Protozoa as Precursors of Metazoa: German Cell Theory and Its Critics at the Turn of the Century

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In 1902, when the new German journal for protozoology, the *Archiv für Protistenkunde*, published its first issue, Richard Hertwig was chosen to write the lead article, which he entitled "Protozoa and the Cell Theory."[1] Both the author and the subject were appropriate and significant choices, for Hertwig, as professor of zoology and comparative anatomy and director of the Munich Zoological Institute, was the founder of one of the leading centers for protozoological research in Germany. His credentials in the field of cell theory were no less impressive. In the 1880s, he and his brother Oscar (both former students of Ernst Haeckel at Jena) had carried out cytological studies of invertebrates that figured prominently in the development of embryology and cell theory.[2] Infused with a love of protozoa through his association with Max Schultze at Bonn, Hertwig had subsequently turned his attention to investigating the processes of fertilization and nuclear division in various groups of protozoa. He was therefore well qualified to discuss the current status of protozoa vis-à-vis cell theory and, on the basis of this evaluation, to suggest a future research program for protozoology.

Hertwig's article proved to be an important one for the

1. Richard Hertwig, "Die Protozoen und die Zelltheorie," *Arch. Protist., 1* (1902), 1—40.

2. For the careers of the Hertwig brothers, see Richard Weissenberg, *Oscar Hertwig (1849—1922): Leben und Werk eines deutschen Biologen* (Leipzig: J. A. Barth, 1959). The articles by several of Richard Hertwig's students (written on the event of his seventieth birthday) in *Naturwissenschaften, 8* (1920), 767—782, provide information on his various research interests. Reminiscences of Hertwig by Richard B. Goldschmidt, in *The Golden Age of Zoology: Portraits from Memory* (Seattle and London: University of Washington Press, 1956), and by Karl von Frisch, in *Erinnerungen eines Biologen* (Berlin: Springer Verlag, 1957) (or *A Biologist Remembers*, trans. Lisbeth Gombrich [Oxford: Pergamon Press, 1967]), treat both Hertwig's work and his direction of the Munich Zoological Institute.

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development of the discipline in the first two decades of this century. It influenced the work of several major protozoologists, including Fritz Schaudinn, who used Hertwig's interpretations of his own recent studies to suggest a new conceptual approach to the organization of protozoa — the so-called chromidial theory. This theory, moreover, spread beyond the confines of protozoology when Richard Goldschmidt presented it as valid for metazoan cells as well. The research program that Hertwig proposed obviously guided the work of his many students at Munich, but its experimental approach to investigating the organization of these organisms appeared attractive to numerous protozoologists at other institutions in Germany as well as abroad.

Ultimately, however, the vision of the cell reflected in the work of Hertwig and his German counterparts prompted the criticism of a number of British biologists. As expressed by the most vocal advocate of this view, Cecil Clifford Dobell, the particular theories arising from German protozoology were grounded in the recapitulation theory of the nineteenth century, which he regarded as both outmoded and erroneous. He, and others who shared his views, therefore rejected the chromidial theory and, in some respects, German cell theory in general. In the present study, I will trace the major developments in this episode, examining Hertwig's essay and the work of several German biologists it influenced. I will then consider the arguments of the critics of German cell theory in Britain and conclude by suggesting ways in which the historian can evaluate their criticism.

"PROTOZOA AND THE CELL THEORY"

Hertwig began his 1902 essay on a historical note, reminding his readers that the study of protozoa had played a major role in the reform of cell theory in the middle of the previous century. Protozoa had been central to investigations into the nature of the living substance of the cell, and to formation of the concept of the protoplasm, particularly in the work of Félix Dujardin, in France, and Max Schultze, in Germany. For three decades, however, the major strides made in understanding the functioning of the cell — particularly the role of the nucleus in cell division, or karyokinesis — had been gained through the investigation of multicellular organisms. This, of course, was not accidental, for despite all the differences exhibited by various metazoan cells — be they muscle, bone, nerve, or sex cells — all the cells of multicellular organisms possess a high degree of uniformity in both structure and function. Such was not the case in protozoa, in which, Hertwig wrote, "all the processes of differentiation and diversity that are expressed in organisms and make possible a discrimination between innumerable species are here expressed within the cell itself."[3]

Despite the complexity of protozoan organization, Hertwig nonetheless followed Theodor von Siebold and Otto Bütschli in maintaining that protozoa were unicellular organisms.[4] The identification of protozoa with cells was crucial to Hertwig's program, but it also had ramifications outside of protozoology. For example, it addressed an important aspect of contemporary evolution theory: the hypothetical precursor of multicellular organisms. As E. B. Wilson put the matter, the view that the body of a protozoon consisted of a single cell suggested that "the multicellular body of higher forms is equivalent to an assemblage or colony of one-celled individuals; and from this grew the further conception that the multicellular organism may be regarded as a 'cell-state' the one-celled members of which have undergone a physiological division of labor."[5] Hertwig was well aware of the evolutionary implications of his views; indeed, the argument that the nucleus of protozoa was comparable to that of metazoa was essentially based on an evolutionary perspective, where the former represented stages in the development of the latter.

Exploiting the full implications of the unicellular hypothesis of protozoa, Hertwig deduced that protozoa must abide by all the "laws of cell life" valid for metazoa. That is, the knowledge of cellular structures and processes of metazoan cells acquired over the past two decades could be used to illuminate the study of protozoa. Yet here Hertwig offered a word of caution. He recognized that too often in the recent past protozoa had been subordinated to the metazoa, both in terms of perceived importance as well as through an incautious application of findings gained from higher organisms. With this in mind, Hertwig embarked upon a reexamination of precisely how the organization of protozoa could be compared with the structure of metazoan cells, and, based upon this comparison, he formulated a new program that he believed would advance protozoology as well as general cell theory.

Hertwig delineated two major ways in which protozoa and

3. Hertwig, "Die Protozoen," p. 4.

4. For a treatment of Siebold's and Bütschli's views on the unicellularity of protozoa, see Frederick B. Churchill, "The Guts of the Matter. Infusoria from Ehrenberg to Bütschli: 1838—1874," *J. Hist. Biol.*, this issue.

5. Edmund B. Wilson, *The Cell in Development and Heredity*, 3rd ed. (New York: Macmillan, 1925), p. 101. Paul Weindling has studied the social dimensions of this conception in "Theories of the Cell State in Imperial Germany," in *Biology, Medicine and Society, 1840—1940*, ed. Charles Webster (Cambridge: Cambridge University Press, 1981), pp. 99—155.

metazoa differed: (1) in their nuclear structure, and (2) in their various modes of reproduction. With respect to the nuclear structure of infusoria (or ciliates), for example, biologists had long known of the curious presence in paramecia of two different nuclei — the micronucleus and the macronucleus — each apparently charged with distinct functions: reproduction and general metabolism, respectively. Within the past few years, further novelties in the nuclear organization of protozoa had emerged.

In his own study of nuclear division and fertilization in the heliozoan *Actinosphaerium*, for example, Hertwig had discovered, upon the application of standard nuclear dyes to his preparations, the presence of granules dispersed throughout the protoplasm. Because these granules stained identically to the nuclear chromatin, he named them *chromidia* and assumed that they were of nuclear origin.[6] This relationship was given empirical support the following year: investigating the mode of reproduction in *Arcella vulgaris*, Hertwig also identified chromidial structures dispersed in the protoplasm of this rhizopod; although they appeared netlike rather than granular. The nuclear nature of this so-called chromidial net was established by its ability to form new daughter nuclei (see Fig. 1).[7] He later found a chromidial net in other siliceous-shelled rhizopods possessing a single nucleus.

Hertwig took the opportunity of the informal format of his 1902 essay to generalize from these findings, revealing the way in which evolutionary considerations were implicit in his work. He speculated that the chromidia and the chromidial net of protozoa represented "an ancient process of cell division, in which the nucleus dissolves, the chromidial net divides, and a new nucleus concentrates gradually from these portions."[8] In short, he viewed the chromidial net as a precursor of the more complicated mechanism of karyokinesis seen in metazoa. This suggested that a study of the various modes of reproduction in protozoa could ultimately augment the understanding of nuclear reproduction in metazoa.

Hertwig, accordingly, next discussed the nature of reproduction in protozoa. This topic, reflecting the recent concerns of cytology, was currently the object of considerable attention. From the

6. Richard Hertwig, "Ueber Kernteilung, Richtungskörperbildung und Befruchtung von *Actinosphaerium Eichhorni*," *Abh. bayer. Akad. Wiss.* (*Math. phys. Kl.*), *19* (1898), pp. 631–734.

7. Richard Hertwig, "Ueber Encystierung und Kernvermehrung bei *Arcella vulgaris*," in *Festschrift zum siebenzigsten geburtstag von Carl von Kupffer*, 2 vols. (Jena: Gustav Fischer, 1899), 1: pp. 367–382.

8. Hertwig, "Die Protozoen," p. 8.

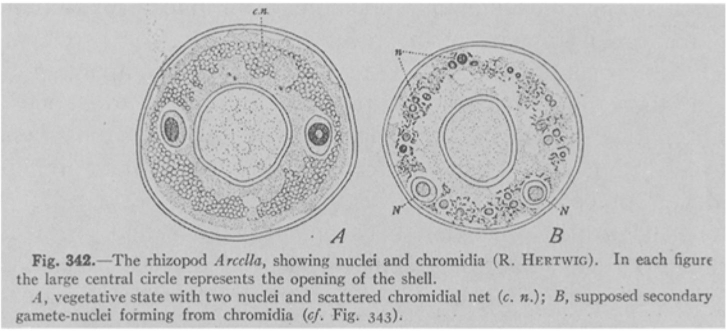

Fig. 1. Chromidia and the chromidial net in the rhizopod *Arcella vulgaris*, after Hertwig. (From E. B. Wilson, *The Cell in Development and Heredity*, 3rd ed. [New York: Macmillan, 1925], p. 700.)

present vantage point, it appeared that the mechanisms of reproduction in single-celled individuals were incredibly diverse, and this, Hertwig believed, was due not so much to the different conditions of life to which the various groups were subjected, but rather to the remarkable plasticity of the nucleus. The seemingly primitive yet complicated nuclei of protozoa exhibited, in the lowest taxa, the apparently lawless mechanism of simple division; yet in the higher taxa the process approached the highly complicated mechanism of karyokinesis in metazoa. It was in this respect, Hertwig stated, that the findings of cytology, particularly the study of nuclear division in metazoa, had most informed protozoology.[9]

Despite the differences in cell structure and in cell division, Hertwig believed that there was undoubtedly a great deal of similarity between protozoa and metazoa. Again, he based this conclusion on the assumption that the protozoa were the precursors of metazoa. If higher organisms had evolved from unicellular organisms, metazoan organization should retain resemblances to these precursors. As Hertwig expressed this idea, "Since animal life possesses certain generally recurring principles, so must there also be definite principles generally preserved in the structure of living substance."[10]

9. Ibid., pp. 24—29.
10. Ibid., p. 4.

This statement was a powerful one, enabling parallels to be drawn throughout the animal kingdom, from unicellular to multicellular organisms and in the reverse direction. Yet, as Hertwig had earlier cautioned, a simple *morphological* comparison between the cells of metazoa and protozoa could lead to erroneous assumptions. It was therefore necessary to ascertain the *physiological* significance of the individual cell parts — their ultimate function in cell life, as well as their structure — in order to establish proper analogies between protozoan and metazoan cells.[11] But this was not a simple task. It required a means by which the functional roles of the various cellular components or organelles of protozoa could be assessed. Yet, he believed, such an approach was forthcoming in his notion of a relationship between the nucleus and the cytoplasm.

HERTWIG'S KARYOPLASMIC RATIO

In the remaining pages of "Die Protozoen und die Zelltheorie," Hertwig outlined a research program for protozoology that centered on his discovery of what he called the "Kernplasmarelation." Briefly stated, Hertwig's karyoplasmic ratio (to use Wilson's designation rather than the modern "nucleocytoplasmic relationship") postulated that in cells of the same species a ratio existed between the nuclear mass and the cytoplasmic mass, usually varying only during the different stages of cell life. Any upset in the balance of this relationship brought about a change in cell state. He believed, for example, that a disturbance of this karyoplasmic ratio in favor of the cytoplasm was ultimately the cause of cell division. If, however, the nucleus grew at the expense of the cytoplasmic mass, a moribund condition ensued; such an overabundance of nuclear matter could perhaps explain the recently discovered phenomenon of "depression" in protozoa.[12]

Primarily a physiological view of the functioning of the cell, Hertwig's karyoplasmic ratio helped him to understand the significance of the morphological entities he called chromidia. Chromidia were possibly the means by which the cell could

11. Ibid., pp. 35—36.

12. First discussed by Hertwig in "Ueber das Wechselverhältnis von Kern und Protoplasma," *Ges. Morph. Physiol. München, 18* (1902), 77—97, the karyoplasmic ratio was further developed in his "Ueber Korrelation von Zell- und Kerngrösse und ihre Bedeutung für die geschlechtliche Differenzierung und die Teilung der Zelle," *Biol. Centralbl., 23* (1903), 49—62, 108—119. For a detailed discussion of this theory, see Wilson, *The Cell*, pp. 727—733.

redress an imbalance caused by an inordinate growth of the nuclear mass. That is, the cell perhaps possessed an internal means to adjust the karyoplasmic ratio through the expulsion of nuclear fragments into the cytoplasm in the form of chromidia, whereupon they subsequently disintegrated. In this respect, Hertwig's chromidia became physiologically distinct from his chromidial net. The former were primarily related to the cell's metabolic or "housekeeping" functions; the latter, however, played a role in the reproductive activities of the cell.

Hertwig was convinced that the karyoplasmic ratio was a major empirical breakthrough in understanding the causal mechanisms governing cell life. It was potentially a powerful tool for protozoology, providing an empirical standard by which all the multifarious nuclear organization presented in unicellular organisms could be compared and analyzed. But given the "generally recurring principles" throughout life, findings gained in the study of the protozoa should also inform the understanding of the metazoan cell.

Because of the diversity in nuclear structure and in the reproductive mechanisms displayed among the protozoa — possessing, as they did, a single nucleus, several nuclei, or even a distributed nuclear system — they exhibited an array of different karyoplasmic ratios. Moreover, protozoa were generally good experimental subjects, easy to maintain and to monitor under controlled conditions. This was an important point for Hertwig, given his further assumption that stimuli external to the cell could alter the karyoplasmic ratio, and hence indirectly influence cellular activities. In short, for both practical and theoretical reasons, the study of protozoa offered a promising approach to advancing the general knowledge of the cell as much as that of the individual organisms themselves.

Hertwig's program for protozoology, then, contained all the necessary ingredients of a satisfactory research program. It was founded on the theory of the karyoplasmic ratio as a major regulative mechanism in cell life. By satisfactorily explaining such phenomena as depression in protozoa and the appearance of chromidia, this theory had gained credence. Even more importantly, perhaps, the postulated relation between nuclear and cytoplasmic mass was eminently testable, a particularly strong point in the highly charged experimentalist mode of turn-of-the-century biology. This program offered the discipline a new experimental methodology, and one with potentially far-reaching consequences. To Hertwig, it appeared that the means were finally at hand to be able to provide, after many years of autonomous development, "a unified conception of the cell valid in the same way for protozoa and for metazoa."[13]

THE INFLUENCE OF HERTWIG'S PROGRAM FOR PROTOZOOLOGY

Hertwig's essay bore fruit immediately. Only a year after it was published, Fritz Schaudinn, director of the Institute for Marine and Tropical Hygiene in Hamburg and one of Germany's most prominent protozoologists, published a paper in which he particularly singled out Hertwig's ideas concerning chromidia.[14] Schaudinn explained that since the commencement of his study of reproduction in protozoa in 1894, he had been puzzled by the appearance of certain phenomena. But now, he said, referring to rhizopod reproduction, "the new ideas of R. Hertwig on chromidia have given this research fresh stimulus and clarified for me many previously unexplainable processes so that now I can complete the developmental cycle of this form."[15]

13. Hertwig, "Die Protozoen," p. 16. The term "depression" was coined by the American protozoologist Gary Calkins to denote the period of physiological stagnation apparent during certain stages of the life cycle of paramecia. Postulating, from the karyoplasmic relation, that depression was caused by an excess of nuclear matter, Hertwig and his students removed from such organisms a portion of their nuclear mass and indeed found that the animals resumed normal physiological activity. Hertwig believed that this experiment provided a major confirmation for the karyoplasmic ratio ("Ueber das Wechselverhältnis," pp. 81—84).

14. Fritz Richard Schaudinn (1871—1906) gained his Ph.D. under F. E. Schultze at the University of Berlin in 1894. Continuing in the Zoology Institute as assistant and habilitating in 1898, Schaudinn also worked concurrently at the Institut für Infektionskrankheiten directed by Robert Koch. In 1901 he was appointed director of the German-Austrian marine biology station in Rovigno and chose Stanislaus von Prowazek, a former student of Richard Hertwig, as his assistant. In 1904 he was called to Berlin, upon Koch's recommendation, to direct the new protozoology institute established in the national ministry of health (Reichsgesundheitsamt). Two years later he went to Hamburg to direct the new protozoology laboratory at the Institute for Marine and Tropical Diseases, but succumbed to a sudden illness the same year. He was particularly noted for his work on the newly discovered parasites of blood — the trypanosomes and the malarial plasmodia — and for his study of the coccidians and of the bacterial organism responsible for syphilis. For biographical sketches of Schaudinn, see Ilse Jahn, Rolf Löther, and Konrad Senglaub, *Geschichte der Biologie. Theorien, Methoden, Institutionen, Kurzbiographien* (Jena: Gustav Fischer, 1982), pp. 726—727; Max Hartmann and Stanislaus von Prowazek, "Fritz Schaudinn," *Arch. Protist.*, *8* (1907), i—x; Franz Doflein, "Fritz Schaudinn," *Allg. Zeitung*, no. 153 (July 5, 1906); and especially Goldschmidt, *Golden Age*, pp. 124—138.

15. Fritz Schaudinn, "Untersuchungen über die Fortpflanzung einiger Rhizopoden," *Arb. kaiserl. Gesundheits.*, *19* (1903), 547—576; esp. p. 549.

Two years later, in a lecture on "Recent Research on Fertilization in Protozoa" delivered before the 1905 meeting of the German Zoological Society, Schaudinn offered a circumspect overview of the present state of the discipline. There was no doubt that protozoological research was still in its infancy. "Our knowledge of the finer processes in the fertilization of protozoa," he stated, "is at present so full of gaps and so contradictory that it is not at all possible to give a comprehensive picture of it or even to construct a theoretical system."[16] Yet Schaudinn was optimistic about the future of the discipline. Hertwig's discovery and interpretation of chromidia in protozoa, he told his learned audience, offered a promising approach for a new theoretical analysis of reproduction in protozoa. Moreover, he believed that some ideas he had recently developed could also assist this process.

SCHAUDINN'S BINUCLEARITY HYPOTHESIS

Impressed though he was by Hertwig's explanation of chromidia, Schaudinn did not adopt it in toto. He himself had been developing a concept of protozoan organization for almost a decade, and rather than laying emphasis on a balance between cellular components — nucleus and protoplasm — as in Hertwig's concept of a karyoplasmic ratio, Schaudinn concentrated primarily on the nuclear material. Stimulated by Hertwig's interpretation of the physiologically distinct functions of the chromidia and the chromidial net — one a regulative mechanism and the other linked to reproduction — Schaudinn used this idea to formulate a unified conception of reproduction and metabolism in unicellular organisms.

The relatively widespread occurrence of chromidia in several groups of protozoa suggested to Schaudinn that chromidia had a general significance in cell life. The chromidial granules appeared to be associated with the elementary "vegetative" processes of the cell: assimilation, dissimilation, and growth. The chromidial net of rhizopods had been shown to be linked to reproduction. Comparing the various manifestations of these phenomena in different organisms, Schaudinn arrived at the following generalization: "In protozoa in general," he declared, "where the developmental history and especially fertilization has been learned, a dualism of the somatic and generative nuclear substances, similar to the nuclear relations in Infusoria, is perceptible at some point in develop-

16. Fritz Schaudinn, "Neuere Forschungen über die Befruchtung bei Protozoen," *Verhandl. deut. zool. Ges.*, *15* (1905), 16—35; esp. p. 16.

ment."[17] In short, the nucleus could be divided into two components. This basic dualism in the nuclear substance was best seen in the ciliates, where in paramecia two morphologically distinct nuclei were present, one responsible for reproduction and one for general metabolism. But chromidia and the chromidial net, interpreted as two different types of nuclear chromatin dispersed in the protoplasm, indicated that there was a fundamental "binuclearity" present in *all* unicellular organisms — indeed, possibly in all cells.

The resemblance between Schaudinn's binuclearity concept and August Weismann's earlier distinction between the somatoplasm and the germ plasm is unmistakable, even if unacknowledged.[18] Originally conceived for multicellular organisms (to segregate in the germ plasm the substance responsible for heredity from that responsible for body maintenance), Weismann's basic dichotomy in the types of cells in individual organisms was simply logically extended by Schaudinn to the level of unicellular individuals. That is, granted that the protozoon was an individual, albeit a single-celled one, the same separation between somatic and reproductive functions envisioned for metazoa should also apply to protozoa. For protozoa, however, Schaudinn proposed a physiological division of labor in the nuclear material itself. This had long been known to be the case for paramecia, with their two distinct nuclei, but the existence of chromidia now revealed a similar binuclearity in organisms with only one nucleus. With the terminology itself reminiscent of Weismann, Schaudinn conceived of the chromidia, or "somatochromidia," as physiologically distinct from the chromidial net, or "gametochromidia."

In addition to a duality of somatic and reproductive nuclear matter, Schaudinn also discerned a further kind of binuclearity in another group of protozoa. In the trypanosomes and other flagellates, his own recent studies and those of others suggested that the basal body of a flagellum — the blepharoplast — was of

17. Ibid., p. 26. For a detailed contemporary discussion of this topic, see Edward A. Minchin, *An Introduction to the Study of the Protozoa, with Special Reference to the Parasitic Forms* (London: Edward Arnold, 1912), pp. 82—99.

18. See August Weismann, "The Continuity of the Germ-Plasm as the Foundation of a Theory of Heredity" (1885), in *Essays upon Heredity and Kindred Biological Problems*, trans. E. B. Poulton, S. Shonland, and A. E. Shipley, 2 vols. (2d ed.; Oxford: Clarendon Press, 1891—92), 1: 161—248. Richard Hertwig clearly recognized the connection between the binuclearity hypothesis and Weismann's views: "The problem is the same (only carried over to intracellular relations) as the problem that Weismann introduced into science with his principal distinction between somatic cells and reproductive cells" (Richard Hertwig, "Ueber den Chromidialapparat und den Dualismus der Kernsubstanzen," *Sitz. Ges. Morph. Physiol. München, 23* [1907], 19—40, esp. p. 25).

nuclear origin.[19] Similarly, the "Bewegungsapparat," or flagellum, itself derived from the nucleus. These two related bodies, both originating from the nucleus and the source of motion for the organism, he viewed as representing the "kinetic" nucleus of the flagellates, in contrast to the normal "trophic" nucleus. Schaudinn, however, did not view this new kind of binuclearity as opposed to the somato/generative dualism he envisioned; rather, he conceived of the former as nested within the latter.

In a boldly speculative series of associations, Schaudinn suggested that the "dualism within a dualism" in the trypanosomes represented nothing less than a sexual differentiation in the generative nucleus. Associating the motile blepharoplast with male characteristics and the larger, passive nucleus with female ones, he claimed that the trypanosomes were unicellular hermaphrodites ("zwitterig"), incorporating both female and male characters in one organism.[20] This led him to suppose that these organisms might represent a primitive stage in the origin of sexuality.

In the concluding remarks to his 1905 paper, Schaudinn associated his views of cellular organization with evolutionary principles. Addressing the question of the origin of life from inorganic matter, he stated that the postulate of a "small, constantly dividing and growing drop of plasma" had no place in his theoretical conception. It was no more difficult to postulate an inherent dualism in the first living matter than to explain the development of complex organization from an originally undifferentiated protoplasm. But the former postulate offered a significant advantage over the latter: "With the assumption of a primary physiological dualism of the organic substance, we have gained a conception both of sexual dimorphism and of fertilization."[21]

19. Schaudinn, "Neuere Forschungen," p. 28. There was considerable discussion among protozoologists at this time about the relation of the nuclear to the kinetic apparatus. Most recognized a connection between the blepharoplast and the centrosome, thereby providing further reason to assume that the former represented a nuclear dualism. Unfortunately for advance in protozoological knowledge, according to John Corliss (personal communication), this was one of the few serious errors of observation/interpretation made by the otherwise brilliant Schaudinn: he mistook the larger DNA-rich kinetoplast (part of the mitochondrion in trypanosomes) for the true basal body in these organisms, an error not to be fully corrected until several decades later (and wrongly labeled in some textbooks still today). See also Wilson, *The Cell*, pp. 690—700.

20. Schaudinn, "Neuere Forschungen," pp. 29—31, in which the arguments represent, to the modern reader, a curious mixture of biological knowledge and contemporary social stereotypes. On an earlier hermaphroditic theory of infusoria, see Churchill, "The Guts of the Matter."

21. Schaudinn, "Neuere Forschungen," p. 34.

FURTHER ELABORATION OF THE BINUCLEARITY HYPOTHESIS

Schaudinn's binuclearity hypothesis, associated (and sometimes confused) with Hertwig's theory of chromidia and of a karyoplasmic ratio, was soon taken up by the protozoologists Max Hartmann and Stanislaus von Prowazek and by the zoologist Richard Goldschmidt.[22] It also soon attracted the attention of, among others, American, English, and French biologists. Only a few months after it appeared, for example, the prominent French protozoologist at the Pasteur Institute, Félix Mesnil, wrote that "one can scarcely open a cytological journal treating protozoology today without encountering the new expressions: chromidia, chromidial net, or chromidium."[23] He urged his colleagues, if they were to keep up with the new developments in this discipline, to familiarize themselves with these seminal ideas.

Hartmann and Prowazek attempted to extend Schaudinn's hypothesis to other protozoa. But they primarily concentrated on developing his second interpretation of binuclearity: the duality between a kinetic nucleus and a trophic nucleus. In a joint paper published the year after Schaudinn's death, for example, Hartmann and Prowazek surveyed organisms that displayed reproductive mechanisms similar to the karyokinesis of metazoa. They developed ideas concerning the origins of the blepharoplast, the karyosome (the chromosomes of protists), and the centrosome (which, following Schaudinn, they associated with the second nucleus of some protozoa).[24] In later years, Hartmann developed further

22. All three, it is interesting to note, had been students of Richard Hertwig in Munich. Prowazek (1875—1915) had studied at the universities of Prague and Vienna and worked at the zoology station in Trieste; after Schaudinn's death, he assumed the directorship of the Institute for Marine and Tropical Diseases in Hamburg (Jahn et al., *Geschichte der Biologie*, p. 718; see also Goldschmidt, *Golden Age*, pp. 138—142). Hartmann (1876—1962), after gaining his doctorate in 1901 under Hertwig in Munich, had been an assistant in Strassburg and in Giessen before joining the Institute for Infectious Diseases in Berlin in 1905; in 1914 he was called to direct the protozoology division of the new Kaiser Wilhelm Institute for Biology (Jahn et al., *Geschichte der Biologie*, pp. 675—676). Goldschmidt (1878—1958) was until 1914 first assistant to Hertwig, when he too joined the Kaiser Wilhelm Institute for Biology as director of the division for animal genetics (Jahn et al., *Geschichte der Biologie*, p. 670).

23. Félix Mesnil, "Chromidies et questions connexes," *Bull. Inst. Pasteur, 3* (1905), 313. Mesnil had studied under Alfred Giard at the École Polytechnique and presently worked in Elie Metchnikoff's department of the Pasteur Institute. In the early 1890s, he and his friend Maurice Caullery had worked in Hertwig's laboratory in Munich.

24. Max Hartmann and Stanislaus von Prowazek, "Blepharoplast, Caryosom

Schaudinn's ideas concerning the origin of sexuality. For his part, Goldschmidt took up the suggestion to explore the validity of these ideas in higher organisms and, synthesizing Schaudinn's views on binuclearity with those of Hertwig on the physiological function of chromidia, soon developed his own conception of the significance of chromidia and nuclear dimorphism for cell life.

GOLDSCHMIDT'S THEORY OF THE CHROMIDIAL APPARATUS

Goldschmidt was first introduced to Schaudinn's concept of binuclearity in 1903 when the two met and became friends while working at the zoological station in Rovigno. A former student of Hertwig in Munich and of Bütschli in Heidelberg (where he gained his doctorate), Goldschmidt had recently become Hertwig's assistant at the Zoology Institute. Interrupting his researches on nerve-cell development in the nematode *Ascaris* to look for chromidia in this simple animal, Goldschmidt was soon rewarded. In 1904 he published a preliminary report, and in 1905 a full report, in which he purported to have discovered chromidial bodies in those cells that were actively functioning: gland cells, egg cells in yolk formation, sperm cells, and intestinal epithelial cells.[25] These findings, he stated, had recently been complemented by several studies on egg-cell maturation carried out by his students. Like Hertwig, Goldschmidt suggested a primarily metabolic role for such chromidia: the nucleus of active metazoan cells emitted chromidia into the cytoplasm to carry out the cell's particular physiological activities.

In 1907, Goldschmidt and his student Methodi Popoff published a paper in which they developed a full-blown theory of the chromidia. Combining the evidence from protozoology with the recent data on metazoan cells, they attempted to unify all the disparate phenomena of nuclear division within the guise of a general principle. They compared, using both homology and analogy, the various cellular structures in protozoa with similar ones in metazoa. Using the umbrella concept of a "chromidial apparatus" (which encompassed Hertwig's simple chromidial

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und Centrosom: Ein Beitrag zur Lehre von der Doppelkernigkeit der Zelle," *Arch. Protist.*, *10* (1907), 306—335.

25. Richard Goldschmidt, "Die Chromidialapparat lebhaft funktionierender Gewebezellen," *Biol. Centralbl.*, *24* (1904), 241—251; and "Die Chromidialapparat lebhaft funktionierender Gewebezellen," *Zool. Jahrb.* (*Anat.*), *21* (1905), 41—140. For Goldschmidt's description of meeting Schaudinn in Rovigno, see *Golden Age*, p. 128.

granules, the chromidial net, and their own discovery of chromidial strands and rods), they equated such recently discovered cell organelles as mitochondria, Golgi bodies, the pseudochromosomes, the *Nebenkern*, the ergastoplasm, and the archoplasm — all currently the focus of considerable discussion by cytologists — with the chromidial apparatus, explaining away the apparent divergences in form among these cellular constituents as resulting from their being distinct stages in the development of the chromidial apparatus (see Fig. 2).[26]

In framing the theory of the chromidial apparatus, Goldschmidt stressed Hertwig's notion of a physiological differentiation between the chromidia and the chromidial net. He did not, however, focus upon the karyoplasmic ratio as the raison d'être for chromidial formations. Rather, like Schaudinn, he saw chromidia as illustrating a basic duality in the nuclear matter of the cell: one type responsible for metabolism (which he called trophochromatin) and one for reproduction (or propagatory chromatin). He interpreted the multifarious cytoplasmic structures as different manifestations of trophochromatin transformed through its particular role in the cell's vital processes — in short, as morphological structures associated with physiological activity.

Goldschmidt formalized his conception of the binuclearity of the nuclear chromatin, and its significance for the life of the cell, in the following three pronouncements in his 1905 paper:

> 1. Every animal cell has, according to its nature, a double nucleus: a somatic and a propagatory nucleus. The former directs the somatic functions, metabolism, and movement. . . . The propagatory nucleus contains, above all, the substance of heredity, and it also possesses the ability to produce a new metabolic nucleus.
>
> 2. The two kinds of nuclei are usually united into one

26. Richard Goldschmidt and Methodi Popoff, "Die Karyokinese der Protozoen und der Chromidialapparat der Protozoen- und Metazoenzelle," *Arch. Protist.*, *8* (1907), 306—335. See also Richard Goldschmidt, "Die Chromidien der Protozoen," *Arch. Protist.*, *5* (1905), 126—144. For discussions of various conceptions of protoplasmic structure in the early twentieth century, see Wilson, *The Cell*, pp. 25—57; Mikuláŝ Teich, "From 'Enchyme' to 'Cyto-Skeleton': The Development of Ideas on the Chemical Organization of Living Matter," in *Changing Perspectives in the History of Science: Essays in Honor of Joseph Needham*, ed. Mikuláŝ Teich and Robert Young (London: Heinemann, 1973), pp. 439—471, esp. p. 465; and Robert Olby, "Structural and Dynamic Explanations in the World of Neglected Dimensions," in *A History of Embryology*, ed. T. J. Horder, J. A. Witkowski, and C. C. Wylie (Cambridge: Cambridge University Press, 1985), pp. 275—308.

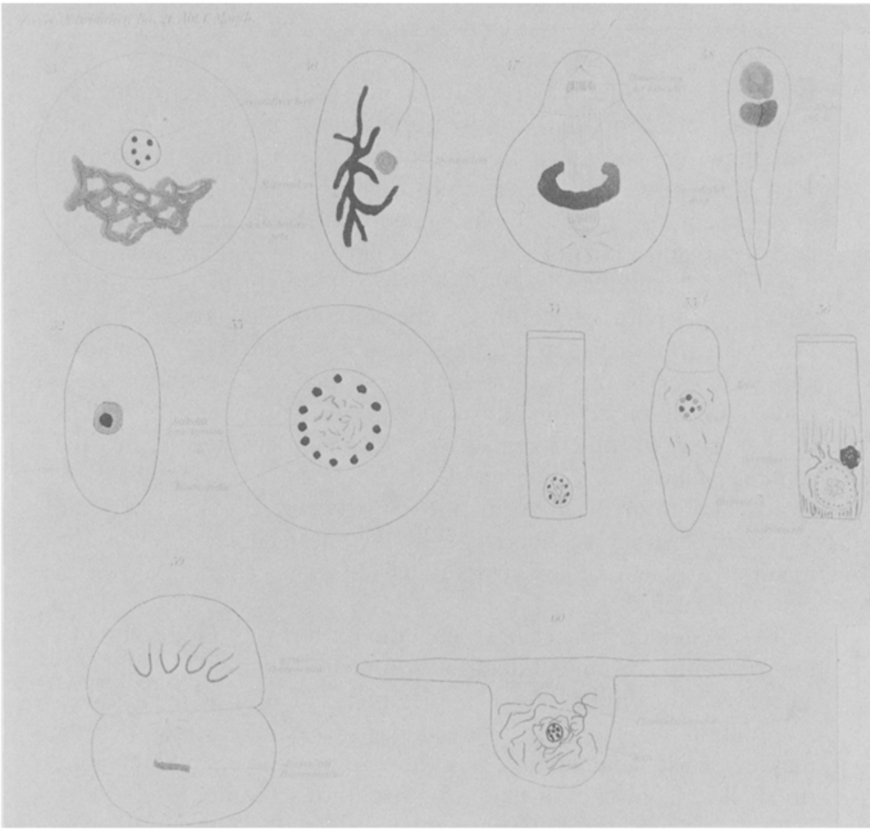

Fig. 2. Examples of chromidial formations in protozoan and metazoan cells. The three rows represent a series of forms: (1) complete separation of the two kinds of nuclear chromatin (vegetative and propagatory) in: rhizopods, infusoria, egg cell of *Dytiscus*, and sperm cell; (2) nuclei containing a mixture of both kinds of chromatin: trypanosome, egg cell before maturation, gland cell at rest, gregarine, and functioning gland cell; and (3) special cases in which the cells have only vegetative chromatin: diminution in *Ascaris*, and *Ascaris* muscle cell. (From Richard Goldschmidt, "Der Chromidialapparat lebhaft funktionierender Gewebezellen," *Zool. Jahrb.* (*Anat.*), *21* [1905], 124—125 and plate 8.)

nucleus, the amphinucleus. Separation can follow, to greater or less degree. A complete division seldom occurs; usually [there is] a division into a predominantly propagatory, yet still mixed, nucleus (the cell nucleus in the usual sense) and the main mass of the somatic nucleus (the chromidial apparatus).

3. The complete division of both types of nuclei may only be

present in a few cases, in connection with reproduction in protozoa or in oogenesis and spermatogenesis in metazoa.[27]

Whereas Schaudinn was primarily interested in the reproductive functions of chromidia, Goldschmidt was more concerned with analyzing the vegetative functions of the chromidial apparatus. That is not to say that he ignored the nucleus, but that it was the nuclear control of metabolism and development rather than nuclear organization per se that particularly captured his attention.

In the chromidial theory, Goldschmidt sought to unify all the seemingly disparate structures of the cell into one general conception, which he considered a basic law of cell life. His chromidial apparatus was a mechanism that could account for the nuclear control of cell physiology (through vegetative chromatin) as well as of heredity (through generative chromatin). Once again the seminal views of Weismann assisted in conceptualization: Goldschmidt borrowed his distinction between an idioplasm and a somatoplasm, but he applied it at the intracellular level as the material explanation for a functional division of labor known to exist in the cell.[28]

To contemporary critics, including Hertwig, Goldschmidt's theory of the chromidial apparatus appeared overly speculative.[29] There is no doubt that he seemingly disregarded Hertwig's admonition in "Die Protozoen und die Zelltheorie" to beware making overly facile homologies between protozoan and metazoan organelles. Goldschmidt ignored morphological criteria for establishing relationships between bodies (since the forms he compared were dissimilar), and yet he claimed a homology between chromidial structures of protozoan cells and organelles of metazoan cells without a proper experimental study of their supposed

27. Goldschmidt, "Die Chromidialapparat" (1905), pp. 119—120.

28. Goldschmidt and Schaudinn may well have been influenced by Weismann's further distinction between the germ plasm and the *nucleoplasm*, the general substance of heredity from which the germ plasm was derived. While only the sex cells contained germ plasm, according to Weismann's view all body cells contained nucleoplasm to direct various cytoplasmic processes and other developmental activities, such as regeneration, that required the inherited tendencies. It was the "definite and varied changes" arising in a cell's nucleoplasm through segmentation that accounted for cellular differentiation. See Weismann, "Continuity of the Germ-Plasm," p. 185.

29. Hertwig, "Ueber den Chromidialapparat." Like his brother Oscar, Richard Hertwig believed that the nuclear chromatin was uniform and that it was the particular cell environment that determined subsequent differentiation: "Somatochromatin is idiochromatin whose *Anlagen* are developed through activity" ("Ueber den Chromidialapparat," p. 16).

physiological identity. His major evidence for this claim came from cytological technique rather than from experiment: because the various chromidial elements stained similarly upon the application of nuclear dyes, he assumed that they derived from the nucleus; and because they ordinarily were more numerous in cells engaged in intense metabolic activity, he maintained that they played a physiological role in cells.

Yet the seemingly tenuous empirical grounding for Goldschmidt's ideas should not be judged too harshly: both Hertwig and Schaudinn had proposed theories with little experimental basis, as, of course, had Weismann before them. In the context of the present study, it appears that each was ultimately concerned with accounting for the evolution of multicellular organisms from unicellular ones, from which emerged a prerequisite and a common goal: to provide a generalized cell theory valid for protozoa and metazoa alike. Goldschmidt well expressed this aim in his 1905 paper, where he argued that all the various cytoplasmic structures of the cell should be conceived of as manifestations of one phenomenon:

> It appears to me that the moment has come to bring together many of these structures, in part also comparable to one another, under the same point of view, and I hope to be able to prove that we stand before a lawfulness of cell form [*Gesetzmässigkeit des Zellenbaus*] which is in agreement with all of our knowledge up to now of the cell. But by this [we] also come closer to understanding previously unexplained matters, and ultimately to bringing together the metazoan cell again with protozoa, which, according to the latest research, threatens to ridicule the old schema of the metazoan cell.[30]

THE IMPACT OF THE CHROMIDIAL THEORY

From a modern vantage point, the theory of the chromidial apparatus perhaps appears but an obscure and speculative episode in the history of biology. But in the context of the concerns of biologists in the first three decades of this century, the theory was indeed an important one. It engaged the attention of some of the leading protozoologists and cytologists of the time, and it was discussed in virtually all the major textbooks of the period. To give but a few leading examples, chromidia and the chromidial theory were discussed in the first general textbooks on protozoology,

30. Goldschmidt, "Die Chromidialapparat" (1905), pp. 89—90.

including Franz Doflein's *Lehrbuch der Protozoenkunde* (2nd ed., 1909) in Germany, Edward A. Minchin's *Introduction to the Study of Protozoa* (1912) in England, and Gary N. Calkins's *Protozoology* (1909) in the United States. Moreover, Goldschmidt's theory of the chromidial apparatus in metazoa sparked a lively debate in cytology that continued into the 1920s, as witnessed by the extensive discussion it warranted in E. B. Wilson's third edition of *The Cell in Development and Heredity* (1925) and in E. V. Cowdry's article in the classic cytological text, *General Cytology* (1924), which he edited.[31]

Not all of these authors were favorably disposed to the theory. Doflein, for one, accepted the presence of chromidia in certain protozoa but without endorsing the theoretical interpretation given to them. In general, however, the ideas were presented favorably and were introduced to an entire generation of biologists.[32]

By far the predominant work on the chromidial theory was that carried out in Munich under Hertwig and Goldschmidt. In addition to Methodi Popoff, Alexander Issakowitsch, Max Jörgensen, Julius Schaxel, Eugen Neresheimer, C. M. Wenyon, Rudolf Blankertz, Paul Buchner, and G. von Kemnitz treated the chromidial theory in their work. These researchers, studying both unicellular organisms and simple metazoa, were generally sympathetic to Goldschmidt's elaboration of the chromidial apparatus of metazoan cells, but it was Hertwig's association of chromidia with the karyoplasmic ratio that primarily interested them. Judging from the number of students working on this problem and the many publications they produced, there is no doubt that Hertwig's program, linking the concerns of protozoology with metazoan

31. See Franz Doflein, *Lehrbuch der Protozoenkunde*, 2nd ed. (Jena: Gustav Fischer, 1909); Minchin, *Introduction to the Study of the Protozoa*, chap. 6; Gary N. Calkins, *Protozoology* (New York and Philadelphia: Lea and Fiebiger, 1909), pp. 115—126; Wilson, *The Cell*, pp. 24—38, 700—704; and E. V. Cowdry, "Mitochondria, Golgi Apparatus, and Chromidial Substance," in *General Cytology*, ed. E. V. Cowdry (Chicago: University of Chicago Press, 1924), pp. 311—382.

32. This is well exemplified by a statement contained in a letter to Goldschmidt from the American cytogeneticist T. S. Painter, December 23, 1943: "I came into zoology via the protozoa route and in the days when it was still common to speak of tropho- and idiochromatin. I have never entirely forgotten these basic concepts and my thinking in cytology has been influenced by this early training. I read your 1904 article several years ago and I recognized then, as I do now, that what you and others like you were trying to explain was the dominant role played by the nucleus in cell physiology. Somehow you had to implement the relation in morphological terms. And in reading this paper one must keep in mind the setting and the interpretations given known facts as of that date" (Richard Goldschmidt Papers, Bancroft Library, University of California—Berkeley).

cytology, greatly contributed to the internationally renowned school that developed in the Munich Zoology Institute in the decade prior to the First World War.[33]

CRITICISM OF THE CHROMIDIAL THEORY: THE ATTACK ON GERMAN CELL THEORY

Hertwig's research program for protozoology, despite its appeal, was not immune to criticism. The theory that guided it soon came under attack by the British protozoologist Cecil Clifford Dobell. Prompted primarily by the profusion of papers claiming to verify the chromidial theory, Dobell published in 1909 a major rebuttal of this theory.[34] Ultimately, Dobell criticized German cell theory for fostering what he perceived to be an overly speculative tendency. The first substantial criticism of the chromidial hypothesis and of the concept of binuclearity on a theoretical as well as an empirical plane, Dobell's paper forced protozoologists to reconsider the basic assumptions underlying their work — including, ultimately, the very postulate of unicellularity.

Adam Sedgwick's Attack on Cell Theory

Dobell was a former student and close friend of the Cambridge embryologist Adam Sedgwick, himself an avid opponent of cell theory. Through his work on the early embryogenesis of *Peripatus*, Sedgwick had begun to be critical of the germ-layer theory, and of the biogenetic law on which it was based, in the 1880s. By the 1890s, he was convinced that cell theory itself, as it was currently formulated, did not actually describe the process of organismic growth during development. In 1894 he published a paper entitled "On the Inadequacy of the Cellular Theory of Development" in which he vigorously attacked cell theory, stating that it "blinds men's eyes" to the true relations of cell organization and of ontogeny.[35]

33. See the *Abhandlungen aus dem Zoologischen Institut zu München*, Zoology Institute Library, Munich. For descriptions of the Munich Zoology Institute under Hertwig's direction, see Goldschmidt, *Golden Age*, pp. 85—88, 95—105; Karl von Frisch, "Eröffnungsansprache," *Verhandl. deut. zool. Ges., 28* (1928), 15—20; and Hansjochem Autrum, "Die Geschichte der Zoologie in München," ibid., *57* (1963), 37—42.

34. Clifford Dobell, "Chromidia and the Binuclearity Hypothesis: A Review and a Criticism," *Quart. J. Micr. Sci., n.s. 53* (1908—09), 279—325.

35. Adam Sedgwick, "On the Inadequacy of the Cellular Theory of Development, and on the Early Development of Nerves, Particularly of the Third Nerve and of the Sympathetic in Elasmobranchii," *Quart. J. Micr. Sci., n.s. 37* (1895), 87—101. One year earlier, the American embryologist C. O. Whitman had

According to Sedgwick, cell theory postulated that nuclear divisions were accompanied by a division of the protoplasm into two parts, resulting in two distinct cells. Yet, he asserted, this type of nuclear division actually seldom occurred — more frequently, a "syncytial" mode of organization could be observed in metazoan cells, which he described elsewhere as nuclear division "accompanied by a rearrangement of the protoplasm around each nucleus, but not by its division into two separate masses."[36] Often numerous nuclei appeared without any "cellular" division in the surrounding protoplasm. In such cases there were, in other words, no unit "cells." Having called into question the existence of cells presumed by the current definition of cell theory, Sedgwick applied his views to a consideration of the protozoa. If noncellularity was actually a frequent mode in metazoan organization, the view that protozoa were unicellular organisms was also open to question.

Perhaps it is not surprising to find that Sedgwick's conception of the cell was closely related to his own particular understanding of the evolution of higher organisms. In a subsequent essay, responding to a critic of his views, Sedgwick explicitly addressed the implications his views had for evolution studies. Unicellularity rested, he believed, on an evolutionary argument that assumed that "organisms of Metazoa are aggregations or colonies of individuals called cells, and derived from a single primitive individual — the ovum — by successive cell divisions." This interpretation derived from recapitulation theory, which assumed that "the holoblastic cleavage of the ovum represents the process by which the ancestral Protozoon became multicellular, and the differentiation of the cells into groups the beginning of cellular differentiation."[37] Yet, according to Sedgwick, this view was no longer tenable; ontogeny did not, in fact, proceed in this fashion. Therefore the contem-

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expressed similar views in "The Inadequacy of the Cell-Theory of Development," *J. Morph.*, *8* (1893), pp. 639—658, a paper originally presented as an evening lecture at Woods Hole Marine Biological Laboratory and published in its *Biological Lectures* (1894).

36. Adam Sedgwick, "Embryology," *Encyclopedia Britannica*, 11th ed. (1910), 9: 314—331.

37. Adam Sedgwick, "Further Remarks on Cell Theory, with a Reply to Mr. Bourne," *Quart. J. Micr. Sci.*, *38* (1895—96), 331—337; esp. p. 332. Sedgwick was responding to a critique of his earlier paper by the Oxford zoologist (later Linacre Professor of Zoology) Gilbert C. Bourne in "A Criticism of the Cell-Theory; Being an Answer to Mr. Sedgwick's Article on the Inadequacy of the Cellular Theory of Development," ibid., pp. 137—174. Brief but informative discussions of this question can be found in Arthur Hughes, *A History of Cytology* (London and New York: Abelard-Schuman, 1959), pp. 138—144; and John R. Baker, "The Cell-Theory: A Restatement, History, and Critique. Part III," *Quart. J. Micr. Sci.*, *93* (1952), 157—190, esp. pp. 175—177.

porary view of phylogenetic history, and the cell theory arising from it, required revision.

Sedgwick offered such an alternative view of evolution. He held that "the differentiation of the Metazoa had been effected in a continuous multinucleated plasmatic mass, and that the cellular structure had arisen by the special arrangement of the nuclei in reference to the structural changes."[38] That is, multicellular organisms had not evolved from colonies of individual unicellular organisms; rather, they had originated from multinucleated protozoons whose parts had subsequently evolved specialized functions, gradually forming the various tissues and organs of metazoa. This view of the evolution of life, Sedgwick realized, had profound repercussions for protozoology. Protozoa could no longer be viewed as unicellular organisms — they were complex organisms-as-a-whole which should, therefore, be studied in their own right and not simply treated as adjuncts to a fundamentally false phylogenetic hypothesis that homologized them to the ovum.

Dobell's Criticism of the Chromidial Theory

Dobell fell strongly under the influence of his mentor and friend, Sedgwick, while at Cambridge. One of Britain's first biologists to specialize in protozoology, Dobell went to Germany in 1907, at Sedgwick's urging, to work with Hertwig. In Munich, he found himself in the midst of the current research into the chromidia of protozoa and metazoa, including the attendant discussion of Hertwig's karyoplasmic ratio, Schaudinn's notion of binuclearity, and Goldschmidt's theory of the chromidial apparatus. According to his biographers, commenting on his sojourn in Germany, Dobell was strongly repelled by "the speculative views and slapdash methods that he found current among the majority of protozoologists he met."[39] A year after returning to England, he responded to this experience by publishing "Chromidia and the Binuclearity Hypothesis: A Review and a Criticism."

The purpose of the paper, Dobell stated, was to summarize "the state of knowledge regarding the existence of chromidia and their probable function in the Protista (Protozoa and Bacteria) and Metazoa."[40] Dobell did not dispute the existence of chromidial bodies in some protists; indeed, he himself later described chro-

38. Sedgwick, "Further Remarks," p. 334.

39. Cecil A. Hoare and Doris L. MacKinnon, "Clifford Dobell, 1886—1949," *Obit. Not. Fell. Roy. Soc., 19* (1950), pp. 35—61, esp. p. 38.

40. Dobell, "Chromidia," p. 282.

midia in the primitive rhizopod *Arachnula* (see Fig. 3).[41] His own interpretation of the meaning of chromidial structures was that they exemplified a kind of reproductive specialization in protozoa, an efficient method of multiple division whereby "a larger brood of gametes can be eventually produced than by the sudden multiple division of a single nucleus." Such a conception meshed well with Sedgwick's belief that higher organisms had arisen through the differentiation of multinucleated protozoa. "Whatever theoretical value we may give to the chromatin itself," he wrote, "it cannot be denied that chromidia represent an intermediate stage in the simultaneous formation of a number of nuclei from a single nucleus."[42]

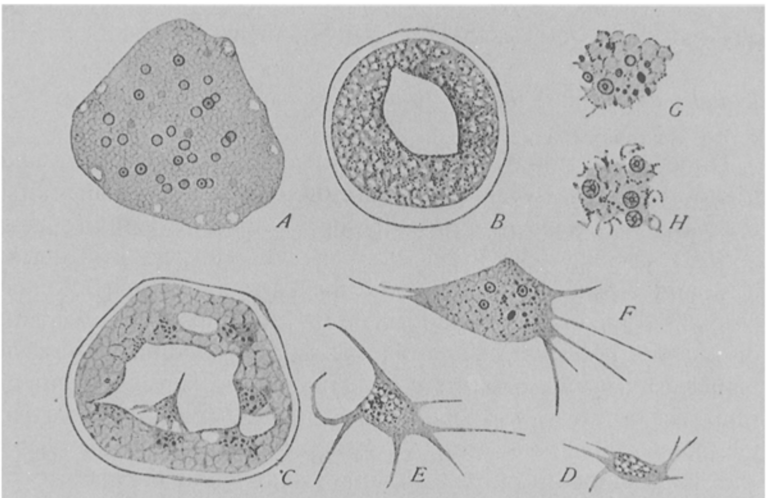

Fig. 343.—Chromidia and nuclei in the rhizopod *Arachnula* (Dobell) (from fixed and stained specimens).

A, Individual ready for encystment, with many nuclei, no chromidia; *B*, encysted individual with large vacuole, nuclei broken down into scattered chromidia; *C*, endogeneous formation of daughter-cells; *D*, *E*, young chromidial daughter-cells, recently escaped; *F*, older form with nuclei forming, *G*, detail from individual similar to last, stages in formation of vesicular nuclei form chromidia; *H*, detail from mature specimen, nuclei and chromidia.

Fig. 3. Chromidia in the rhizopod *Arachnula*, after Dobell. (From E. B. Wilson, *The Cell in Development and Heredity*, 3rd ed. [New York: Macmillan, 1925], p. 702.)

41. Clifford Dobell, "Observations on the Life-History of Cienkowsky's *Arachnula*," *Arch. Protist.*, *31* (1913), 317.

42. Dobell, "Chromidia," p. 305.

Dobell's major grievance, then, was not with chromidia per se but with the theory that had been based on them. He particularly opposed Schaudinn's binuclearity theory, of which Goldschmidt's theory of the chromidial apparatus was essentially only an elaboration. Although most recently and fully expressed by Schaudinn, this concept, he believed, was implicit in the earlier work of Otto Bütschli and of Richard Hertwig on the origin of the centrosome.[43] While Schaudinn had merely refurbished and embellished this idea, Goldschmidt, on the other hand, had altered Schaudinn's original conception by claiming that the presumed binuclearity further revealed a fundamental principle underlying cellular structure and functioning. The empirical basis for both theories, according to Dobell, was insufficient to support such a theoretical edifice, and he therefore dismissed them as overly speculative. His conclusion, after reviewing the current literature on the subject, was that "the facts relating to chromidia are not yet sufficiently strong to bear the weight of the binuclearity hypothesis which rests upon them: that, therefore, this binuclearity hypothesis, however suggestive it may be as a working hypothesis, is far from being a 'law,' as some would have it called: and that the tropho-kinetic binuclearity hypothesis is equally unworthy to rank as a cytological truth."[44]

Two years later, Dobell struck another, more direct, blow at German cell theory. Resurrecting Sedgwick's earlier argument, Dobell threw down the gauntlet to his colleagues in a paper in the *Archiv für Protistenkunde.* There he asserted:

> the evolution theory and the cell theory, formulated as they were in the middle of last century, have had a paralysing effect upon the study of the Protista. These theories have forced men to see the Protista from an entirely subjective point of view, and have prevented Protistology from throwing any light upon

43. Ibid., p. 312. Dobell refers to the lively discussion of the origin and function of the centrosome carried out in the 1890s. At this time cytologists were debating whether the centrosome was, along with the nucleus and cytoplasm, a primary component of the cell and the initiator of cell division. Otto Bütschli, Richard Hertwig, Theodor Boveri, and Schaudinn had proposed three different interpretations of the possible relationship between the centrosome and the nucleus: (1) the achromatinic theory (Hertwig), which postulated the cytoplasmic origin of the centrosome; (2) the nucleolo-centrosomic theory (Bütschli), which held that the centrosome originated in cytoplasm but was later incorporated into the nucleus; and (3) the nuclear theory (Boveri and Schaudinn), according to which the centrosome derived from the nucleus, thereby representing a kind of binuclearity.

44. Dobell, "Chromidia," p. 318.

> biological problems in general. So long as the Protista are "primitive unicellular organisms", so long will their biological significance remain unrecognised.[45]

He further declared that the conception of protists that dominated both specialist and general biological literature — namely, as "primitive, lower, simple, unicellular" organisms — greatly hindered progress in this field.

To illustrate how this perception pervaded the mentality of contemporary protozoologists and led to "absurd" conjectures, Dobell quoted a passage from Max Verworn's influential text on general physiology:

> The Protista seem to have been created by Nature for the physiologist, for, besides their great capacity of resistance, of all living things they have the invaluable advantage of standing nearest to the first and simplest forms of life; hence they show in the simplest and most primitive form many vital phenomena that by special adaptation have developed to complexity in the cells of the cell-community.[46]

Dobell adamantly opposed such a view, maintaining that the protists were not unicellular organisms; they were, rather, non-cellular. Harking back to Christian Gottfried Ehrenberg's conception, he stated that the protists were complete organisms, just as complex in their own right as metazoa and metaphyta. Therefore, they should be studied, not as adjuncts to cell theory or to evolution theory, but as autonomous life forms possessing an organization fundamentally different from that of metazoa.

Ultimately, it was contemporary cell theory itself that was faulty. The definition of a cell proposed in the 1860s by Max Schultze — "a cell is a mass of protoplasm containing a nucleus" — was, strictly speaking, not valid. Rather, a "correct definition" would also have to include: "the cell is a part of an organism and not a whole organism." However, Dobell's criticism of cell theory

45. Clifford Dobell, "The Principles of Protistology," *Arch. Protist.*, *23* (1911), 269—310; esp. p. 270.

46. Dobell, "Principles of Protistology," p. 301, citing, somewhat loosely, a passage from Max Verworn, *General Physiology*, trans. F. S. Lee, 2nd ed. (London: Macmillan, 1899), p. 51. Verworn was particularly vulnerable to incurring Dobell's wrath: his entire physiological program assumed that the protists, as the simplest manifestation of life, offered the most accessible means of investigating the question of cellular function, and that results gained from such studies could be directly applied to cells in higher organisms.

was more radical. The very basis of conceptualization of the cell required reformation, taking into account recent advances in both cytology and protozoology. "The cell," he wrote, "must be defined in terms of the organism, and not the organism in terms of the cell."[47] Taking a holistic stance, Dobell concluded that protists were not homologous with a single cell in a metazoan individual, as the unicellular theory would have it: they were homologous with an *entire* individual. In other words, protists were organisms-as-a-whole, not simply "cells."

Dobell next criticized the evolutionary assumptions upon which contemporary cell theory was based. Protists could not, as they had too often in the past, be used as models for research into the origin of life. On the one hand, they were just as far removed, in phylogenetic distance and in time, from the hypothetical unicellular progenitors of metazoa as were the so-called "higher" organisms (a label that he opposed); on the other, there was no *unicellular* precursor of metazoa. The "protozoa to man hypothesis," as he labeled this view, rested on the recapitulation theory, which supposed that "when the egg undergoes segmentation in ontogeny, it repeats the processes which occurred in phylogeny when the Metazoa arose from 'unicellular' ancestors." At the core of this argument was the assumption that both the egg and protists were analogous, and both cells. But this Dobell refuted:

> A metazoan egg undergoing segmentation is a non-cellular organism undergoing differentiation by forming cells. Before segmentation, the egg is a whole organism: after segmentation it is the same whole organism, but more differentiated. After segmentation, the organism is not a colony of individuals each of the same value as the original egg. A protozoon undergoing division, on the other hand, is one organism dividing into two: it is one whole organism becoming two whole organisms of the same value as the original whole organism. If segmentation were really analogous to the divisions of a protozoon, it would produce a cluster of eggs and not a differentiated organism. This is a fact which is so obvious, that it is quite surprising that the use of the word "cell" should have prevented it from being realized. There is no real analogy between an egg dividing into two blastomeres and a protist dividing into two protists.[48]

Few people would follow Dobell in believing that the metazoan

47. Dobell, "Principles of Protistology," pp. 284—285.
48. Ibid., pp. 302—303.

egg was not a cell, that it only gained a cellular status when it cleaved. Yet his view, shared with Sedgwick, that evolution had proceeded through the specialization of individual organelles within multinucleated protists rather than from an aggregation of individual protists, did gain adherents. Most generally, however, his arguments opposing both the recapitulation theory of evolution and the unicellular hypothesis of protists were taken up by other biologists who agreed with Dobell that "the theory of organic evolution will soon have to be recast."[49]

RESPONSE TO DOBELL'S CRITICISM

Dobell's attack on cell theory and on the unicellular concept of protozoa launched a debate within the biological community. In 1916, for example, the noted British protozoologist Edward A. Minchin published an article in the *American Naturalist* entitled "The Evolution of the Cell," in which he assumed that "amongst the Protista all stages of the evolution of the cell are to be found, from primitive forms in which the body can not be termed a cell without depriving the term 'cell' of all definable meaning, up to forms of complex structure in which all the characteristic features of a true cell are fully developed."[50] Minchin's position could not have been more opposed to that of Dobell.

In an appendix to his essay, entitled "The Cell-Theory," Minchin discussed Dobell's recent criticism. Singling out one aspect of Dobell's argument — his use of *homology* in comparing a protist individual with a metazoan individual — he virtually ignored Dobell's remaining points. Minchin did concede that "any Protist, as an organism physiologically complete in itself, is clearly analogous to the entire individual in the Metazoa — a comparison, however, which leaves the question of genetic homology quite untouched." But certainly in terms of genealogical ancestry, Minchin maintained, "a Protozoon is truly homologous with a single body-cell of a Metazoon."[51]

Yet Minchin considered this type of reasoning rather abstruse.

49. Ibid., p. 297. For a more recent discussion of precisely these same issues, see John R. Baker, "The Status of the Protozoa," *Nature, 161* (1948), 548—551, 587—589.

50. Edward A. Minchin, "The Evolution of the Cell," *Amer. Nat., 50* (1916), 5—38; 106—118; 271—283; esp. p. 281. Minchin, a graduate of the Department of Zoology at Oxford and Jodrell Professor of Zoology of the University of London, was at the Lister Institute of Preventive Medicine, Chelsea. He had spent a year in Germany in the early 1890s working with Hertwig and also with Butschli.

51. Ibid., p. 282.

What was more important was the great similarity — both in nuclear organization and in the processes of nuclear and cell division — between protists and metazoa. Like Hertwig and other German biologists, he believed that this illustrated a basic continuity in their cellular structure:

> Thus in the Protozoa we find the protoplasmic body differentiated into nucleus and cytoplasm; the nucleus in many cases with a structure comparable in every detail to that of the nucleus of an ordinary body-cell in the Metazoa; reproduction taking place by division of the body after a karyokinetic nuclear division often quite as complicated as that seen in the cells of the Metazoa and entirely similar both in method and in detail; and in the sexual process of differentiation of the gametes on lines precisely similar to those universal in Metazoa, often just as pronounced, and preceded also in a great many cases by phenomena of chromatin-reduction comparable in principle, and even sometimes in detail, with the reduction-process occurring in Metazoa.[52]

An avowed "chromatinist" (that is, favoring the chromatin rather than the cytoplasm as the critical aspect of cell organization), Minchin believed that because the process of karyokinetic nuclear division in protozoa was in general comparable to that in metazoa, their genetic relationship was established.[53] Dobell, on the other hand, strongly disputed this. He always maintained that organization in protozoa was distinct from that found in metazoa. In his 1924 study of the coccidian *Aggregata*, for example, Dobell declared that "the chromosome cycle of *Aggregata* is not the same as that of a metazoon, with trifling variations in detail, but radically different."[54] In other words, diverging evolution between protista

52. Ibid., p. 281.

53. Minchin believed, for example, that the substance of the chromatin was "to be regarded as the primitive constituent of the earliest forms of living organisms, the cytoplasmic substance being a later structural complication" (ibid., p. 28). By contrast, Hertwig was a *cytoplasmist.* Although readily acknowledging the importance of the nucleus for cell life, he maintained that "this in no way shakes the old statement that the protoplasm is the bearer of the functions of life" (Hertwig, "Die Protozoen," p. 34). This distinction deserves further historical study.

54. Clifford Dobell, "The Life-History and Chromosome Cycle of *Aggregata eberthi* [Protozoa: Sporozoa: Coccidia]," *Parasitology, 17* (1925), 1—136; esp. p. 121 n. 2. The views Dobell expressed in 1911 continued to surface in his later work; in the sporozoa study, for example, he described *Aggregata* as "a non-cellular organism possessing a nuclear system, and not as a cell containing a nucleus" (ibid., p. 111).

and multicellular organisms meant that there were no generally recurring principles throughout the two kingdoms.

It is seemingly ironic that Goldschmidt later accepted the validity of Dobell's claim of the noncellularity of protozoa. In his book on sex determination, published in Germany in 1920 and translated into English in 1923, Goldschmidt stated: "The Protozoan is neither morphologically nor physiologically comparable with any cell of a Metazoan; it is comparable to the whole organism."[55] This analogy helped him to take a stand in the current discussion of immortality in protozoa. Goldschmidt compared a protozoon with a metazoon, assuming that as a "whole organism" a protozoon would exhibit a differentiation between somatic elements and reproductive structures similar to that in metazoa. Since the structures in protozoa that he analogized to the body cells of metazoa did pass away, he believed protozoa were also mortal. It is obvious, however, that Goldschmidt, in adopting the noncellularity of protozoa, abandoned neither his belief in binuclearity nor his implicit view of protozoa as the precursors of metazoa. He did eventually give up his theory of the chromidial apparatus — and yet, in many respects, Goldschmidt's later work in developmental genetics exemplifies a conceptualization of the nuclear control of cell functions similar to that expressed in his theory of the chromidial apparatus.[56]

One biologist who fully agreed with Dobell's criticism was D'Arcy Wentworth Thompson, also a graduate of the Cambridge school of embryology and a close friend of both Sedgwick and Dobell. In the first edition of his influential book *Growth and Form* (1917), Thompson criticized the chromidial theory of the "extreme cytologists of the Munich school."[57] Stating that "physio-

55. Richard Goldschmidt, *The Mechanism and Physiology of Sex Determination*, trans. William J. Dakin (London: Methuen, 1923), p. 17.

56. See Marsha L. Richmond, "Richard Goldschmidt and Sex Determination: The Growth of German Genetics, 1900—1935," Ph.D. diss., Indiana University, 1986, chap. 4.

57. D'Arcy Wentworth Thompson, *Growth and Form* (Cambridge: Cambridge University Press, 1917), p. 286. In his obituary of D'Arcy Thompson, Dobell discussed the relationship between Sedgwick, Thompson, and himself: "Sedgwick was my tutor at Trinity, my father in zoology, and my best friend until the day of his death. He was also a lifelong friend of D'Arcy Thompson, to whom he introduced me while I was still an undergraduate — saying, I remember, that he was a member of our College and '*a man well worth knowing.*' *How plain and true — like everything else that Sedgwick ever said or wrote*" (C. Clifford Dobell, "D'Arcy Wentworth Thompson, 1860—1948," *Obit. Not. Fell. Roy. Soc., 6* [1949], 599—617, esp. p. 603; emphasis in the original).

logical science has been heavily burdened in this matter, with a jargon of names and a thick cloud of hypotheses," Thompson outlined his opposition to all such morphological theories. His own view of the cell stressed physical forces and chemical reactions as dominating cellular phenomena. In this particular case, Thompson ascribed chromidial formations to

> the gathering or "clumping" together, under surface tension, of various constituents of the heterogeneous cell-content, and to the drawing out of these little clumps along the axis of the cell towards one or other of its extremities, in relation to osmotic currents, as these in turn are set up in direct relation to the phenomena of surface energy and of adsorption. And all this implies that the study of these minute structures, if it teach us nothing else, at least surely and certainly reveals to us the presence of a definite "field of force," and a dynamical polarity within the cell.[58]

Thompson's eschewal of the tendency among German cell theorists to ascribe primacy to morphological structures rather than to physicochemical mechanisms — to form rather than to function — was a criticism shared by other biologists in the early years of this century. E. S. Russell, for example — another Cambridge-educated biologist — expressed similar sentiments in his classic work, *Form and Function* (1916).[59] Dobell's criticism, then, should not be viewed as an isolated rebellion against the predominant paradigm in protozoology. It indicates a deeper and growing dissatisfaction with a cell theory founded upon a particular evolutionary conception that was beginning to be seen as faulty. And this, in turn, had profound repercussions for all the many biological disciplines whose own programs were implicitly as well as explicitly linked to the recapitulation theory of evolution, protozoology included.

58. Thompson, *Growth and Form*, pp. 286—287.

59. E. S. Russell, *Form and Function. A Contribution to the History of Animal Morphology* (London: John Murray, 1916). The most extensive treatment of the Cambridge school of embryology is that by Mark Ridley, "Embryology and Classical Zoology in Great Britain," in Horder et al., *History of Embryology* (above, n. 26), pp. 35—67. Ridley implies that the decline of embryology at Cambridge after the death of Frank M. Balfour in 1882 was in some measure a result of Sedgwick's abandonment of Balfour's recapitulationist program. One might argue, however, that the critique of recapitulation by Sedgwick and his students was an important contribution to both embryology and general biology.

CRITICISM OF THE BIOGENETIC LAW AND ITS IMPACT ON PROTOZOOLOGY

The demise of the theory of the chromidial apparatus eventually came through "morphological" cytology and through biochemical studies of the cell, which indicated that the various cell organelles, such as mitochondria and the Golgi bodies, should not be seen as elements of one system but rather as having independent functions in cell life.[60] But such research could not resolve the debate over the hypothesized unicellularity of protozoa, upon which this theory had been built. Unable to be decided through empirical means, the question of the unicellular versus "acellular" status of the protists continues to be discussed to the present day. John Corliss, for example, protozoologist and historian of his discipline, reviewed Dobell's arguments in recent years and concluded: "Dobell deserves credit for focusing fresh attention on the fundamental truth of Ehrenberg's idea: in general a *single* protozoon is as capable of independent locomotion, feeding, growth, reproduction, regeneration, and so on, as is any *entire* metazoan organism."[61] In general, modern protistologists treat protists as organisms-as-a-whole, while occasionally applying a unicellular definition when it seems useful. Such a vacillation indicates that in many respects this issue is no longer of great importance, the reason perhaps being that the evolution theory that implicitly spawned the turn-of-the-century debate has long since ceased to guide biology. When the biogenetic law began to be revealed as untenable, the necessity for the unicellular view of protozoa collapsed as well.

German recapitulation theory had regarded the organism as a historical being and held that the earliest stages of ontogeny revealed the evolutionary history of life itself. Problems of embryology and, indirectly, of morphology were linked together into one grand scheme. Heredity and development were but different stages of the same process. Embryology showed that metazoa developed from a fertilized ovum that cleaved into two cells, these again dividing and eventually forming the ball-like blastula, which subsequently invaginated to form the future gut-cavity of the organism. Indeed, the germ-layer doctrine of embryology rested upon these facts. According to the recapitulation theory of evolution, embryology revealed the historical sequence

60. Wilson, *The Cell*, pp. 700—717.

61. John O. Corliss, "Concerning the 'Cellularity' or Acellularity of the Protozoa," *Science, 125* (1957), 988—989.

of phylogeny: metazoa had likewise derived from unicellular ciliated protozoa united into a blastula-like colony. But when embryological studies began to call this evolutionary scheme into question, the concept of protozoa as single-celled organisms, and cell theory itself, began to be scrutinized.

Sedgwick, for example, was a leading critic of the germ-layer theory in embryology. He and many of his students clearly saw the implications his arguments had for protozoology. If one did away with Haeckel's hypothesized gastrula, his monera concept of protozoa went as well.[62] E. S. Russell, in fact, viewed the "criticism of the concepts or prejudices of evolutionary morphology" as one of the major developments in biology in the last decade of the nineteenth century. After discussing, in *Form and Function*, the experimental study of form (the cytological study of heredity coupled with Mendelism), he continued: "More significant is the revolt against the cell-theory started by Sedgwick and Whitman, on the ground that the organism is something more than an aggregation of discrete, self-centred cells."[63] Sedgwick recognized no cell territories, only nuclei and surrounding protoplasm. Hence, multinucleated protozoa were the precursors of metazoa, not colonial single-celled organisms. Dobell concurred with this view and reintroduced it at a critical point in the development of protozoology in the first decades of the twentieth century.

CONCLUSION

With historical hindsight, it can be little questioned that the view of protozoa as unicellular organisms was important for the development of the discipline of protozoology. In the early years of this century, the assumption of unicellularity provided a sound justification for the study of protists: it linked them to the metazoa and supported the claim that the study of these "simple" unicellular organisms could shed light on the organization of the metazoan cell. This prospect was significant, given the state of cytology circa 1910. In the wake of the major gains made in understanding nuclear division in the last two decades of the nineteenth century, cytology was suddenly confronted with many, seemingly less penetrable, problems. Several aspects of nuclear

62. This was clearly stated, for example, by E. W. Macbride in "Sedgwick's Theory of the Embryonic Phase of Ontogeny as an Aid to Phylogenetic Theory," *Quart. J. Micr. Sci., 37* (1895), 325—342. Macbride had been a student of Sedgwick at Cambridge but later broke with him and advanced neo-Lamarckian ideas of evolution (see Ridley, "Embryology," p. 47).

63. Russell, *Form and Function*, p. 346.

organization still remained unexplained, and recent research had revealed the presence in the cytoplasm of structures whose functions in cell life were unknown. Classical methods of cytology, relying on descriptive, morphological analysis, seemed ill equipped to resolve these questions.

Hertwig's program for protozoology, grounded in the assumption of the fundamental unity of organization in protozoa and metazoa, offered a potential means for investigating these and other problems of cell theory. Linked to mainstream cytology, protozoology was advocated as a means of experimentally investigating key biological processes — reproduction, metabolism, and organelle morphology and physiology — less accessible in higher organisms. Protozoa were hailed as prime experimental organisms, in which cell structure and function could be more easily studied. Unlike the metazoan cell, they could be subjected to controlled experiments in which the external environment was modified and the effects monitored. Protozoa offered, in other words, a promising experimental means by which to investigate the cell — its structures and its processes.

The success of this program within Germany was soon apparent. In contrast to the rather neglected state of the discipline in 1900, protozoology began to be recognized as more than a somewhat obscure area of study for specialists. In practical terms, this translated into greater numbers of students attracted to the field, increased institutional support for the discipline, and its elevation in status within the biological sciences as new developments, particularly in connection with medical applications, began to draw attention to the field.[64]

The unicellular hypothesis also promoted the internal development of the science. It provided a rationale for introducing the various techniques used in cytology, embryology, physiology, and the new field of biochemistry as suitable research tools for

64. One of the best illustrations of this point comes from the preparatory discussions for the new Kaiser Wilhelm Institute for Biology, established in Berlin-Dahlem in 1914. Virtually all of Germany's major biologists who were solicited favored protozoology as one of the four areas to be included in the institute. It was included, in addition to genetics (*Vererbungslehre*) and embryology (*Entwicklungslehre*), in Theodor Boveri's initial proposal to the Kaiser-Wilhelm-Gesellschaft. (See the documents in the dossier "Vorbereitung der Gründung biologischer und medizinischer Institut," 1222, in the Bibliothek und Archiv zur Geschichte der Max-Planck-Gesellschaft, Berlin-Dahlem.) One should not, however, unduly stress the intellectual rationale underlying the support for the discipline at this time. Certainly the potential practical advantages to be gained from this field, as the recent progress in identifying the malarial vector well illustrated, enhanced its chances for funding in colonial nations.

protozoology as well. This vastly extended the research possibilities and facilitated the understanding of, among other things, protozoan organization, modes of reproduction, and evolutionary relationships. The new experimental grounding of the discipline in turn fitted in well with developments in biology at large: in contrast to the descriptive methodology that had predominated in the nineteenth century, this new experimental program placed protozoology at the forefront of the early twentieth-century movement to make biology an experimental science comparable to physics and chemistry.

Yet the criticism of the unicellular hypothesis can also be seen as having served a valuable function within the development of the discipline. It focused attention on the study of protists as organisms in their own right, not simply as models for metazoan cells. More generally, it helped to remind biologists of the particular evolutionary assumptions that supported this conception. Dobell and other British critics pointed out, among other things, the association between the theory of recapitulation and the interpretation of protozoa as unicellular organisms. At the time when the recapitulation theory and the germ-layer doctrine were in decline, it was important to stress how these evolutionary ideas also entered into the contemporary concepts of subsidiary specialties. This was as true for protozoology as it was for cell theory itself. The chromidial theory, in its various guises, and the binuclearity hypothesis did in fact contain elements of recapitulationist reasoning, and they were open to criticism for the same kind of overly speculative theorizing that characterized this evolution theory. Dobell's critique forced protozoologists and cell theorists alike to review the theoretical postulates guiding their investigations.

In the absence of further historical studies, it is hard to evaluate the consequences of this debate in later years. The issue was not whether protozoa were the precursors of metazoa — both sides accepted this. They disagreed over which particular protozoon had served as the ancestral form, and this, in turn, influenced their stance on the question of unicellularity. The situation is little changed today. Because the former question is still an open one, the latter remains so too. Both of the models for the origin of multicellular organisms — colonies of ciliates versus multinucleate protists — are still presented as possible mechanisms in modern textbooks of evolution. Unable to judge the dispute in terms of the ultimate validity of the competing conceptions, the historian requires other criteria. It perhaps becomes more important to evaluate the issues in the context of the internal and external stimulus they provided the discipline.[65] In these terms, and from the present historical vantage point, Hertwig's research program for protozoology, based upon the unicellular hypothesis, appears to have been a successful one.

65. In my analysis of this controversy, involving both different research schools and differing interpretations among members of the same school, I have benefitted from the approach outlined by Gerald L. Geison in "Scientific Change, Emerging Specialities, and Research Schools," *Hist. Sci., 19* (1981), 20—40. In addition, Harry M. Collins has offered a promising sociological perspective on how to interpret the kinds of controversies represented in the debate over the chromidial theory. See H. M. Collins, "The Place of the 'Core-Set' in Modern Science: Social Contingency with Methodological Propriety in Science," *Hist. Sci., 19* (1981), 6—19.