

THE IMPORTANCE OF BEING ELEGANT: A DISCUSSION OF ELEGANCE IN NEPHROLOGY AND BIOMEDICAL SCIENCE*

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Abstract

Elegance is pursued and appreciated in virtually all aspects of our lives, from fashion to visual and performing arts, from literature to architecture. While most of us praise the elegance and beauty of science when we see it, elegance is typically treated as something that need not concern our research and thus does not belong inside the laboratory. In this article, we provide an alternative perspective, according to which elegance is more than an accessory ornament of scientific theories. We endorse and defend the view that elegance is an intrinsic feature of successful scientific practice and observation, a benchmark that demarcates between good experiments and bad ones. In support of our conclusions, we present and discuss three paradigms of scientific elegance: Jenners discovery of vaccination, Bricker and Slatopolsky's *trade-off hypothesis*, and Brenners hypothesis regarding the role of residual nephrons in the decline of renal function.

1 Introduction

Elegance is pursued and appreciated in virtually all aspects of our lives, from fashion to visual and performing arts, from literature to architecture. What about *science*? Can science be elegant? *Prima facie*, the answer seems obvious: of course science can be elegant. Indeed, we all have our favorite examples of elegant scientific work and the elegance of science is often what fascinates and

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attracts young scholars, getting them interested in science in the first place. Nevertheless, upon further scrutiny, two important questions arise, which are seldom articulated: *what* makes science elegant? And *why* should science be elegant?

What makes science elegant?

With respect to the former question, attempts to isolate the characteristic features of elegant science are stilled by the difficulty of providing a clear yet informative definition. Our inability to define elegance in science (as in all other domains) is paradoxical. We constantly perceive, recognize, admire and pursue elegance; yet we seem to be incapable of providing an adequate definition. Now, surely we can single out some features—such as *clarity*, *geniality* and *simplicity*—that contribute towards a general characterization of elegant science (4). Yet these features can, at best, provide some useful landmarks for spotting elegance; they fall short of a rigorous definition. For one thing, all of these properties are no less vague and hard to capture as elegance itself: dubbing a piece of scientific work as ‘clear,’ ‘simple’ or ‘work of genius’ is as controversial and in need of clarification as the claim that such piece of work is ‘elegant.’ Furthermore, these properties are not specific to elegance as it pertains to scientific research, but can be applied across the board to identify elegant music, elegant poetry, elegance in fashion and so forth. A characterization so general as to be applicable to virtually any domain can hardly be employed to single out the defining features of elegance in a field so diverse, complex and constantly evolving such as modern science.

Living without definitions

In short, we fall short of rigorous definitions of elegance *per se* and of elegant science. Yet, this lack of precise definition should not frustrate an attempt to examine the importance of elegance in science. Indeed, one of the important lessons philosophy teaches us is that the search for necessary and sufficient conditions for the application of concepts is often chimerical and unnecessary. The lack of definitions grounding basic concepts such as *knowledge*, *justice* or *probability* never hindered our capacity to engage in meaningful and critical debates in epistemology, ethics and statistics. The same is true of elegance. Thus, in the present article, we shall not attempt to provide an abstract theoretical definition that captures the ‘essence’ or the ‘true nature’ of elegance. More modestly, in what follows, we shall provide a brief analysis of some paradigmatic instances of elegant science in support of our main claim, that elegance has an important role to play in scientific research.

The significance of elegance in science

Moving on to the second question raised above, the significance of elegance for scientific research raises an important and controversial issue. While most

of us praise the elegance and beauty of science when we see it, elegance is typically treated as something that need not concern our research and thus does not belong inside the laboratory. We are in the business of solving problems, finding cures to diseases; we cannot—and should not—waste our time pursuing elegance. At most, elegance is treated as an accessory, a way to make the presentation of our theories more interesting to colleagues, more palatable to students and more appealing to grant committees and financing institutions. Elegance is not a goal of scientific research *per se*. In what follows, we suggest an alternative perspective, according to which elegance should be viewed as more than an accessory ornament of scientific theories. We endorse the view that—just like accuracy, generality and testability—elegance is an intrinsic feature of successful scientific practice and observation, a benchmark that demarcates between good experiments and bad ones. Hence, elegance belongs inside the laboratory, not to textbooks, coffee breaks and grant proposals.

2 Paradigms of scientific elegance

According to a widespread tendency, the elegance of a scientific theory can be identified with its mathematical structure. This idea is by no means new; it is already present in Leibniz's *Monadology*, where the German philosopher defines the 'best of possible worlds' as that possessing greatest multiplicity and diversity, harmonized by the fewest and simplest formal (in general, mathematical) laws. A similar intuition is also found in Kant's *Critique of Pure Reason*, where modern science is characterized as an enterprise whose basic aim is the unification of phenomena under universal laws. Yet, we contend that reducing elegance to mathematics overlooks the various facets and dimensions of scientific elegance. The following examples emphasize how the elegance of science transcends mathematical simplicity once we move away from the physical science and focus on biological and biomedical research.

Jenner's discovery of vaccination

To begin, let us consider a celebrated chapter in the history of medicine: Edward Jenner's discovery of vaccination. Contrary to popular knowledge, the idea underlying the process of vaccination was not invented and developed from scratch. A similar practice, called *variolation*, was widely employed in various countries, such as China and India, in order to minimize the devastating effects of smallpox epidemics. Variolation involved the voluntary infection of a person with a mild form of smallpox, followed by a relatively mild contagion, which would make the person immune to future infections from the smallpox virus. While variolation is a relatively effective means against smallpox epidemics, it could become extremely dangerous because the—generally mild—infection, could occasionally (in roughly 2% of cases) become serious, or even deadly. Furthermore, the exposed subject could herself become a source of contagion. Jenner employed folk knowledge to find a more effective and less dangerous

alternative to variolation. From the observation that dairymaids infected with cowpox were also immune to smallpox, he realized that a disease different from smallpox, though similar in some of its manifestations, could provide preventive measures against the devastating disease as effective as variolation, with a much lower risk of contagion. In other words, Jenner realized that the cowpox virus causes an immune response that prevents future infections with smallpox, while, being a different virus, it does not cause smallpox in the individual, and does not cause smallpox contagion. The origin of the cure also explains the name ‘vaccination,’ which derives from the Latin name for ‘cow’ (*vacca*), the animal which provided the cowpox virus that is injected in humans by scarification under the skin and causes an immune response where the antibodies can react with the smallpox virus. It is said that Jenner himself was so confident about the efficacy of his method of immunization that he did not hesitate to vaccinate young boys—including his own son—and then expose them to smallpox, which they failed to contract.

Jenner’s intuition, which allowed him to promptly foresee the wide-ranging clinical applications of vaccination, was undoubtedly important. Furthermore, the anecdote according to which he was confident enough to vaccinate his own son added strong drama. Yet, this is only part of the story. It seems to us that what makes Jenner’s story an effective paradigm of scientific elegance lies, at least in part, in his ability to capture the analogy between smallpox in humans and its variants, and to apply his discoveries in the broader field of immunology. This goes to show how elegance sometimes emerges in the form of *synthesis*—in the literal sense of collecting data and ‘placing them together.’ The elegance of Jenner’s discovery transcends the mere discovery of a new cure for a deadly disease. Otherwise, it would be hard to appreciate why vaccination is much more than a substantial improvement in the longstanding practice of variolation. In addition to its epidemiological control, the discovery of the efficacy of vaccinations provided an innovative systematization of various disconnected pieces of existing knowledge, opening up new and fruitful avenues for subsequent research.

Bricker and Slatopolsky’s trade-off hypothesis

While the history of science is replete with cases of elegance, for our second paradigm, let us restrict our attention to a more contemporary example: Bricker and Slatopolsky’s trade-off hypothesis. The fundamental intuition underlying Bricker and Slatopolsky’s discoveries is the idea that organisms pay a biological ‘price’ in order to maintain the invariance of mineral metabolism (calcium and phosphate homeostasis). The empirical basis of this research was presented in a study performed in dogs that were experimentally subjected to progressive renal failure (10; 11). The importance of equilibrium for the organism was already present in Hippocrates and Galen’s ancient theory of *humorism* (8) and, more recently, in Claude Bernard’s postulation of the critical importance of the constancy of a *milieu interieur* for the survival of the organism (1). The fundamental step introduced by Bricker and Slatopolsky, however, which lies

at the foundation of their *trade-off hypothesis*, resides in the intuition that the organism ‘pays a price’ in order to maintain equilibrium. The currency employed by organisms in such trades is constituted by the progressive increase of parathormone synthesis and secretion by parathyroid glands in order to increase renal phosphate excretion. An additional remarkable feature of this series of experiments was the understanding of the key role of phosphate accumulation, as trigger of a series of biological consequences, leading to secondary hyperparathyroidism.

Bricker and Slatopolsky’s trade-off hypothesis provides an effective example of how elegance can manifest itself through a combination of simplicity and equilibrium, which have been landmarks of elegance long before the 20th century, especially in connection with the physical and mathematical sciences. The trade-off hypothesis was a simple idea, if ever there was one. Yet it required elegant minds to engineer an ingenious solution to design an experimental model that could then be effectively applied to clinical practice.

Brenner’s hypothesis

As a final paradigm of scientific elegance, let us consider an important chapter of contemporary nephrology: Barry Brenner’s hypothesis regarding the role of residual nephrons in the decline of renal function. For those unfamiliar with basic nephrology, *nephrons* are structured into a cluster of vessels (glomeruli) that filter blood thus producing glomerular urine, which is then manipulated by tubular structures. Brenner *et al.* observed that residual glomeruli are constantly under pressure, and the amount of pressure is inversely proportional to the number of glomeruli: the fewer glomeruli present, the higher the pressure needed to sustain the filtering process (2). This observation was confirmed by noting that, in patients lacking a kidney, the volume of the residual kidney increases, thus supporting the hypothesis of an increased intraglomerular pressure (9). Brenner also showed that small-for-date newborns exhibit a reduced number of working nephrons and, as a consequence, are more prone to experience hypertension and renal failure throughout their lives (7). Brenner’s hypothesis for this fact was simple and effective: the fewer the working nephrons that are present in an individual, the higher the working load that each nephron has to endure. The increase of intraglomerular pressure deteriorates the glomerular structures eventually leading to sclerosis and organ failure. Brenner’s hypothesis was further confirmed and extended by subsequent work, revealing that proteinuria (a marker of glomerular damage) is also correlated with an increase in glomerular pressure, and therefore, potentially affected by compounds able to interfere with the reninangiotensin axis (5; 3).

We maintain that the elegance of Brenner’s hypothesis lies in a combination of its simplicity and linearity. Despite its remarkable essentiality, it is a unifying hypothesis that contributed to a deeper understanding and explanation of the possible mechanisms of progressive renal failure under non-immunological clinical conditions.

3 Discussion

All the examples we cited resulted in extremely successful research. Indeed, elegance is often correlated with success; nevertheless, success in research does not necessarily imply that the research method or the intuition responsible for the research was elegant. In a word, elegance should not be straightforwardly identified with success.

This point is well illustrated by the increasing importance of mathematical and statistical techniques applied to clinical research. Most discoveries nowadays are achieved through plodding repetitive application of some procedure. For instance, one looks at the latest or most promising chemotherapeutic drug. The molecule under scrutiny is then massively cloned and continuously altered a bit at a time, until a more promising and effective variant is discovered. When that happens, scientific progress is undoubtedly achieved. The employment and application of formal techniques divide the medical community between enthusiastic praises of the objectivity of quantitative methods and skeptical mistrust of statistical tricks (12). What is indisputable is that statistical methodology has become a successful and indeed irreplaceable feature of contemporary scientific research. Yet is this research elegant? It seems to us that the answer is clearly negative (at least unless the alteration of the protein is geared towards the discovery of a new compound that reveals some innovative therapeutic property that distinguishes it from all the previous clones). A critical assessment of the role of meta-analysis in clinical research greatly transcends the scope of this article. Our point is simply that it is only when the brute force of the mathematical framework is backed up by some creative act that meta-analysis can enter the empyrean world of elegance.

What would be a more elegant alternative to the ‘blind,’ mechanistic application of statistical techniques? Imagine that, instead of producing a massive array of ‘random’ variation of the existing molecule, a team of researchers could take the original molecule and engineer a link that allows it to attach right to the chemical receptor in the target cell. Furthermore, let us assume that the molecule could be modified in a way that it perfectly fits the receptor. Ideally, at this point, the researchers could test this single molecule, instead of experimenting thousands of almost-identical clones of the original protein. It is hard to deny that this more selective alternative would be preferable: in addition to being more elegant, it would save the research team a massive amount of time and resources. The problem, of course, is that this can seldom be done in practice. Statistical methodology is useful precisely because we rarely know how to engineer the optimal molecule to be tested. In such cases, meta-analysis might not be the ideal strategy, but it is typically the only available one.

We are clearly aware of the fact that a ‘brute force’ methodology is often the only route to scientific knowledge, and it would be preposterous to flatly criticize the general use of statistical techniques in medical science. Our remark is simply that contemporary research often stops too soon. In the grip of an Academic system that requires constant results and massive publication records, much scientific work has fallen short of a full understanding of its value, and of

its placement in a broader spectrum of knowledge. Comprehending the deeper significance of an experiment often requires time and patience, even though many contemporary researchers lack the former and ignore the latter. Understanding the impact and significance of an experiment is frequently tantamount to innovation and is associated with elegance.

In conclusion, when designing an experiment—be it clinical or laboratory-based—it is important to take a step back and look at what one is trying to find, see how it fits in with previous knowledge or expands it, and whether it can use concepts deriving from different areas of expertise and use them to create a new experiment that generates greater, novel knowledge. In this respect, so-called ‘me-too studies’ and other varieties of confirmation protocols constitute a significant and necessary part of contemporary scientific methodology, but do not belong to the world of elegant science. In addition, scientific progress also requires original, innovative studies that deepen our foundational insights. We expect that, while inevitably increasing the time taken to perform the research, a more consistent pursuit of elegance will lead to a substantial increase in the long-term impact of published work, which—as revealed even by a cursory glance at the half-life of articles—has constantly and inexorably decreased over the last few decades. Pursuing elegance is often a matter of moving away from the microscope and looking into the telescope. It requires setting some details aside and focusing on the foundation, structure and architecture of our scientific work. Details are crucial, but it is easy to get lost in them if we lose sight of the core message.

With all of this in mind, let us return to the paradigms of scientific elegance presented above. What all the examples have in common is the audacity of breaking existing schemata. Elegant thinkers have been able to go beyond the boundaries of conventional research, guided by their willingness to open new avenues of research or shedding new light on old questions. Much of current scientific research is focused on problems that have narrow scope, sometimes too narrow. Specialization is a characteristic and important feature of contemporary science. However, even if brute-force solutions are sometimes the easiest route towards solving a problem, we should also pursue elegance in our work. While meta-analysis is, and should continue to be, an important tool for scientific progress, elegance too should leave the textbooks and hallways and make its way inside the laboratories.

4 Conclusions

A systematic study of elegance requires an interdisciplinary approach that involves attention to contemporary biomedical research, a historical perspective, and a philosophical understanding of the structure and foundations of science. As Kuhn (6), 88 famously remarked, ‘it is . . . particularly in periods of acknowledged crisis that scientists have turned to philosophical analysis as a device for unlocking the riddles of their field.’ We believe that history and philosophy have a role to play in everyday scientific practice, not only when crises occur. Histor-

ical perspective and philosophical reflection are not tangential, but fundamental components of scientific research. In particular, they allow us to develop the features of science that make it elegant and better understand why an elegant mind is a propeller for scientific progress.

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