidence or intuitions) but not others? What are the consequences for halting unpromising projects that, while economizing on expenditure, may pre-empt serendipity by abandoning projects too soon?

Last but not least, in redefining serendipity as the junction of a-causal but meaningful events, we can finally make out a structure to serendipity. The legendary status of such 'chance' discoveries as penicillin, Velcro, X-rays, aspirin, Post-It Notes, the HP Inkjet printer, or Scotchguard are no longer justified. Rather, the seeds of discovery were brewing long before the chance observations credited with innovations. As Szent-Györgyi, who discovered vitamin C, insightfully surmised: "discovery is seeing what everybody else has seen, but thinking what nobody else has thought".

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¹ Thus conceived, serendipity is not inconsistent with Burt's (2004) 'brokering' of structural holes in social networks so as to generate new ideas. According to Burt (2004: 349-50), "people who stand near the holes in a social structure are at higher risk of having good ideas...New ideas emerge from selection and synthesis across the structural holes between groups". Thus, Burt also places agency squarely at the centre of idea generation. "To be sure, ideas come over a variety of paths from a variety of sources [...], but idea generation at some point involves someone moving knowledge from this group to that, or combining bits of knowledge across groups" (Burt, 2004: 356).

² From *The Serendipity of Science*, a series of radio programmes aired between 15 and 29 August 2002 at 9.02pm on Radio 4. Produced by Simon Singh. The author acknowledges the kind help of Simon Singh in making his interview transcript with Dr Ian Osterloh available.

³ Ely Lilly, in collaboration with ICOS Corporation, referred to three documents – two journal articles and a PhD dissertation – each of which was considered 'prior art' and independently could have warranted the invalidation of Pfizer's patent for lack of novelty. In fact, the tribunal uncovered a copy of one of these articles, marked by a Pfizer scientist with: '*Should we not try out [sildenafil citrate] in impotence*?' Thus, Lilly claimed that Pfizer had done little more than to put into practice the suggestions offered in these three documents. The UK High Court of Justice, in November 2000, ruled in favor of the plaintiffs and revoked Pfizer's patent. Viagra's discovery was considered inevitable.

⁴ But of course, not all serendipitous discoveries are equally valuable. Christopher Columbus, for instance, never had the sagacity to recognize the significance of his discovery. As Roberts explains, he died a disappointed man, "believing he had found new areas of the Orient rather than a new continent" (1989: 5). Ironically, Columbus' calculations grossly underestimated the size of the earth, yet legitimized his decision to sail West in an effort to reach the Indies. His calculations, which were far less accurate than those of the sages of Salamanca, proved useful in discovering America precisely because they were so far off the mark. "And so you see how complicated life is, and how fragile are the boundaries between truth and error, right and wrong...Columbus, while he was wrong, pursued faithfully his error and proved to be right – thanks to serendipity" (Eco, 1999: 7).