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THE CHALLENGE OF DISAGREEMENT

Scientists engage in solving problems. However, they sometimes disagree about the solutions. They may even disagree about the problems themselves. That is where this book begins. Scientists begin by probing phenomena. They collect and analyze data. They discern patterns and formulate ideas about them. But imagine the challenge when interpretations differ. Accounts can sometimes conflict even when each seems consonant with observation and experiment. How do we reconcile them? How do we fit all the apparently conflicting facts together to construct reliable knowledge? How do scientists resolve disagreement?

Popular images of science tend to simplify disagreement. Typically, science is the triumph of discovery, as portrayed playfully by Abraham Tulp in Figure 1.1 (Nicholls 1982, xii). Here, 1978 Nobel Prize-winner Peter Mitchell is cast as the Christopher Columbus of energy transformations in the cell. His colleague, experimentalist Jennifer Moyle, accompanies him on deck. Various reagents, laboratory equipment and assistants crowd the ship. Afloat in a cellular membrane-sea, the experimenters venture into the great unknown. Looming on the horizon is a giant enzyme. It produces the basic molecule of energy transfer in the cell, *adenosine triphosphate*, or ATP. Spouting from the enzyme's headdress are the protons that Mitchell will "discover" are crucial to its function. His dramatic reconceptualization of these energy reactions in the cell earned Mitchell the Nobel Prize.

But Mitchell also sets sail "despite dire warnings that he will be consumed." The cartoon reminds us of Mitchell's skeptics. The naysayers on the dock exclaim emphatically, "~"! The squiggle is a symbol for a high-energy chemical bond, central to consensus about how ATP was produced. Echoing the Columbus metaphor, the high-energy squiggle reappears as a serpent in the sea which, critics warn, will doom Mitchell. In this view, scientitsts who disagreed were, quite simply, wrong from the outset.

In retrospect, opposition to Mitchell may seem embarassing. In particular, chemists searched for over a decade for molecules that contained the high-energy ("squiggle") bond. Indeed, many claimed to have isolated or identified them. But all the claims later dissolved. As one researcher noted, they met with "conspicuous non-success." Why? As textbooks now tell us, these compounds do not exist. They were not just elusive. They were illusionary. These 20th-century biochemists thus seem just like early Renaissance alchemists who searched for the Philosopher's Stone or 18th-century chemists who pursued phlogiston. They all chased phantoms. Here, disagreement stemmed from *error*.

Mitchell's insights were profound and we now have a much fuller understanding of how cells process energy. But the episode of reaching this knowledge was turbulent. The cartoon loses much of the original drama and sense of uncertainty. A history privileged by retrospect discounts Mitchell's critics. It disregards what justified their approach. These scientists believed that they had good reasons. By recovering the historical context, one can reconstruct and appreciate these reasons. One can thereby revive the excitement—and confusion—that fueled this debate for nearly two decades. It is easy to dismiss the controversy as a case of scientific irrationality, the inevitability of trial-and-error, or the tentativeness of scientific knowledge. I find such accounts uninformative, however, and certainly not very helpful. Hence, I focus on what such a historical episode can reveal about the process of resolving disagreement in science.

While this debate and its fascinating science may not be widely familiar, nearly anyone can appreciate the stakes. Everyone knows that breathing oxygen is vital, even without understanding why. Cells throughout the body "burn" food. They use oxygen, just as fire does. Cells thereby secure their basic energy in the form of ATP (as noted earlier). Sense perception, nerve signaling and muscle contraction all use energy harvested via this process. Whenever we walk, talk, write, breathe, glance, smile or gesture, we use muscles—all fueled by ATP. The scientists in this debate focused on the energy transformations that produce ATP using oxygen. The reactions are known, impressively, as *oxidative phosphorylation*. Biochemists, however, typically refer to them much more simply as **ox-phos** (pronounced as an assonant, nearly rhyming 'OX-FOSS'). I will happily "respect" their streamlined jargon. The ox-phos debate originated in a relatively specialized area of cellular biochemistry. But it soon expanded into a major controversy of revolutionary proportion. Even introductory biology texts, usually reserved for presenting only well established background knowledge, profiled the disagreement (e.g., Keeton 1972; Becker 1977; Curtis 1979; also Lehninger 1971; Dyson 1975). The debate persisted and intensified, involving what one textbook described as "contentious, often rancorous, discussion" (McGilvery and Goldstein 1979, 390). "The opposition was in some cases quite vitriolic," another observer noted. "It was the norm in the field at the time. Particularly in the 60s, the oxidative phosphorylation field had the reputation that if you went to a Federation meeting, all the meetings were crowded because everybody went along because they knew there would be a damned good fight there" (Gilbert and Mulkay 1984b, 36). Such testimony indicates, if only briefly, how the ox-phos episode is a prime case for understanding disagreement in science.

In what follows (Chapters 3-8), I delve more extensively into the ox-phos episode as a model case. I articulate its subtleties in order to address (with ample attention to historical detail) general epistemic questions about how scientists resolve disagreement. For robust conclusions, however, one must go beyond one case. Hence, I also sketch how my characterizations of the ox-phos case resonate with several other debates in science: the Chemical Revolution, the "Great Devonian Controversy" and continental drift, for example (Chapter 9). To close, I consolidate my conclusions and frame them as they may be relevant for different readers (Chapter 10). Abundant cross-references will highlight conceptual connections and allow readers to follow their own trajectories through the text without missing relevant sections. Those interested primarily in the history will find it unfolded in Chapters 3-8 and capped by a comparative analysis in Chapter 9. Scientific background is included in §1.1 below. The philosophical problems are framed primarily in §1.2; conclusions are summarized at the end of each chapter (3-9) and recapitulated and generalized in Chapter 10. I profile my analytical perspective and methods in Chapter 2 (and, further, in the Appendix). I hope that scientists, science administrators, scholars in science studies, and science educators will all find something interesting and useful by considering the whole.

On one level, the challenge of resolving divergent conceptions in science poses broad philosophical problems: How are theories and scientific communities structured? How do they interact? How can two groups each see themselves as right, while simultaneously seeing each other as wrong? How do scientists delineate the empirical scope of concepts? How do various types of experiments function? At another level, relevant to those engaged in research, the problems are more practical: What strategies lead to reconciling conflicting interpretations advanced by different scientists? How does one construct an effective research agenda, or design an appropriate experiment? What type of social organization promotes productive interactions among scientists who disagree? I trust my analysis of the ox-phos episode and other debates offers a deeper understanding, both philosophical and practical, of how scientists resolve disagreement.

1.1. A Textbook History

To understand the controversy between Mitchell and his critics, one may begin with the scientists' own accounts. In textbooks, review articles and honorific speeches, scientists frequently adopt a historical perspective. They convey an appreciation of new ideas, dramatize their development and characterize how they view the nature of science. Such folk histories, like Tulp's cartoon, may well be misleading. Nevertheless, they document roughly how the field developed. At the same time, they teach the basic concepts. Equally important, perhaps, the widespread perceptions form a baseline for posing quetions (§1.2) and for guiding further analysis (Chapter 2). Here, then, in a mosaic of the scientists' own voices, is a 'textbook history' of the ox-phos controversy:

In the early 1960s disagreement developed over **oxidative phosphorylation**, a process of energy conversion in the cellular organelle, the mitochondrion (Figure 1.2). 'Oxidative' refers to the use of oxygen by one system of molecules in releasing energy. This is precisely why we breathe oxygen. The centrality of this process to our lives, in fact, helps explain why a researcher might devote his or her career to a topic that may otherwise seem abstruse. 'Phosphorylation' refers to the energized bonding of phosphate to a specific molecule: this molecule, adenosine triphosphate, or **ATP**, is how energy becomes generally accessible in cells and, ultimately, it fuels the chemical reactions throughout our bodies: building proteins, contracting muscles, preparing nerve cells to transmit signals. ATP allows us to blink, to pump blood, to speak, to think, to grow. The mechanism for how the energy is transfered from the first, oxidative system to the phosphorylation of ATP is what the debate was all about. "All living organisms need energy to survive. . . . Adenosine triphosphate (ATP) . . . serves as a universal energy currency for living cells. The regeneration of ATP by way of oxidative . . . phosphorylation thus plays a fundamental role in the energy supply of living cells" (Ernster 1979, 94). How the energy-releasing reactions and energy-using reactions forming ATP were '**coupled**' "was for two decades the most contentious issue in bioenergetics" (Harold 1986, 44). In the late 1950s, just before the controversy about ox-phos flared, chemists already understood a fair amount about energy pathways in the cell. They were gaining familiarity with the enzyme that produces ATP, **ATPase**. They had also established that in a step prior to ATP production, energy was stored in the form of high-energy electrons (located in carrier molecules). These high-energy electrons (e- or 2e-) shifted to successively lower energy levels, releasing energy, while moving through a series of proteins and large molecular complexes, known variously as the cytochrome chain, respiratory chain, oxidative chain or, more plainly, **electron transport chain (ETC)** (Figure 1.3). At three points, the energy drop was large enough to produce the high-energy bond in ATP (Figure 1.4). Originally, chemists viewed this process as similar to other energy-conversion reactions in the cell (glycolysis and the citric acid cycle). That is, energy in the form of high-energy chemical bonds would pass, like a baton in a relay race or like pails of water in a bucket brigade, from the ETC to a **high-energy intermediate** or series of intermediates and then finally to ATP. The symbol '**~**' represented the critical high-energy bond in various molecules (note $\sim_1$ and $\sim_2$ in Figure 1.4b and I~X in Figure 1.4c).

"Many hypotheses were formulated, most of which postulated the occurrence of 'energy-rich' chemical compounds of more or less well-defined structures as intermediates between the electron-transport and ATP-synthesizing systems. Despite intensive efforts in many laboratories, however, no experimental evidence could be obtained for these hypotheses" (Ernster 1979, 24-25). "After the demonstration of the direct utilization of the energy of biological oxidations [from the ETC, but without ATP] the search for the hypothetical intermediate A~C was intensified. The rest of the 1960's is not one of the happiest periods in the history of mitochondrial research. Apparently spectacular successes proved unfounded" (Slater 1981b, 29). "Many laboratories tried to find a high-energy intermediate composed of a respiratory chain enzyme or coenzyme and a component of the ATP synthetase mechanism. Although this intermediate held a central position in the chemical scheme, no one had either observed or isolated it" (Skulachev 1988, 399). "Despite a number of red herrings, no intermediates could be positively identified" (Nicholls 1981, 13-14). Chemists conducted a "frustrating and ultimately fruitless search for chemical intermediates" (Harold 1986, 61). "Years of fruitless investigation had to pass" (Green and Young 1971). The chemical-coupling, or simply **chemical hypothesis**, was nevertheless "widely accepted" until the late 1960s (Ernster and Schatz 1981).

"By the early 1960s, the perplexity and frustration among biochemists studying oxidative phosphorylation was great indeed. The answer to their difficulties came from Peter Mitchell, a British biochemist who had, for reasons of health, retired from academic life and was working in his private laboratory in Cornwall. . . . In 1961, he put forth the ingenious—and radical—proposal that the phosphorylation of ADP to ATP . . . [was] powered by a proton gradient" (Curtis 1983, 200). Mitchell suggested that there were no separate intermediate molecules or high-energy bonds between the ETC and ATPase. Rather, he claimed, another type of energy coupled them: an **electrochemical gradient** of protons across a membrane--what he called a 'chemi-osmotic' potential. The different concentrations of electrically charged particles inside and outside of the mitochodrional membrane acted something like a reservoir or (as Mitchell sometimes portrayed it) a battery, ready to release its energy (Figure 1.6).

"Historically, . . . the **chemiosmotic hypothesis** grew out of Mitchell's fascination with the concept of chemical reactions organized in space, and its formal presentation included explicit . . . mechanisms for proton translocation" across the membrane (Harold 1986, 228). "The basic idea of this hypothesis is that enzymes of the electron-transport and ATP-synthesizing systems are localized in the membrane [of the mitochondrion] with a well-defined orientation and are functionally linked to a vectorial transfer of positively charged ions" (Ernster 1979, 25). "According to the model, the process depends on two characteristcs of the electron-transport molecules" (Keeton 1980, 179). First, the ETC components are embedded in the membrane of the mitochondrion and, Mitchell claimed, their physical position on different sides of the membrane is essential (Figure 1.7). "It is an asymmetrical arrangement of the carrier molecules across the membrane that allows the proton gradient to be established" (Hinkle and McCarty 1978, 104). As electrons traveled "down" levels from one cytochrome to another (energetically), they also travelled back and forth across the membrane (spatially). Second, Mitchell postulated further, the electron acceptors on each side of the membrane differ. On one side, the molecules have an affinity not only for the electrons, but also for protons (i.e., hydrogen ions—H^+). The negatively charged electrons draw positively charged protons from the internal fluid compartment. As the electrons move, the protons do also. The electron carriers on the other side of the membrane, however, have no affinity for protons, which are then released into the solution outside.[1] "Thus, electron transport will give rise to an electrochemical proton [or pH] gradient across the membrane which can serve as a driving force for ATP synthesis" (Ernster 1979, 25). The ability of the membrane to keep two regions (inside and outside) separate was thus the crucial element in energy conservation (Hinkle and McCarty 1978, 104; Harold 1988, 76-77). Mitchell wholly rearranged knowledge about the ETC and its relationship with the membrane in a revolutionary but subtle mechanism.

In addition to dispensing with the need for a high-energy chemical intermediate, Mitchell ably provided an "elegant rationale" for several phenomena that chemists had found anomalous under the chemical view (Becker 1977, 121; Jones 1981, 74). First, "a group of compounds of very different chemical structures was found to induce the same characteristic change in mitochondrial energetics, known as uncoupling. These '**uncouplers**' halted phosphorylation and stimulated both respiration and ATP hydrolysis" (Skulachev 1988, 339). Mitchell explained that while the uncouplers differed chemically, they all shared the potential to disrupt the membrane or to transport ions across the membrane, thus releasing the stored energy. Second, "the chemical scheme failed to explain the fact that both respiratory and photosynthetic phosphorylations require topologically closed membranous structures" (Skulachev 1988, 339). For Mitchell, though, "a requisite for the establishment of a proton gradient is, of course, that the membrane itself is impermeable to protons, which explains the need for an intact membrane structure in oxidative and photosynthetic phosophorylation" (Ernster 1979, 25).

"However, intellectual inertia prevented the Mitchellian concept from being generally accepted" (Skulachev 1988, 342). "When, in 1961, I proposed the so-called chemiosmotic hypothesis," Mitchell later remarked, "according to which the energy-rich chemical intermediates simply did not exist, . . . the response of most my scientific colleagues varied between indifference, incredulity and outrage" (Mitchell 1989/Japan, 7). "The chemiosmotic hypothesis was received with reservation by many workers in the field which is, in a way, understandable, since it was unorthodox, fairly provocative, and based on little experimental evidence" (Ernster 1979, 25; see also Harold 1986, 61, 63). "The energy-linked transport of various ions by isolated mitochondria remained essentially a side-show curiosity, largely because nothing was then known of the stoichiometric [or numerical] relationships between electron transport and ion transport. To many investigators ion transport appeared to be a trivial process of second-order importance" (Lehninger 1972, 6). "Contemporary thinking concerning the mechanism of ATP synthesis was dominated by the chemical coupling hypothesis and did not readily envision a role for the membrane" (Ernster 1984, ix). The development of bioenergetic research for the next two decades was "tempestuous and debates on crucial problems . . . uncompromising" (Skulachev 1988, v). "'Nature may be difficult, but she is never malicious'" one researcher quoted Einstein as saying. Einstein, he then commented, "obviously had never worked on oxidative phosphorylation" (Efraim Racker, see Rowen 1986; see also Lardy and Ferguson 1969, 991). Confusion, frustration and disagreement continued through this "turbulent period" (Nicholls 1981, 13).

In the mid 1960s, yet another hypothesis appeared. In this alternative, the intermediate energy stage was neither chemical nor electrochemical, but rather mechanical on a molecular scale. One version focused on the conformational strain of proteins, which can undergo changes in shape when their energy changes; the energy was akin to a coiled spring (Figure 1.8). In another version, the whole mitochondrial membrane served as a form of energy storage--analogous perhaps to an entire set of bedsprings (Figure 1.9). Both versions were known as the **conformational hypothesis**. Three (or perhaps four) major hypotheses now crowded the field. "Chemical, chemiosmotic, and conformational models, each in several versions, were vigorously promoted and roundly condemned" (Harold 1986). The hypotheses "are not accepted with equal enthusiasm by specialists in the area, but each appears to be the best explanation for certain experimental observations while remaining apparently inconsistent with others" (Dyson 1975, 189). "Each [had] its passionate devotees and its skeptics" (Becker 1977, 121). "Hypothesis after hypothesis was proposed, experiment after experiment was designed and run, but the process occurring in the mitochondria remained baffling" (Curtis 1984). "This was a time of strife, dominated by controversy over the essential nature of energy coupling whose flavor was at times almost Byzantine" (Harold 1986).

Although chemists initially received Mitchell's hypothesis with scepticism, "in the mid-1960s evidence began to accumulate" in its favor (Ernster 1984). Researchers could not escape the persistent association of proton gradients and closed membranes with energy coupling, not only in isolated mitochondria, but also in laboratory-prepared vesicles "reconstituted" from membrane fragments, in artificial membrane-systems and in other energy-processing units--chloroplasts (in plants) and several types of bacteria. One could measure the electrochemical gradients produced by the ETC (or comparable structures); in each case the direction of the gradient (some of them inside-out) matched the sidedness of the membrane: "the dual polarity of membranous structures explained many observations that had long been puzzling" (Harold 1986, 77). More dramatically, perhaps, chemists showed that one could synthesize ATP with *artificially* imposed gradients—that is, without the ETC. "The first observation of this kind was made in 1966 by Jagendorf and Uribe, who described dark ATP formation after transfer of chloroplasts from an acidic to an alkaline solution" (Skulachev 1988, 342). Likewise, ATP could generate measurable gradients by partially reversing the whole process (Arms and Camp 1983; Harold 1986; Skulachev 1988). "Confidence in the chemical coupling hypothesis began to falter. To use an apt American expression, it was now a new ball game" (Lehninger 1972, 4).

"Logically, the above evidence was sufficient for considering the chemiosmotic hypothesis as being experimentally proved. . . . [But] people wanted to see more and more 'miracles' predicted by the founder of the new bioenergetics. . . . They said that intact membrane systems were too complicated and reconstituted ones, too artificial. Experiments with artificially imposed [electrochemical gradients] were criticized because of small absolute values of synthesized ATP, which were limited by the small internal volume of the studied vesicles. . . . Experiments with bacteriorhosopsin tipped the scales. In 1971, Oesterfelt, Blaurock and Stoeckenius described a new type of bacterial pigment, bacteriorhodopsin, which proved to be responsible for the use of light-energy by halophilic bacteria. In 1973, Oesterfelt and Stoeckenius demonstrated light-dependent, bacteriorhodopsin-mediated H^+ extrusion from intact bacteria which was sensitive to uncouplers" (Skulachev 1988, 342-343; also 1981, 12-13). In 1974, Racker and Stoeckenius did the same for artificial chimeric vesicles, "composed of constituents from the three kingdoms of living organisms (bacteria, animals and plants). . . . The results of bacteriorhodopsin studies shattered the 'anti-Mitchellian' concepts, bringing about a drastic change in public opinion" (p. 343). They "swung the pendulum toward the chemiosmotic hypothesis. It was no longer possible to talk about a high-energy intermediate of the respiratory chain" (Racker 1981, 381).

"The debate concluded with the general (albeit not universal) acceptance of the chemiosmotic central dogma, that a current of protons is the sole link between respiration [in the ETC] and phosphorylation. Consensus was fittingly celebrated by the issuance of a joint communiqué (Boyer et al. 1977) in which the leading investigators spelled out areas of agreement" (Harold 1986; see also Wikstrom and Saraste 1984, Ernster and Schatz 1981, and Nicholls 1982, 22, on the "central dogma of bioenergetics"). "This is not to say of course that there are no doubts or dissenting voices, but the weight of opinion in the field appears to be solidly in favor of Mitchell's views" (Crofts 1979, 6). "Many of the details remain to be worked out, but the initial chemiosmotic hypothesis has been elevated to the status of the *chemiosmotic theory*" (Curtis 1983, 200). Mitchell himself noted, "the altruism and generosity with which former opponents of the chemiosmotic hypothesis not only came to accept it, but actively promoted it to the status of theory is a remarkable testimony of an admirable social quality of the scientific social system" (Mitchell 1989, 8). "In 1978, Mitchell received the last piece of evidence testifying to the triumph of his concept ... a Nobel Prize" (Skulachev 1988, 343). The Nobel Committee lauded Mitchell for "a breakthrough that has opened up new insights into the fundamental problems of bioenergetics" (Ernster 1979, 26); he had "intertwined riddles of oxidative phosphorylation, photosynthesis and active transport, sparking a revolution in cell biology that continues today" (Harold 1986, xi, 63).

1.2. Puzzles from the Textbook Narrative

The textbook history celebrates the success of chemiosmotic concepts. And it dramatizes the shift from innovative (yet scorned) hypothesis to widely accepted theory. But, of course, this is not idle history. It is a fable that moralizes science. Its literary elements echo the Christopher Columbus image in Tulp's cartoon. Various narrative devices, or tropes, enhance the rhetorical power of the story (Allchin 2003). For example, as a literary character, Mitchell is larger than life. He is heroic. He exudes virtue. Others, by contrast, are flawed. By inflating the struggle, the resultant triumph becomes more vivid. It is the stock David-and-Goliath storyline (Gilbert and Mulkay 1984b, 18-38). Mitchell, as underdog, defeated all odds and won against a more powerful, but vulnerably overconfident opposition (pp. 35-36). In this and other instances, the historical facts are subtly shaped to fit a familiar narrative pattern. The result is heightened drama—or melodrama (e.g., Saier 1997, Orgel 1999). These histories function primarily to justify the narrator's position (Kuhn 1962, Chap. 11). Right opposes wrong, and truth ultimately wins over error. Moreover, everything on the path to our current knowledge reflects the right method and way of thinking. All else is pathological. The textbook history thus appears to convey implicit philosophical lessons.

But the textbook history can puzzle someone interested in the process of science. For example, the extensive but "fruitless" search for the high-energy intermediates seems odd given that "many gifted individuals" worked on the problem. If the intermediates were fictional, why did researchers not abandon their search for them earlier (§4.2)? While the importance of the problem clearly inspired researchers in the field, was there any warrant for defending the "rear-guard" so adamantly (§5.2)? How was the chemical hypothesis ever deemed plausible (Chap. 3)? If the novel hypothesis was ultimately correct, how could anyone reject it? Why did researchers not gradually shift their focus as new evidence appeared? What allowed the controversy to persist for so long? "Frustrating" and "perplexing" may describe the mood of the period, but this fits uncertainty, not disagreement. *Why did the scientists disagree at all?*

The sharp dichotomy of right and wrong in the textbook history implies that disagreement was due to error. Vast error. To make sense of history, it seems, one must explain error—and lots of it. In Gilbert and Mulkay's interviews, researchers in ox-phos also accounted for each other's views. Error, they said, was due to personal, psychological and social factors (1984b, 63-89). The list is rather colorful. Participants attributed error variously to: succumbing to charisma, a rethorical "aura of fact," personal rivalry, dislike, and an "ostrich approach" of willfully disregarding the facts (pp. 66, 71, 81, 93, 96). They cited "intellectual inertia" and confrontation with "unorthodox" views. Some researchers were deemed "dogmatic," others apparently only "tenacious" (pp. 49, 65, 66). Others mentioned "prejudice, pig-headedness, strong personality, subjective bias, emotional involvement, naivity, sheer stupidity, thinking in a woolly fashion, fear of losing grants, threats to status and so on" (p. 79). For one participant, the whole generation was simply "unequal to the task" (p. 81). Contingent facts of personality thus permeate popular accounts of error. By contrast, empirical findings apparently explain correct belief. The scientists' interpretations thus resonate with many conventional philosophies of science that relegate irrational conclusions to non-empirical (and therefore non-scientific) factors (Laudan 1977, Longino 2002). The explanations for "true" and "false" beliefs are distinctively asymmetrical.

Worse, perhaps—though perhaps not unpredictably—individuals with conflicting conclusions faulted each other's errors simultaneously. Each participant viewed himself as right (due to the evidence) and the others as wrong (due to contingent factors). The asymmetrical interpretations were reciprocal. Indeed, the mutual asymmetry may express the controversy itself. How can an observer interpret the history and its outcome without privileging any one perspective? At this point, Gilbert and Mulkay abandoned their analysis. Indeed, their sense of being overwhelmed by the "Pandora's box" of variable conflicting interpretations may exemplify the postmodern malaise. After deconstruction, what next? I address this challenge and take the analysis further by restoring symmetry, especially empirically (§2.3), and by adopting a community-level perspective of interacting individuals (§2.4).

To solve the puzzles of the folk textbook history, then—and to provide a complete account of the resolution of the controversy—one must accommodate the mutual asymmetries. Two elements are primary. First, one must recover the reasons for ideas now abandoned. Why were erroneous conclusions once defended—empirically? For example, what experimental evidence indicated that the high-energy chemical intermediates were real? Somewhat paradoxically perhaps, one must "justify" the error. One must defend the "rear-guard" of the controversy. That is, a fuller history includes a rational reconstruction of the *wrong* ideas. Second, one must revive criticism of ideas that, now, seem inevitable. Why did many researchers not accept the chemiosmotic hypothesis at the outset, if it was ultimately correct? Here, conversely, one must find evidence for why it seemed wrong. I will show, for example, that the chemiosmotic hypothesis was not without flaws initially and was revised significantly before gaining full acceptance (§5.2). These two elements help restore empirical symmetry. While perhaps far fetched from a scientific or philosophical perspective, this task is familiar to any historian of science. Recapturing "science-in-the-making" is also a tool of many sociologists of science. Recovering the context of the past (§2.1) is the first step to understanding how the disagreement emerged, then persisted. My analysis, therefore, focuses primarily on the reciprocal views not represented in the simple textbook history (especially Chapters 3-6).

Once the status of disagreement is vividly reestablished, one can reconsider what led to its resolution. For example, were pig-headedness and prejudice subtly transformed into open-mindedness? Did some chemists merely stop "thinking in a woolly fashion"? How did the evidence itself change? What motivated and guided new investigations? What shaped interpretations of the evidence? Consider, for instance, E.C. Slater, who originated the chemical hypothesis. After the controversy he recognized the value of Jagendorf and Uribe's "acid-bath" experiment, the "significance of which slowly became apparent" (Slater 1981b). Yet in the midst of the controversy he claimed that it was "insufficient evidence for the [chemiosmotic] postulate." He even dismissed its potential relevance. For him at that time, it revealed nothing novel beyond "general experience" (Slater 1967, 317). What shaped how he perceived the significance of the same results at different times? How did the context change? Here, one finds clues in the experiences of multiple individuals as the evidential horizon edged forward historically (Chapters 7-8). Replacing a retrospective view with a contextualized, prospective view enables one to solve the ultimate puzzle: *how was the disagreement* *actually transformed into agreement?*

READER'S GUIDE

Readers may follow many trajectories from here.

- • • ▶ Those who enjoy knowing the conclusions at the outset may find them summarized in Chapter 10, presented in more detail perhaps in §7.3 and §8.3.
- • • ▶ The history and analysis of the main controversy itself begins in Chapter 4.
- • • ▶ This history gains more meaning, however, with further context. That is, researchers disagreed about ox-phos even *before* the controversy about chemiosmotic concepts. I explore this important baseline, valuable for contrast and integral to my conclusions, in Chapter 3.
- • • ▶ Readers concerned about historiography and philosophical method will find the tools of interpretation addressed in Chapter 2 (next) and elaborated in a more formal model in the Appendix.

Endnotes

1. This model appeared in the textbooks just after Mitchell received the Nobel Prize and was borrowed from Mitchell's earliest formal presentations of the theory. 'Redox loops' were widely challenged as too simplistic (see, e.g., Greville 1969) and, even now, they are only part of the story.