Introduction
Challenging Times

Evolution of Galilean–Newtonian Scientific Thinking

Some people are sufficiently fortunate to have their most creative years coincide with great mysteries in human knowledge. One thinks of the magnificent Seventeenth Century. It began with Francis Bacon moving the study of Nature from haphazard experience to designed experiments, and Galileo placing scientific knowledge within the frame of mathematics, not requiring explanation in terms of human physical categories. It ended with Isaac Newton grounding scientific knowledge on mathematical laws applicable to a wide variety of phenomena. The human condition, that is, man's place in the world, changed radically in 1687 with Newton's publication of *Philosophiæ Naturalis Principia Mathematica*.

There was a profound enigma lurking in the thinking of Galileo and Newton. It was genius to declare that knowledge of Nature is constituted within mathematics, not within human categories of understanding; yet, as long as the mathematical laws were consistent with human cognition, the full implication of this thinking lay hidden. The advent of quantum mechanics in the first part of the Twentieth Century brought it to light: a theory may be preposterous from the perspective of human intelligibility but lead to predictions that agree with empirical observation—and therefore be scientifically valid. Man can possess knowledge beyond the limits of his physical understanding. There was excitement in the air. The human condition was changing again, and young scientists dove headlong into the maelstrom.

Today, slightly more than a century since Niels Bohr hypothesized that an electron can jump to a different level without continuously passing through space, and almost a century since Louis de Broglie argued that particles of matter exhibit wave–particle duality, once again science faces an epistemological conundrum, but this time it appears that the resolution does not lie implicitly within Newton's thinking.

Toward the end of the Twentieth Century, the emergence of high-performance computing allowed scientists to construct huge models consisting of thousands of variables and parameters. The complexity of these models prevents them from fulfilling the most basic requirement of science: validation by the successful prediction of future events. System complexity has resulted in data requirements that cannot be met. Model parameters cannot be accurately estimated, thereby resulting in model uncertainty. On the other hand, model simplification means that there can be many models aiming to describe the same complex phenomena, all being inherently partial and hence yielding different predictions. The desire to obtain scientific knowledge of complex systems runs up against the requirements for scientific knowledge. In addition to complexity, there is also an aspiration for systems covering large time scales, so that validating data cannot be obtained. The inability to validate theory via observations constitutes an existential crisis for science.

The first part of this book, comprising Chapters 1 through 5, tells perhaps the greatest saga of the human mind: the evolution of scientific knowledge from explanations of natural phenomena in terms of everyday physical understanding to mathematical models that possess no such understanding and require mathematical formulation of their experimental relation to Nature. The chapters are populated by many of history's greatest scientists and philosophers. Their struggle involves a most perplexing problem: How does mind characterize what mind can know? It is a story that should be known not only to every scientist and engineer, but also to every scholar and educator, for in a world so influenced by science, no discipline can be taken seriously if it does not account for itself in relation to science.

A Radical Shift in the Narrative

A radical shift in the narrative begins with Chapter 6. A chronicle that seemed to be complete runs abruptly into the quandary of complex systems. The issues are essentially mathematical and statistical. Thus, the presentation takes on a more mathematical tone. Many of the specifics are set in the context of biology, which some have proclaimed to be the key science of the Twenty-first Century. In fact, the underlying problems of system complexity and data paucity span the range of scientific investigation, from biology to economics to social science. While our computational ability continues to grow, thereby fueling the demand for modeling complex phenomena, limitations on human conceptualization and data appear to preclude the formation of valid scientific theory in many domains—at least insofar as scientific epistemology has thus far evolved. We are in the midst of a new epistemological crisis. What could be more exhilarating for a scientist, engineer, or philosopher? Yes, we are confused, but confusion is the norm when one is on the frontier–and where else would one want to be?

The last chapter of the book considers the impact of scientific uncertainty on the translation of scientific knowledge into means to alter the course of Nature—that is, the effect of uncertainty in engineering. It proposes a course of action based on integrating existing partial knowledge with limited data to arrive at an optimal operation on some system, where optimality is conditioned on the uncertainty regarding the system. It explains the classical paradigm of optimal operator design based on a scientific model, a class of potential operations, and a quantitative measure of performance, all of which presupposes a system description whose predictions are concordant with observations. It then postulates an alternative optimization paradigm grounded in a Bayesian framework to take advantage of existing partial knowledge pertaining to the physical system of interest. The ultimate scientific problem of model validation is not solved; rather, the thinking here is that of an engineer: find an optimization framework in which pragmatic goals can be achieved. As for a new scientific epistemology in which valid knowledge can be defined, that awaits the bold efforts of fertile minds enriched with the mathematical, scientific, and philosophic education required for such a quest.

Chapter 1
Why Epistemology?

1.1 The Desire to Know

The opening line of Aristotle's *Metaphysics* states, "All men by nature desire to know." But what does it mean to know? While one might wish for a universal answer to this question, none as yet has been forthcoming. As we understand the question, what it means to have knowledge depends on one's standpoint. Moral knowledge is of a different kind than scientific knowledge. Even in science, the domain of scientific knowledge and what is accepted as authentic knowledge, meaning that it is accepted as "true," has changed dramatically over time.

The domain of scientific knowledge for Aristotle was much smaller than it is today. He could not make observations of the atom or of distant galaxies. He could not observe the genes and proteins in a cell, nor could he measure electrical impulses in the brain. His concept of truth was limited by his ability to observe and measure, but it was also limited by the mathematical systems he had available to represent the behavior he viewed. It is naïve to think that our concept of knowledge in today's world of quantum physics and microbiology would be the same as it was for Aristotle in 340 BC, what it was for Newton in 1687, or what it will be in 2500.

Scientific knowledge relates to the manner in which the mind formulates and operates on ideas concerning Nature. These must ultimately be related to our senses that provide the data from which the neural system formulates ideas. My idea of a rock is not outside my mind. Something is out there that results in sensations, that in turn results in the idea of a rock. Such ideas are the raw material of theories that describe the interaction of the ideas—and if a theory is valid it should produce consequences that can be checked against future sensations. The fundamental point is that theoretical operations in the mind correspond to physical operations in Nature that are not directly experienced, but whose activity is reflected in new sensations resulting in new ideas concordant with outcomes the original operations predicted. This very general description of scientific knowledge has been developed over many centuries and is not Aristotle's view.

The first aim of this book is to trace this development up to and including the turbulent effects of quantum mechanics in the Twentieth Century. The second aim, which cannot be accomplished absent an appreciation of the subtle relations between reason, science, and metaphysics, including their historical evolution, is to scrutinize the new and rapidly accelerating crisis of scientific knowledge that has accompanied the desire to model extremely complex systems such as those arising in biology, environmental science, economics, and social science.

1.2 What is Epistemology?

Implicit in these aims is that it is possible to characterize a specific kind of knowledge to be called "scientific." This characterization lies outside of science and must be constructed prior to the organization of experience within scientific categories. Such characterization amounts to having a theory of scientific knowledge. *Epistemology* is defined as the theory of knowledge, so a scientific epistemology is required. What would it entail?

Wilhelm Windelband (1848–1914) defines epistemology in the following way: "The problems, finally, which arise from the questions concerning the range and limit of man's knowing faculty and its relation to the reality to be known form the subject-matter of epistemology or theory of knowledge." [Windelband, 1958] Taking the word "range" to refer to the kind, or nature, of the knowledge under consideration, the nature of scientific knowledge is determined by its manner of representation and its criteria for truth; its limitations are determined by the limits of its form of representation and the degree to which its criteria of truth can be applied; and its relation to reality is determined by the manner in which its representation is connected to physical phenomena and the relation between scientific truth and physical phenomena.

Many researchers appear to believe that epistemological issues are too arcane and irrelevant to their everyday efforts. One just has to get on with gathering data, building models, and justifying the models. But how should one gather data, what kind of models should be constructed, and, most importantly, what constitutes genuine validation? These questions relate to Windelband's definition of epistemology. Absent some understanding of their answers, one might spend years wandering about aimlessly, producing meaningless results, simply because a bona fide theory must conform to the epistemological requirements of science.

José Ortega y Gasset (1883–1944) phrases the matter this way: "Whoever wishes to have ideas must first prepare himself to desire truth and to accept the rules of the game imposed by it. It is no use speaking of ideas when there is no acceptance of a higher authority to regulate them, a series of standards to which it is possible to appeal in a discussion." [Ortega y Gasset, 1994]

The foundations of a discipline are inseparable from the rules of its game, without which there is no discipline, just idle talk. The foundations of science reside in its epistemology, meaning that they lie in the mathematical formulation of knowledge, structured experimentation, and statistical characterization of validity. Rules impose limitations. These may be unpleasant, but they arise from the need to link ideas in the mind to natural phenomena. The mature scientist must overcome the desire for intuitive understanding and certainty, and must live with stringent limitations and radical uncertainty.

Inattention to epistemology results in research that appears scientific but fails to have depth, or even worse, is scientifically unsound. Albert Einstein (1879–1955) writes, “The reciprocal relationship of epistemology and science is of a noteworthy kind. They are dependent upon each other. Epistemology without contact with science becomes an empty scheme. Science without epistemology is—insofar as it is thinkable at all—primitive and muddled.” [Einstein, 1949]

Only through deep reflection on epistemology can one come to grasp what it means to possess scientific knowledge of Nature and therefore be in a position to effectively seek such knowledge. Significant effort must be spent escaping a naïve realism that would attempt to force one’s conceptualizations of Nature to conform to ordinary everyday understanding.

In a letter, Einstein wrote the following:

> I fully agree with you about the significance and educational value of methodology as well as history and philosophy of science. So many people today—and even professional scientists—seem to me like somebody who has seen thousands of trees but has never seen a forest. A knowledge of the historic and philosophical background gives that kind of independence from prejudices of his generation from which most scientists are suffering. This independence created by philosophical insight is—in my opinion—the mark of distinction between a mere artisan or specialist and a real seeker after truth. [Einstein, 1944a]

“Independence from the prejudices of his generation!” Only in this way can one break free of the run-of-the-mill grind that never gets to the heart of the matter.

1.3 Modern Science

Starting in the early part of the Seventeenth Century, a radical new understanding of natural science took shape. On the one hand, Francis Bacon proposed ordered observations in the context of experimental design; on the other, Galileo contended that scientific knowledge must be constituted within mathematics and not be bound by the need to explain matters in ordinary language. Isaac Newton manifested Galileo’s conception with his laws of motion, which he proclaimed free of non-empirical, metaphysical notions such as substance and causality. This was indeed a “new science.” What is gravity? Who knows? All that matters is that science provides mathematical descriptions of behavior. It would no longer be required to satisfy the human desire for explanations in a deeper reality.

Mathematics was not new to science; Archimedes, the greatest scientist of antiquity, was a great mathematician and this was reflected in his scientific thinking. Now, however, instead of supporting a theory whose status as authentic knowledge was rooted in causality, mathematics was the theory. Knowledge was constituted within it, and its validity depended solely on its ability to make predictions confirmed by observation. The birth of modern science was the greatest revolution in human history. It radically changed the human condition because it altered man’s perspective on himself and Nature.

The full extent of the change did not become apparent until the arrival of quantum mechanics in the Twentieth Century. Only then did the unintelligibility of Nature become forcefully apparent with the uncertainty principle and strange notions like wave-particle duality. The theory was mathematically sound and agreed with predictions, but defied human understanding.

Hannah Arendt (1906–1975) frames the dilemma brought about by science in the early Twentieth Century: “To understand physical reality seems to demand not only the renunciation of an anthropocentric or geocentric world view, but also a radical elimination of all anthropomorphic elements and principles, as they arise either from the world given to the five senses or from the categories inherent in the human mind.” [Arendt, 1977a]

It is not just that the senses cannot be trusted; neither can the categories of our understanding, which form the womb in which modern science was conceived. Indeed, Nature is not even thinkable. Arendt writes, “The trouble, in other words, is not that the modern physical universe cannot be visualized, for this is a matter of course under the assumption that Nature does not reveal itself to the human senses; the uneasiness begins when Nature turns out to be inconceivable, that is, unthinkable in terms of pure reasoning as well.” [Arendt, 1977b]

A vast number of scientists have not even taken Newton to heart, let alone come to terms with the strangeness of Nature to which Arendt is referring. Many appear to hope that a light will go on, Nature will become transparent, and simple explanations will emerge. Engaging the subtleties of epistemology will quickly rid one of such a puerile outlook. Indeed, as technology provides more detailed observation, Nature is becoming more unfathomable.

1.4 The Crisis of Complexity

With the advent of the Twenty-first Century, it has become apparent that the epistemology that began with Galileo, took shape with Isaac Newton, and came to fruition in the first half of the Twentieth Century with Niels Bohr, Hans Reichenbach, and others cannot support the desire to model complex systems. Across disciplines, scientists and engineers want to gain knowledge of large-scale systems composed of thousands of variables interacting nonlinearly and stochastically, often over long time periods. This massive complexity makes the standard modes of discovery and validation impossible.

The unverifiable character of many proposed systems is most troubling because the proliferation of such systems compromises the notion of scientific truth and threatens to erode the credibility of science. Consider medicine, which confronts huge complexity in physiological systems. In 2011, Janet Woodcock, Director of the Center for Drug Evaluation and Research at the FDA, estimated that as much as 75% of published biomarker associations are not replicable. She went on to comment, “This poses a huge challenge for industry in biomarker identification and diagnostics development.” [Ray, 2011] This dismal record could only have been produced by a widespread lack of attention to legitimate scientific method. A large number of studies involving immense complexity or dimensionality have been undertaken in which there is no possibility of obtaining scientifically meaningful conclusions.

If, as Aristotle says, all men desire to know, and in the Twenty-first Century the desire is for knowledge of complex systems, then, in Windelband's words, scientists must address "the questions concerning the range and limit of man's knowing faculty," as these pertain to systems involving high dimensionality, complexity, and uncertainty.