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Introduction

Cell Mechanisms and Cell Biology

> In order to succeed in solving these various problems, one must so to speak progressively dismantle the organism, as one takes to pieces a machine in order to recognize and study all its works.
>
> (Bernard, 1865, Part II, Chapter 1)

1. A DIFFERENT KIND OF SCIENCE

To many people, cell biology is an unlikely domain to impart impetus for a major shift in the way philosophy of science is practiced. Cells appear to be the object of straightforward empirical observation, not of bold theories that challenge the status quo. In high school or at the museum you look into the microscope and struggle to see what you are told you should see – structures that are never as sharp and well delineated as in the drawings in textbooks. What could cell biology be but a tedious descriptive science? This popular conception, however, is quite erroneous. Cells, as Theodor Schwann first concluded in the 1830s, are the basic units of life. They perform all essential vital functions: extracting energy and building materials from their environment, constructing and repairing themselves and synthesizing products for export, regulating their own internal operations, reproducing themselves periodically by dividing, cleaning up their own waste, and so forth. Beginning in the 1940s an initially small cadre of investigators who were pioneers in the modern discipline of cell biology began to figure out the biochemical mechanisms that enable cells to perform these functions. Although miniaturized, the mechanisms they found to be operative in each cell are staggeringly complex. Their work and that of their successors, primarily in 1940–70, revolutionized our understanding of the basic processes of life. Now, half a century later,

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I am drawing on that lively period of scientific enterprise to find fuel for yet another revolution, one that focuses on the very conception of science itself.

The science of cell biology is very different from the textbook image of science, including that advanced in traditional philosophy of science. That picture, grounded on some of the great successes of the scientific revolution and subsequent developments in some areas of physics, emphasizes bold unifying generalizations – the laws of nature. Newton's laws of motion promised to explain all motion, both terrestrial and celestial. The laws of thermodynamics and electromagnetism are similarly broad in their sweep. In biology, Darwin's insight that evolution by natural selection occurs when there is heritable variation in fitness (Lewontin, 1970) has provided a similarly powerful unifying generalization. However, most areas of biology – including cell biology – do not fit into this picture. Instead of unifying generalizations, cell biology offers detailed accounts of complex mechanisms in which different component parts perform specific operations, which are organized and orchestrated so that a given type of cell can accomplish the functions essential for its life. Not elegant generalizations, but exquisitely detailed accounts of mechanisms, are the products. This difference in product has broad implications for our overall understanding of science, including the challenges of generating evidence, advancing new hypotheses and theories, and evaluating and revising them.

In proposing an alternative characterization of science as the search for mechanisms, I am not seeking to eradicate the old picture of science as the quest for bold generalizations but to complement it. There are domains in which the Newtonian vision is appropriate – ones in which the aim of inquiry is best served by far-reaching generalizations that can be economically stated, often in a single equation. In many domains, though, the aim of inquiry leads to meticulous accounts of complex mechanisms. This is particularly true in the functional domains of biology – cell biology, molecular biology, physiology, pathology, developmental biology, neurobiology – and also in related areas of physics (biophysics) and chemistry (biochemistry). It does not advance our understanding of these sciences to impose an ill-fitting model. Rather, we need to develop a conception of science that is appropriate for them. Only then can we adequately address some of the traditional questions about science – what it is to explain a phenomenon, how explanations are discovered, and how they are evaluated.

The idea that much of science is a quest to articulate mechanisms is not news to biologists. Frances Crick (1988, p. 138) put it succinctly:

"What is found in biology is *mechanisms*, mechanisms built with chemical components . . ." Biologists do not always reach as far down as chemistry in characterizing biological mechanisms, but they do use the term *mechanism* naturally and often. A search I undertook of titles of articles in *Science* from 1880 to 1998 revealed 656 articles that included *mechanism*, *mechanisms*, or *mechanistic* in their titles. Only one appeared before 1900, and that concerned a psychological mechanism. Titles referring to biological mechanisms began in 1904 and are far more frequent than articles about non-biological mechanisms. They also outnumber articles that include *theory*, *theories*, or *theoretical* (584) or *law* or *laws* (165) in their title (the count for law discounted 25 titles clearly referring to political laws). A few of the early papers referring to mechanisms in their titles involved the vitalism–mechanism controversy that was still very active at the turn of the twentieth century. Most, however, focused on specific biological mechanisms. The following are some illustrative examples:

Edwin G. Conklin (1908). The mechanism of heredity.
Frank R. Lillie (1913). The mechanism of fertilization.
E. Newton Harvey (1916). The mechanism of light production in animals.
Jacques Loeb (1917). A quantitative method of ascertaining the mechanism of growth and of inhibition of growth of dormant buds.
W. J. V. Osterhout (1921). The mechanism of injury and recovery of the cell.
John H. Northrop (1921). The mechanism of an enzyme reaction as exemplified by pepsin digestion.
F. H. Pike and Helen C. Coombs (1922). The organization of the nervous mechanism of respiration.
Caswell Grave and Francis O. Schmitt (1924). A mechanism for the coordination and regulation of the movement of cilia of epithelia.

These titles reveal an interesting variation in generality, with Conklin discussing *the* mechanism of heredity while Grave and Schmitt discuss *a* mechanism within a particular cell type. The latter reflects the sort of engagement of individual scientists and research teams that became the norm in the twentieth century. Individual scientists and research teams honed in on much more delimited phenomena at a scale that can be fruitfully investigated in a single laboratory across a period of perhaps a few years. At the general level a broad research community might devote itself to a general phenomenon such as protein synthesis and seek to identify the general nature of the mechanism of protein synthesis. Specific researchers, though, focus on particular components of the mechanism or on the mechanism that is operative in particular cells or particular organisms. This is reflected by considering some typical titles of papers referring to mechanisms and protein synthesis in their titles[1] in the period 1950 to 1970:

Winnick, T. (1950). Studies on the mechanism of protein synthesis in embryonic and tumor tissues. I. Evidence relating to the incorporation of labeled amino acids into protein structure in homogenates. *Archives of Biochemistry*, 27, 65–74.

Novelli, G. D. and Demoss, J. A. (1957). The activation of amino acids and concepts of the mechanism of protein synthesis. *Journal of Cell Physiology,* 50 (Supplement 1), 173–97.

Yoshida, A. (1958). Studies on the mechanism of protein synthesis: bacterial alpha-amylase containing ethionine. *Biochimica et Biophysica Acta*, 29, 213–4.

Goodman, H. M. and Rich, A. (1963). Mechanism of polyribosome action during protein synthesis. *Nature,* 199, 318–22.

Griffin, B. E. and Reese, C. B. (1964). Some observations on the mechanism of the acylation process in protein synthesis. *Proceedings of the National Academy of Sciences, USA*, 51, 440–4.

Carey, N. H. (1964). The mechanism of protein synthesis in the developing chick embryo. The incorporation of free amino acids. *Biochemical Journal,* 91, 335–40.

Mano, Y. and Nagano, H. (1966). Release of maternal RNA from some particles as a mechanism of activation of protein synthesis fertilization in sea urchin eggs. *Biochemical and Biophysical Research Communications,* 25, 210–15.

Although the conception of a mechanism is widely invoked in the biological sciences, it has only recently become the target of philosophical inquiry. Chapter 2 will articulate the conceptions of mechanism and mechanistic explanation that figure in biology, especially cell biology. The quest to understand nature mechanistically has its roots in the scientific revolution and, although challenged by vitalist critics, figured prominently in the attempts to understand physiological systems throughout the eighteenth and nineteenth centuries. The key to the mechanistic approach was not the analogy of physiological systems to human made machines, but the quest to explain the functioning of whole systems in terms of the operations performed by their component parts. Beginning with Bernard, biologists also recognized the importance of the way in which the parts and their operations were organized. Increasingly, biology became a science in which phenomena were explained by discovering the organized parts and operations by which a mechanism performed its function.

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[1] Another interesting class of papers uses the term mechanism not for the general phenomenon, protein synthesis, but for the way in which a particular substance alters that phenomenon. A characteristic example is the following: de Kloet, S., van Dam, G., and Koningsberger, V. V. (1962). Studies on protein synthesis by protoplasts of Saccharomyces carlsbergensis. III. Studies on the specificity and the mechanism of the action of ribonuclease on protein synthesis. *Biochimica et Biophysuca Acta*, 55, 683–9.

As I explore in Chapter 2, recognizing that the goal of many scientific inquiries is to describe the mechanism responsible for the phenomenon of interest provides a different perspective on many aspects of scientific inquiry. Diagrams often provide the most fruitful way of representing a mechanism, in which case scientists may relate the mechanism to the phenomenon of interest by mentally simulating its operation. In part this involves a reductionistic strategy of decomposing the mechanism into its parts and operations, but equally significant is figuring out how these are organized to work together and how various environmental conditions affect the mechanism's functioning. Finally, although traditional philosophy of science has had little to say about the process of discovery, when the focus is on mechanisms we can set out what the challenge of discovery is and analyze typical experimental strategies – strategies that figured prominently in discovering cell mechanisms.

2. THE ORGANIZATION OF SCIENCE INTO DISCIPLINES[2]

Although a central feature of my discussion will be the discovery of cell mechanisms, my broader focus is on the establishment of cell biology as a discipline. In 1940 no one would have listed cell biology when identifying scientific disciplines. By 1970 it was a well-established discipline. My goal is to trace and account for this change. First, though, a preliminary issue must be addressed. The word *discipline* is familiar enough, but what exactly is a scientific discipline? In the disciplines that analyze science (philosophy of science, history of science, and sociology of science, which are collectively referred to as *science studies*), a variety of criteria have been offered.

Perhaps the most common way in which people identify disciplines is in terms of the objects they investigate. Thus, astronomy is described as the study of suns, planets, and the like, whereas psychology investigates mental activities or behaviors. Dudley Shapere captured this feature of our ordinary conception of disciplines when he introduced the term *domain* for "the set of things studied in an investigation" (Shapere, 1984, p. 320; for his classic treatment of domains, see Shapere, 1974). Shapere's conception of a domain is more sophisticated than the lay conception, however, for he argued that domains are not simply presented to scientists but result from their decision as to what items (his term for the constituents of domains) to group together to constitute a domain. Thus, he showed how during the nineteenth century chemists made facts about basic elements a domain for study, because they

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[2] The discussion in this section draws in part upon Bechtel (1986a).

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construed them as the constituents of ordinary substances. Crucially, Shapere drew attention to the fact that scientists' reasons for grouping items together into a common domain may change over time. Moreover, as Toulmin noted, an item may be grouped with different items into different domains depending on the questions asked, and different investigators may ask different questions:

> If we mark sciences off from one another (using Shapere's term) by their respective 'domains', even these 'domains' have to be identified, not by the types of objects with which they deal, but rather by the questions which arise about them. Any particular type of object will fall in the domain of (say) 'biochemistry' only in so far as it is a topic for corresponding 'biochemical' questions; and the same type of object will fall within the domains of several different sciences, depending on what questions are raised about it. The behavior of a muscle fibre, for instance, can fall within the domains of biochemistry, electrophysiology, pathology, and thermodynamics, since questions can be asked about it from all four points of view . . . (1972, pp. 149)

While the objects of study are an important part of what characterizes a discipline, both Shapere and Toulmin made it clear they are insufficient. To identify the set of objects comprising the domain of a discipline, we need to consider why scientists group them together. Scholars who study science generally split over two approaches to addressing this issue, roughly differentiated by their respective disciplines. Philosophers and historians of ideas adopt what is often characterized as an *internalist* approach to understanding science, emphasizing cognitive factors such as theories and evidence, while sociologists and social historians adopt an *externalist* approach, focusing on social and institutional factors. In the 1970s and 1980s these two approaches were often portrayed as competing and mutually exclusive; more recently, many in science studies have recognized a role for both.

Through most of the twentieth century, philosophers of science focused on the theories advanced by scientists and the relation theories bore to evidence. To the extent that disciplines were considered at all, they were characterized in terms of theories. For example, in discussions of the unity of science – the question of how different sciences related to one another – the logical empiricists identified disciplines with their theories and asked whether they could be related to one another logically. Thus, the question of the relation of biology to physics and chemistry became the question of whether the theories (laws) of biology could, with the aid of bridge principles and boundary conditions, be derived from those of chemistry and physics (Oppenheim & Putnam, 1958; Nagel, 1961). If so, biology was said to be *reduced* to, and thereby unified with, physics.

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Finding this singular focus on theory misguided, a number of philosophers have proposed alternative accounts that are more multifaceted and naturalistic. Best known is Kuhn's (1962/1970) notion of a *paradigm* and distinction between *normal science* and times of *paradigm shift*. In its more restricted sense, a paradigm for Kuhn was an exemplar – a solution to a particular problem that became a model for solving other problems. In its more extended sense, a paradigm was a general theory or theory schema that characterized a domain, identified problems to be solved, and specified strategies for solving them and criteria for evaluating proposed solutions. Kuhn's notion of a paradigm (both the restricted sense of an exemplar but especially the extended sense of a general theory) provided a way to characterize a group of scientists engaged in a similar enterprise and to tell a historical narrative of how the enterprise developed.[3] The extended notion of a paradigm was sufficiently vague, however, that it also became the focus of severe criticism and has largely ceased to figure in philosophical accounts of science.

Adopting the term *field* rather than discipline, Lindley Darden and Nancy Maull advanced a multifaceted conception in which no single element dominated (though it did not extend so far as to include externalist elements). Incorporating Shapere's notion of a domain, they defined a *field* as consisting of the following elements:

> a central problem, a domain consisting of items taken to be facts related to that problem, general explanatory facts and goals providing expectations as to how the problem is to be solved, techniques and methods, and sometimes, but not always, concepts, laws and theories which are related to the problem and which attempt to realize the explanatory goals. (Darden and Maull, 1977, p. 144)[4]

Especially relevant here are the explanatory goals, types of accounts offered (e.g., laws or theories), and conceptualization of the central problem, a cluster that I will call, for convenience, the field's *mission*. As I noted in Section 1, in many areas of biology explanation takes the form of an account of the mechanism responsible for a phenomenon. The central problem is then the discovery and refinement of this mechanism.

A second important component of fields, to which Darden and Maull drew attention, is its array of techniques and methods for solving problems. These

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[3] Kuhn inspired several other attempts to characterize larger-scale units that served to unite the practitioners of a discipline. Two examples were Lakatos' (1970) notion of a research program and Laudan's (1977) notion of a research tradition.

[4] Shapere (1984) largely endorsed Darden and Maull's conception of a field but cautioned that one must be sensitive to the fluidity of fields and to the fact that often different practitioners within a field will not share exactly the same methods.

are not just cognitive or reasoning strategies but include instruments, and techniques for using instruments, that enable the scientist to observe and manipulate objects in the domain. Ian Hacking (1983) pioneered discussion within philosophy of the importance of techniques for intervening in nature. Historians such as Kathryn Olesko have also emphasized the importance of techniques of investigation in delimiting a discipline. She nicely noted that a discipline *disciplines* its practitioners by requiring them to master a particular body of knowledge and techniques of investigation (Olesko, 1991, p. 14). Steven Shapin (1982), focusing on the differences between biometricians and Mendelians, illustrated the importance of differences in techniques and methods in demarcating these two groups of investigators.

In contrast, sociologists and social historians of science tend to focus on the social networks and institutional structures within which scientists work. One role such social units play can be related to the cognitive elements emphasized by philosophers and historians of ideas – they insure compliance with a discipline's mission and accepted methods. Thus, Michael Polanyi introduced "the principle of mutual control," which

> consists . . . of the simple fact that scientists keep watch over each other. Each scientist is both subject to criticism by all others and encouraged by their appreciation of him. This is how *scientific opinion* is formed, which enforces scientific standards and regulates the distribution of professional opportunities. (1966, p. 72)

This aspect of the social structure of disciplines was much emphasized by Robert Merton (1973) and the tradition in sociology of science which he inspired.

Subsequently, though, sociologists of science pushed beyond the Mertonian tradition to address how the institutional structure of disciplines influences the content of scientific research by, for example, focusing a particular scientist's endeavors. Rosenberg commented,

> It is the discipline that ultimately shapes the scholar's vocational identity. The confraternity of his acknowledged peers defines the scholar's aspirations, sets appropriate problems, and provides the intellectual tools with which to address them; finally, it is the discipline that rewards intellectual achievement. (1979, p. 444)

Contemporary sociologists emphasize that the factors that shape a scientist's identity are not limited to ideas internal to the science itself but can include those of the broader society. Thus, Robert Kohler characterized such institutions as “mediat[ing] between science and the political, cultural, and economic institutions on which science depends for material and support” (1982, p. 2). Accordingly, Kohler characterized disciplines such as biochemistry, on which he focused, as “political institutions that demarcate areas of academic territory” (p. 1).

Sometimes the emphasis on the roles played by the broader social, cultural, and economic institutions is presented as repudiating the significance of cognitive factors in shaping science (Barnes, 1977; Bloor, 1991; Collins, 1981; Latour & Woolgar, 1979). Such a stance has provoked equally ardent responses from philosophers who have construed any acknowledgment of social factors as undermining the epistemic warrant of science (Laudan, 1981; Kitcher, 2001; and several of the papers in Koertge, 1998). Other philosophers (Longino, 1990; Longino, 2002; Solomon, 2001) have developed a more moderate response, articulating how social factors figure in the intellectual development of science without sacrificing its epistemic warrant. While my sympathies lie with the last position, I will not advance arguments for it here; instead I will briefly discuss how scientists create institutions and how their decisions help shape research in a discipline.

The candidate political institutions of a discipline are academic departments, professional societies, and journals. Of these, departments are the most problematic for tracking scientific disciplines. There are a plethora of ways in which universities divide faculty into departments, often having to do with very local politics and ease of administration. Especially in the biological sciences, the differentiation into departments depends upon the size of the institution and whether the biological sciences are situated among the arts and sciences or in a medical school (or both). Small undergraduate colleges will typically group all the biological disciplines within one department, although they may have separate tracks for majors that correspond to divisions within biology. Research universities tend to have separate departments for different biological disciplines, although they may be grouped in pairs (e.g., cell and molecular biology, ecology and evolution). Although departments may not correspond exactly to disciplinary units as differentiated by such criteria as professional societies and journals, they ensure the historical continuity of disciplines by training subsequent generations of researchers and thereby securing the cognitive and social allegiances of members of a discipline. Richard Whitley commented, “Educational institutions form the basic commitments of scientists in nearly all fields, and constitute the fundamental unit of social and cognitive identity in the sciences, which is one reason why the term ‘discipline’ is usually understood to refer to units of organization in universities” (1980, p. 310).

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Outside of the context of the local university, professional societies and journals are the major institutions that provide disciplinary identity. Given the importance of publication both in establishing a scientist's career and in disseminating results of research, the availability of journals influences the direction of a field. They determine not only what topics of research can most readily be published, but also what methods investigators can employ in investigating those topics. An important step in developing a new area of research and a research community that will carry out the research is the creation of new journals that will publish the results. In many cases, professional societies manage journals. Societies typically also hold regular meetings that provide a context in which scientists meet formally and informally to share results and formulate directions for future research. Although talks at professional society meetings often receive less credit in terms of professional advancement, they are favored vehicles for rapid communication and provide important opportunities for personal interaction.

Beyond formal institutions, sociologists have also focused on informal networks of scientists. Derek de Solla Price (1961; see also Crane, 1972; Chubin, 1982) coined the concept *invisible college* for groups of researchers who are in regular communication and share a common conceptual framework, problem focus, and set of techniques for dealing with a problem, although they may disagree on empirical claims or proposed theories. Sociologists identify such networks using such techniques as tracking citations and identifying clusters (Garfield, 1979). A variety of quantitative techniques have been developed for identifying and graphing social networks (Wasserman & Faust, 1994). A recent approach focuses on collaboration networks characterized in terms of coauthorship of papers (if two scientists have coauthored a paper, they are directly linked; if two scientists have not coauthored a paper but have each coauthored a paper with another scientist they are linked through that scientist, etc.). These networks have been shown to constitute structures known as *small worlds* in which randomly chosen pairs of scientists are typically separated by only a short path of intermediate collaborators (Newman, 2001). Such networks can also be studied more qualitatively and in detail to reveal the interactions that shape the direction of science. Jean-Paul Gaudillière (1996), for example, studied collaborative networks of scientists in France in the 1960s as specimens that could be revealing of the relationship between biochemistry and the emerging molecular biology.

As it turns out, despite the frequent conflict between theorists pursuing cognitive and social accounts of science, the various cognitive and social criteria for delineating units in science tend to converge on the same units. That is, institutional structures, methods of inquiry, domains of inquiry, and