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The architecture of a biographical pathway

FREDERIC L. HOLMES. *Hans Krebs. Volume I: The formation of a scientific life 1900–1933*. New York: Oxford University Press, 1991. xx, 491 pp.

FREDERIC L. HOLMES. *Hans Krebs. Volume II: Architect of intermediary metabolism, 1933–1937*. New York: Oxford University Press, 1993. xvi, 481 pp.

THE KREBS CYCLE is one of the most striking visual images in cell biology and biochemistry. Visitors to experimental biology laboratories encounter it on the wallcharts of biochemical pathways published by major pharmaceutical companies. Representing the stepwise oxidative breakdown of carbohydrates, the Krebs cycle (also known as the citric acid cycle) is situated in the middle of the chart like a large spider in the intricate web of thousands of enzymatic reactions that constitute intermediary metabolism.

The central position of the citric acid cycle in the charts corresponds to that of Hans Krebs himself in the history of 20th century life science. Krebs was born in 1900 in a small town near Hannover, the second child in an assimilated Jewish physician's family. He studied medicine in Göttingen and Freiburg, completing his degree in Munich at the age of twenty-three. After two years of hospital practice and biochemical work in a pathology department, he moved to the Kaiser-Wilhelm-Institut für Biologie in Berlin, where he spent three formative years as an assistant to the authoritarian and demanding Otto Warburg.

Warburg was already known for his studies of enzymes and for his cellular respiration investigations of oxygen consumption in thin tissue slices by means of a sensitive manometric method. Krebs quickly mastered the techniques, adopted Warburg's experimental skills and parsimonious writing style, and soon began to publish papers independently. After a sojourn in an Altona hospital, he was invited in 1931 to Freiburg to introduce the manometric methods. He decided to study the formation of urea in the liver and, hovering over the effect of the amino acid ornithine, he succeeded in 1932 in depicting the synthesis of urea as a cyclic metabolic pathway. This was the first cyclic reaction pattern in biochemistry. You will find it in the vicinity of the citric acid cycle on the wallchart.

In 1933 Krebs recognized the Nazi threat and emigrated to England where Frederick Gowland Hopkins recruited him to the Biochemical Laboratory in Cambridge. In this creative center, which housed such scientists as Dorothy and Joseph Needham and microbiologist Marjory Stephenson,

Krebs continued his study of amino acid metabolism. After two years of hard work he added the synthesis of glutamine to the repertoire of metabolic reactions. After a brief inquiry into the synthesis of uric acid in birds, he turned his attention to the intermediate stages of oxidative carbohydrate metabolism, a question that had been brought to the attention of biochemists by Albert Szent-Györgyi in Hungary a few years earlier. In 1937 Krebs published his famous paper on the citric acid cycle which earned him the Nobel Prize in medicine or physiology sixteen years later. Subsequently the importance of the stepwise cyclic breakdown of carbohydrates releasing energy into the respiratory chain became an obligatory part of every high school student's biology reading.

Larry Holmes was introduced to Hans Krebs in Oxford in 1976. Until Krebs' death in 1981 they met for a couple of weeks every year to reconstruct from the pages of Krebs' laboratory notebooks the thought and experimental events that led to the discovery of the urea and citric acid cycles. From tape-recorded interviews, scientific papers, correspondence, and an autobiography that Krebs finished with Anne Martin shortly before his death,¹ Holmes has woven a masterly and fine-grained two-volume narrative of Krebs' path from medical school to the discovery of the citric acid cycle. The first volume deals with Krebs' early life, cultural background and scientific career in Germany until 1933; the second starts with Krebs' arrival at Victoria station in London and ends with his marriage in 1937 to the daughter of a Yorkshire family.

In light of Krebs' achievements one would expect Holmes' study to be a lens enabling the reader to view the history of 20th century biochemistry and intermediary metabolism. This particular lens has its kaleidoscopic distortions, however. A reader who wants to extract a history of interwar biochemistry out of the two volumes will have a hard time at it. True, Holmes sets the scene in the first volume with a dense and erudite review of research on intermediary metabolism in the 19th and early 20th centuries before Krebs entered Warburg's laboratory in 1926—but otherwise references to the development in the field in the late 1920s and early 1930s are scattered throughout the text, and there are no concluding remarks about the impact of the discovery of the ornithine and citric acid cycles on later developments in biochemistry. So, Holmes' account can not easily be read as an introduction to the history of 20th century biochemistry.

Holmes rather wants to fulfil two closely interrelated aims: he wants to describe how a major creative 20th century scientist conducted his daily work, and he wants to tell the story of a life in science; the latter entails discussing Krebs' work habits, moral leanings and patterns of human in-

1. Hans Krebs, with Anne Martin, *Reminiscences and reflections* (Oxford, 1981).

teraction, and his style of thinking and how it contributed to his rise to fame in biochemistry. The two volumes close a cycle themselves—the third step toward understanding creative processes in science. In 1974 Holmes published a study of Claude Bernard and animal chemistry, ten years later came another study of Lavoisier and the chemistry of life.² The basic concept behind the Holmes cycle is that of an “investigative pathway” and the method that of “fine-grained analysis” of the daily work of the scientist as it is reflected in the pages of laboratory notebooks and experimental protocols. Hence the format: the reader is introduced to a problem that Krebs picked up from the scientific literature at the time; day after day the experimental procedures and results in the laboratory notebooks are elucidated; each trail is followed by a thorough discussion of the particular thought pattern and scientific work style involved; and often the trail ends with a commentary from Krebs himself.

Exploring “research style” is a central concern in the volumes under review. From Warburg Krebs learned “not to hedge,” as he told Holmes in an early conversation, “not to come down on either side of the fence and be diffuse. . . [but] to be quite clear about what one thinks even if it turns out to be wrong, rather than to be woolly” (vol. I: p. 348). He was a trial-and-error searcher; he gleaned experimental questions from the literature, rather than developed a rationale of his own and work out in advance the experimental line with the best chance for success. Almost daily he let himself be diverted from one problem to another. He described himself as someone who picked “pebbles on the beach:” the pebble had to be suitable to the method, but instead of worrying whether it was worth picking up he usually decided just to try and see. Sometimes the short-term order of his experimental practice “defies logical analysis,” says Holmes, who characterizes Krebs’ style as that of a “grasshopper” (vol. II: pp. 329–30). Krebs was “an investigative scanner, gazing back and forth across his experimental horizon for an unusual effect, waiting patiently for something to appear sufficiently out of place to warrant focusing his effort” (vol. I: p. 273). Holmes’ description indicates that a kestrel hovering over a field waiting for a mouse to show up might be a more suitable metaphor; the architect metaphor in the subtitle of the second volume is misleading.

Holmes partly attributes this style to Krebs’ insufficient training as a chemist. According to Holmes, Krebs did not have the basic chemical knowledge to reason deeply about possible metabolic processes. Instead he relied on the manometer technique and waited for suggestions and hints in the current research literature. Lacking a long-range imaginative conception

2. *Claude Bernard and animal chemistry: The emergence of a scientist* (Cambridge, 1974); *Lavoisier and the chemistry of life: An explanation of scientific creativity* (Madison, 1985).

of possible roads ahead, he was rather a pragmatic explorer of what he encountered along the way. In the introductory chapter on the history of intermediary metabolism, Holmes says that he wants to challenge the general opinion among historians of 20th-century science that biochemists were nitty-gritty empiricists compared to the theoretical and visionary molecular biologists. His own study of Krebs, however, does not convince me that general opinion is mistaken.

Although the major strength of this work lies in the philosophy and psychology of science, Holmes does not have the passion for generalization characteristic of philosophers and psychologists of science. Whereas they build large theoretical edifices about scientific creativity on slender empirical material, Holmes is extremely careful not to do so from the Krebs case he has worked up in detail—he emphasizes instead that there are great individual variations in thought patterns and work styles. A general philosophy or psychology of creative research is not impossible, but Holmes prefers to wait until enough microstudies have been accumulated to refine and generalize findings already made. He warns against the urge to generalize too quickly.

Holmes' warning is well placed in an age in which everybody wants to build his own general theory of science, and few have the patience to spend decades laboring at empirical investigations of the kind that Holmes has done. It is easy to believe Holmes when he says that he arrived in Oxford in 1976 with a tape-recorder, some knowledge about Krebs' early scientific papers, "and little further idea about how to proceed" (vol. I: p. xvi). Yet there are limits to strong empiricism. Holmes' reader is presented with a wealth of detail and must have much biochemical knowledge to evaluate the experimental work. Readers with no specific interest in intermediary metabolism will have a hard time panning such creative gold nuggets from the pathway streams as the lucid three-page discussion about the role of Gestalt switches and sudden insight experiences in creative activity hidden in the chapter on the formation of urea (vol. I: pp. 326–28).

Holmes' empiricism goes hand in hand with a strong historicist awareness. Although sympathetic to his approach, I doubt it always works in practice just because it hides the gold in the stream. Part of the anti-Whig argument is that the scientist did not know where his work would end, and Holmes seems to believe the reader should not know either. When starting the reconstruction of yet another research trail Holmes takes care not to indicate the outcome in advance, and the reader is left alone trying to figure out whether the following 15–50 pages is one of the many useless pebbles, or whether it happened to be the one that eventually led Krebs to the urea and citric acid cycles. Many dead-end trails are mapped and we follow them all before we are allowed back on the main trail. For a much smaller

case-study of a single discovery this strategy might work, but Holmes' heavily loaded text often made me wish I had some merciful guide-lines.

Holmes trusts Krebs. He does not uncritically subscribe to the often held opinion among historians and sociologists of science that scientists are unreliable witnesses to their own creations. He does not support the hermeneutics of suspicion that governs so much of recent history of science written from a sociological perspective. There are important lessons to be learned here. Discussing the steps by which Krebs arrived at the solution of the ornithine effect (namely, that it was a catalytic process), Holmes must grapple with the fact that there are no surviving documents. Should he believe Krebs' "spontaneous, unrehearsed" oral response when questioned about the effect? Or should he trust his own reconstruction of the day-to-day record? In contrast with some recent dismissals of scientists' autobiographical stories, Holmes never discounts Krebs' account of events:³ he repeatedly contrasts Krebs' autobiographical accounts with his own reconstructions, finds discrepancies between the two stories, and attributes them to differences between the scientist and the historian concerning the objectives of reconstruction. But he does not "too readily" choose his own reconstruction of the notebooks (vol. II: p. 258). It is not a matter of one of them being naive and the other not, "but of priorities that differ in accordance with their respective purposes" (vol. I: p. 341).

Holmes will probably be labelled old-fashioned in certain circles because he does not fall easy prey to the siren calls of social constructivism and sociological relativism. With occasional exceptions, his references to the sociology of science do not go far beyond the Mertonian tradition. Yet, Holmes' lack of interest in the now established post-Kuhnian tradition in the history of science is fully compensated by his investigative thoroughness and clarity. Ignoring the jargon of science studies, his writing and terminology is straightforward. He does not try to lure the reader with catchy metaphors. His narrative is honest. It reminds you of an often forgotten virtue, "[t]he honesty and humility required of the student—not to pretend to know what one does not know."⁴ Honesty is a virtue that goes together with empiricism, and may be enhanced by the explicit presence of the narrator-subject. Contrary to the opinion of David Cassidy, who maintains in his recent Heisenberg study that "the less the biographer intrudes the better,"⁵ Holmes is constantly present as narrator. Humbly, never falling

3. Pnina Abir-Am, "Noblesse oblige: Lives of molecular biologists," *Isis*, 82 (1991), 326–43; Ilana Löwy, "Variances in meaning in discovery accounts: The case of contemporary biology," *HSPS*, 21:1 (1990), 87–121.

4. Iris Murdoch, *The sovereignty of good* (London, 1985), 89.

5. David C. Cassidy, *Uncertainty: The life and science of Werner Heisenberg* (New York, 1992), x.

into the narcissistic trap known as “self-reflexivity,” he nevertheless often pauses to make a historiographical comment, discuss the status of the sources, or his conversations with Krebs. By making himself visible and vulnerable Holmes allows the reader to follow his own research trail and thereby invites the reader to dialogue.

The description of Krebs’ creativity and scientific style is impeccably researched, narratively rich and convincing; this is probably the best narrative study of the creative process of a scientist ever written. The portrait of the life and personality of Krebs is more problematic, however. More than any other kind of history, biography is a literary genre. As the former doyen of literary biography Leon Edel once pointed out, it is the outcome of the interaction between facts and imaginative composition. As long as you do not tamper with the facts, you have great freedom as an author: “The biographer may be as imaginative as he pleases—the more imaginative the better—in the way in which he brings together his materials.”⁶

And what else brings a life together better than following the exigencies of personal life? The genre is well-suited for understanding the individual’s quest for meaning, personal growth and integrity. Biographies tell us how, in their struggles to overcome the threats of humiliation, suffering, anxiety, and pain of intellectual work, and in their hopes of being able to join with others (or, conversely, stay alone), human beings invoke widely different existential projects. Biography, like literature, is a guide to the drama of human life.

But the force of the narrative of Krebs’ laboratory life is not matched by the narrative of his life as a whole. There is too little biographical imagination in these thousand pages. Part of the reason may be that none of Krebs’ discoveries were revolutionary: they filled out some of the major blanks in the wallchart of intermediary metabolism, but did not break new theoretical or methodological ground. Krebs was a creative puzzle-solver who perused the specialist literature and skillfully utilized Warburg’s manometric method. A solid case-study of normal scientific creativity is quite justifiable, but the same can hardly be said of a two volume life.

Neither was there much drama in the life outside the laboratory. Holmes’ portrait depicts a typically courteous but distant scientist: Krebs was not much of a conversationalist and “tended to regard mediocrity in others with disdain” (vol. I: p. 351). His work habits were Prussian; he was so “extraordinarily methodical” that his colleagues in Cambridge could set their watches according to when he arrived in the laboratory in the morning. His work habits suited his intellectual style and historical role as a major puzzle-solver. His wife Margaret felt he had a certain sense of humor,

6. Leon Edel, *Literary biography* (London, 1957), 1.

but otherwise he seems a bore: punctual, effective, never (according to himself) “worried by inferiority complexes,” an “unusually even tempered” man who avoided showing emotions if possible, he was “reluctant to speak about everything that concerned him” according to his sister, and showed a considerable lack of empathy with his brother in trouble (vol. II: pp. 66, 76, 93). Krebs’ would-be father-in-law did not understand Margaret’s interest: “The chap seems to have no vices,” he said (vol. II: p. 422). Neither theoretical nor revolutionary, disdainful of philosophy, conventional in literary and cultural interests, a hard-working type—Krebs makes a dull subject for a biography.

Holmes’ strategy and writing style do little to entirely Krebs’ dullness. Holmes largely sticks to the narration of factual life events and pays little attention to biographical composition and style. The story of Krebs’ daily work in the laboratory is interspersed with information about vacation trips, occasional romantic meetings or thoughts about emigration to Palestine in the mid-1930s, but soon the reader is brought back to the laboratory. The story of the “investigative pathway” runs parallel with the story of the life outside the laboratory; the two stories are juxtaposed but rarely connected at a deeper level. Holmes also misses some obvious opportunities to address the fundamental problem of biography, the deeper relation between life and work. Krebs’ relation with the German nurse Katherina Holsten in the mid-1930s illustrates this. Gradually Katherina became increasingly dissatisfied with his apparent lack of interest in their common future, and after several months of short, infrequent correspondence she finally gave vent to her frustration and asked Krebs to make up his mind. “There is no reason to infer,” comments Holmes, that Krebs was “not moved” by her letter. “Nevertheless, so preoccupied was he with his relentless laboratory life, that it took him a month and a half to respond” (vol. II: p. 142).

It is hard to believe, however, that a man who is supposed to be moved and concerned about a woman should delay answering her for six weeks because of bench-work. (After all, this episode took place during one of his many pebble-stone picking excursions.) It is reasonable to infer that Krebs retreated into the sanctuary of the laboratory to escape having to confront an unpredictable future with Katherina. Many biographies and life experiences tell about people who fled from the threatening realm of human interaction into manageable activity in science. Science is basically disengagement from the ordinary world.⁷ The Katherina episode seems to illustrate the pessimistic words of Yeats: “The intellect of man is forced to choose/Perfection of the life, or of the work.”⁸ But is this really a neces-

7. Morse Peckham, *Romanticism and ideology* (Greenwood, FL, 1985), 35–43.

8. William Butler Yeats, “The choice,” in Peter Allt and Russel K. Alspach, eds., *The variorum edition of the poems of W.B. Yeats* (New York, 1957), 495.

sary choice? Holmes does not seize the opportunity. If biographers do not, who will?

It is tempting to compare Holmes' study with Adrian Desmond and James Moore's *Darwin*.⁹ The two works epitomize diametrically opposite and influential strategies in writing about individual lives in science today. *Hans Krebs* is written for the specialist, the result of a solitary trek through a series of major events in 20th-century biochemistry based on close textual analysis of thousands of experimental protocols and scientific papers. Aimed at the general public, *Darwin* is a synthesis of a whole generation of Darwin industrialism: a highly contextualized narrative giving colorful descriptions of, among much else, riots on the streets of London and the war drums of rising socialist warriors.

Apart from the differences, however, a common element binds the two works: although both are advertized as biographies and although the personal traits, actions, and thoughts of the subjects receive significant space and attention, in both cases the authors avoid putting the personalities in the center of the narrative. Krebs is continuously decentered toward the text (the laboratory protocols), Darwin toward the cultural context. True, Desmond and Moore's *Darwin* has personal worries. He is plagued by self-doubt, vomiting, disabling stomach aches, personal grief, and constant worries about his respectability. But all this is depicted as "a product of his time" and of the social context: Desmond and Moore's *Darwin* is a thoroughly socialized persona, and their biography is a highly contextualized and "defiantly social portrait."¹⁰ Holmes eschews the larger cultural context. For him, social context is the small inner circle of German and British biochemists; the only connection between larger social events and experimental work is the suggestion that Krebs, although having rather naive views about the Nazi threat, may have speeded up his work with the urea cycle because of the new uncertainties about his future work after the *Machtübernahme* in 1933. But that does not bring personality to the center of the narrative: instead, Holmes' Krebs remains an appendix to the laboratory notebooks, mediating the elements of the creative process the way Darwin's personality mediates the social forces that molded evolutionary theory.

The decentering of personality has become a major trait in contemporary history of science.¹¹ The first blow against personality came from

9. Adrian Desmond and James Moore, *Darwin* (London, 1991).

10. Desmond and Moore (ref. 9), xviii–xx.

11. For an extension of this argument, see Thomas Söderqvist, "Existential projects and existential choice in science: Science biography as an edifying genre," in Richard Yeo and Michael Shortland, eds., *Telling lives: Studies of scientific biography* (Cambridge, 1995).

philosophers who emphasized the logical structure of scientific ideas and disregarded the humanity of the scientist. All but pure cognition—the personality, the passions, and the idiosyncratic aspects of scientific work—was squeezed out. The life—particularly the personal embodied life of the scientist, was made irrelevant for the understanding of science. During the last two decades this philosophically inspired program has gradually been replaced by a concern for the social, cultural, and political context of science. To the philosophical dismissal of the personal has been added a sociological dismissal of the individual.¹² The genre of biography has been challenged by social historians and sociologists who consider studies of individual scientists and their virtues and vices largely irrelevant for the history of scientific disciplines and research schools, for studies of power and gender discourses, or for understanding the social construction of scientific knowledge. As Steven Shapin puts it, “the individualistic reflexes” of the historian of science ought to be “usefully disciplined by the sociologist’s collectivism.”¹³ Likewise, the recent turn toward discourse analysis and rhetoric of science, by concentrating on the text in context, has further weakened interest in the personality of the scientist and severed work from authors’ intentions.

The impact of this serial marriage of history of science with philosophy and sociology has certainly had positive effects on science biography. Biographers today are more aware of the cultural, social, and political context of the lives of their subjects than were biographers of earlier generations. But the relationship has also had negative effects. The most common argument for the use of biography today is that studies of individual scientists can be used as a means of demonstrating the socially constructed character of scientific ideas. Also, philosophers and psychologists of science find studies of lives useful for studies of cognitive processes. Many seem to believe that providing cases for demonstrating the contextual nature of science or the cognitive study of creativity is the only proper use of biography. The renaissance of science biography in the 1980s coincided with a tacit redefinition of the genre as “social biography.”¹⁴ From being an art of telling individual lives in science, biography has largely become an auxiliary to the social history and sociology of science. One reviewer suggests that the problem of biography’s relevance for “the new [i.e., social!] histo-

12. David Kaiser, “Bringing the human actors back on stage: The personal context of the Einstein-Bohr debate,” *British journal for the history of science*, 27 (1994), 129–152.

13. Steven Shapin, “Discipline and bounding: The history and sociology of science as seen through the externalism-internalism debate,” *History of science*, 30 (1992), 333–69, on 354–355.

14. Dale F. Eickelman, *Knowledge and power in Morocco: The education of a twentieth-century notable* (Princeton, 1985), xv.

ry of science” can be solved by redefining the genre: instead of focusing on the personality of individual scientists, the historian should use biographical material as a “convenient indicator of the possibilities for action offered by a particular society.”¹⁵

But biography is not handmaiden to cognitive science or a sociologically reconstructed history of science. The genre has the lives of people as its object of study.¹⁶ Neither social discourses nor cognitive schemas act in the world; people do. And they are not merely mediators of cognitive processes or outcomes of linguistic interaction or power networks; they are irreducible and independent world-makers of their own, with hopes, fears, anxieties, and doubts about their existential projects, social visions, reasoning, and writing.¹⁷ If biographers do not center on personality, who will?

True, neither Holmes nor Desmond and Moore give in to the extreme attacks on personality. Like many other biographies of scientists,¹⁸ *Hans Krebs* and *Darwin* contain long descriptions of personality. But by trying to ride two horses simultaneously—personality and creativity analysis on one hand, personality and contextualization on the other—they compromise the biographical narratives too much. In Holmes’ case, the corrective was close at hand: instead of publishing two consecutive volumes, the overall aim of the work would have gained from making one volume a case study of Krebs the creative scientist and the other the story of Hans Krebs and his life as man and scientist.

To find recent biographies where the person and his quest for meaning in life occupy the central place in the narrative—thereby redeeming biography as an independent genre—we have to go to the margins of the history of science, to biographies about philosophers or scientists-as-philosophers, such as James Miller’s on Foucault, Maila Walter’s on Bridgman, and Ray Monk’s on Wittgenstein.¹⁹ All three authors approach the lives of their subjects in the spirit of Nietzsche’s words: “Gradually it has become clear to

15. Iwan R. Morus, “Industrious people: Biography and nineteenth-century physics,” *Studies in the history and philosophy of science*, 21 (1990), 519–25, on 520.

16. John Macmurray, *The self as agent* (New York, 1957).

17. Roberto M. Unger, *Passion: An essay on personality* (New York, 1984).

18. E.g., Cassidy (ref. 5); Geoffrey Cantor, *Michael Faraday: Sandemanian and scientist: A study of science and religion in the nineteenth century* (New York, 1991); Max Dresden, *H.A.Kramers: Between tradition and revolution* (Berlin, 1988); Kenneth R. Manning, *Black Appollo of science: The life of Ernest Everett Just* (New York, 1983); Walter Moore, *Schrödinger: Life and thought* (Cambridge, 1989); J.L. Heilbron, *Max Planck: The dilemmas of an upright man* (Berkeley, 1986); Evelyn Fox Keller, *A feeling for the organism: The life and work of Barbara McClintock* (New York, 1983).

19. Maila L. Walter, *Science and cultural crisis: An intellectual biography of Percy Williams Bridgman (1882–1961)* (Stanford, 1990); Ray Monk, *Ludwig Wittgenstein: The duty of genius* (New York, 1990); James Miller, *The passion of Michel Foucault* (New York, 1993).

me what every great philosophy so far has been: namely, the personal confession of its author and a kind of involuntary and unconscious memoir.”²⁰

There is no reason to doubt that science in all its aspects also involves strong elements of the personality of its constructors. Not *just* personal confessions, but *also* personal confessions. What Miller’s, Walter’s, and Monk’s biographies have been able to accomplish, other biographers should be able to do. That requires a new look at the foundations and aims of the genre of science biography and a willingness to transcend the now traditional prerogatives of scientific texts and cultural contexts in dealing with the lives and personalities of scientists.

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20. Friedrich Nietzsche, *Jenseits von Gut und Böse* (Leipzig, 1886), trans. Walter Kaufmann: *Beyond good and evil: Prelude to a philosophy of the future* (New York, 1989), 13.