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Mini-Review Article

Cell versus protoplasm: revisionist history

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Abstract

Recent investigations give reason to question anew the historical status of the 'cell theory' as the ultimate driving force in the development of our understanding of life's processes at the most fundamental level. A revisitation of critical research papers and commentaries from the 19th Century shows that the disregarded (and historically maligned) 'protoplasmic theory of life' played a more deterministic role in the early advancement of knowledge on cell structure and function.

Keywords: cell theory; E.B. Wilson; protoplasmic theory; T.H. Huxley

1. The case for protoplasm

The cell is the fundamental structural and functional unit in living beings. Textbooks tell us that this iconic (and nowadays trite) perception of the cell became instituted in the science of biology with the advent of the 'cell theory.' A tenet with a storied past (Harris, 1999), the cell theory's origin is commonly assigned to the work of Schleiden and Schwann in the 1830s. Some spectators of 19th Century science go so far as to place this idea on equal footing to the Darwin–Wallace theory of evolution. Mazzarello's lucid historical perspective, 'A Unifying Concept: The History of Cell Theory' (Mazzarello, 1999) proffers the traditional view, that 'Cell theory stimulated a reductionistic approach to biological problems.... It emphasized the concept of the unity of life and brought about the concept of organisms as 'republics of living elementary units'. The importance of this notion notwithstanding, one might ask what historical role did the emergence of the cell theory actually play in promoting the growth of cell biology and, ultimately, in the advancement of our understanding of life's basic processes at all levels of organization?

A recent communication by Kutschera (2011) evoked an inkling of disbelief in the primacy of cell theory in the annals of biology, hinting that *protoplasm* was a more critical focal point. It has been argued elsewhere (Welch and Clegg, 2010) that the illustrious (though long-forgotten) 'protoplasmic theory of life' played a much more deterministic role in the study of cell structure and function. Far from being instantly embraced, the newborn cell theory was attacked widely, as a superficial perspective that dwelled on the mere housing of life's basic processes. The term 'protoplasm' came to the fore in the 1840s, as an expression for the 'living substance' in cells. In 1850, the botanist Ferdinand Cohn is credited with framing the all-encompassing attitude that 'plants and animals are analogous not only because of their construction from cells, but also – at a more fundamental level – by virtue of a common substance, protoplasm, filling the cavities of those cells' (Geison, 1969). The protoplasmic theory postulated that the physical basis of life (including the foundation of heredity) must be sought in the properties of this universal biological material.

The advocates of the protoplasm viewpoint were plentiful and vociferous – including the likes of the distinguished physiologist, Claude Bernard (1878) (who touted protoplasm as a model for the study of life at all levels), and the founding neuroscientist and later Nobel laureate, Santiago Ramón y Cajal (whose first scientific publication, as a young postdoc in 1880, was titled 'El protoplasma,' published in the Zaragozan journal *La Clínica. Semanario de Medicina, Cirugía y Farmacia*–see Iturbe et al., 2008). Perhaps most noteworthy were Thomas H. Huxley – 'Darwin's bulldog' in Great Britain and Ernst Haeckel – 'Darwin's bulldog' in Germany. On 8 November 1868, Huxley gave a much-heralded public lecture in Edinburgh, entitled 'On the Physical Basis of Life' (published in 1869 in the popular journal *The Fortnightly Review*), which literally made 'protoplasm' a household word and which drew the attention of scientists and non-scientists alike to the role of protoplasm as the 'locus of life' (Welch, 1995). For summary discussion on the thought at the time, see Drysdale (1874) and M'Kendrick (1888).

The protoplasmic theory engendered 'the final repudiation of the tradition comparing living units to utricles, sacks, boxes, bubbles, or any other sort of envelope or container' (Hall, 1969). Protoplasm, as a material form and as a philosophical principle, became the symbol of the functionality of life at the most basic level. As the movement gained momentum, some biologists even argued that the term 'cell' should be dropped, that 'the advance demanded a change in nomenclature, for a cell is a box and lump of protoplasm is not' (Baker, 1952).

An article in 1861 by the prominent anatomist Max Schultze, entitled 'Über Muskelkörperchen und dass was Man eine Zelle zu nennen habe' (investigating the properties of muscle syncytium, appearing in *Archiv für Anatomie, Physiologie und wissenschaftliche Medicin*), was a veritable milestone. As expounded by Geison (1969), ''The publication of this paper, more than any other single event, marked the birth of the protoplasmic theory of life. On physiological rather than structural grounds, Schultze demonstrated that a single substance, called protoplasm, was the substratum of vital activity in the tissues of all living organisms, however, simple or complex.'' More emphatically, Nordenskiöld's early 20th Century historical exposition (Nordenskiöld, 1928) avowed that Schultze's work ''laid the foundations on which cell research has since been built, and this marks a new era in the science of cytology.''

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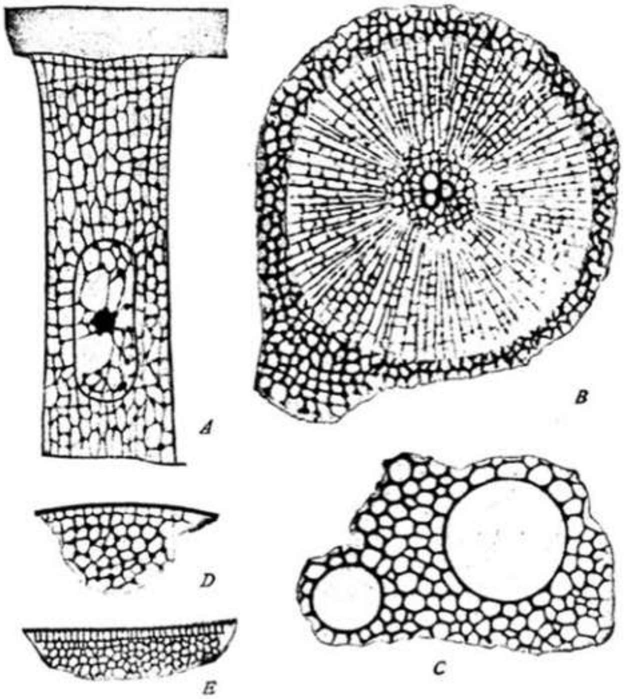

Figure 1 Late 19th century alveolar/foam model of protoplasm, according to Bütschli (1894)
Sketches of various cell types from light microscopy, in comparison to an artificial foam emulsion (from Wilson, 1900).

The protoplasmic theory generated widespread research into the properties of the cell in the latter part of the 19th Century. Initially, protoplasm was pictured as ''a diaphanous semi-liquid, viscous mass, extensible but not elastic, homogenous – that is to say, without structure, without visible organisation, having in it numerous granules, and endowed with irritability and contractility'' (M'Kendrick, 1888). As light microscopy and cytochemical staining techniques steadily improved during the late 1800s, abundant internal cellular structure became evident. Three working models for the protoplasmic make-up emerged: reticular/fibrillar, foam/alveolar and microsomal/granular (Bütschli, 1894; Seifriz, 1936; Hall, 1969) (Figure 1).

The delineation of parts of the protoplasm as 'living' relied on analysis by 'vital staining' – an empirical term that remained in the language of experimental cell biology well into the 20th Century. Visibly active portions of protoplasm were designated by a variety of spin-off names bearing the suffix *-plasm*. 'Ergastoplasm,' for example, was the term applied to what would later be identified as the 'endoplasmic reticulum.' Such idioms as 'cytoplasm' and 'nucleoplasm' in the parlance of modern-day cell biology are vestiges of that era. Investigation of the nature of protoplasm, in conjunction with advances in such fields as colloidal chemistry, spawned enduring interest in the character of the aqueous state *in vivo* (Bütschli, 1894; Heilbrunn, 1928; Gortner, 1930; Seifriz, 1936; Frey-Wyssling, 1948). The debates on the essence of cell water that unfolded later in the 20th Century stand as the legacy of these early studies (Clegg, 1984; Chaplin, 2006).

Biologists of the late 19th Century were not content simply with the assignment of the 'locus of life' to the solid or fluid 'plasms' of the cell. The science of biology, like physics at the time, was heading inexorably towards an atomistic foundation. A wave of molecular protoplasmic theories ensued, as the physical basis of life was pondered as a conglomeration of 'living particles' going by such names as 'biogens,' 'gemmules,' 'idiosomes,' 'plasomes,' 'pangens,' inter alia (Hall, 1969). Early in the 20th Century, with the (re)discovery of Gregor Mendel's work and the birth of modern genetics, the atomistic focus in biology shifted predominantly to the 'germ-plasm'; and the panoply of protoplasmic 'particles' was swept away and replaced with a new unit: the *gene*.

By the end of the 19th Century, espousal of the physiological idea of 'living molecules' was gradually straining the limits of credibility of the protoplasmic theory in scientific circles, with charges of 'abstraction' and 'obscurantism'–and even vitalism – coming from those in the physical sciences (Welch, 1995). Moreover, the protoplasm idea (under such sobriquets as 'Urschleim') had been extended beyond the confines of cell structure and function, becoming associated with such controversial topics as primordial life, spontaneous generation and ontogeny. The new sciences of biochemistry and enzymology, building on a solid base of *in vitro* physical chemistry, were yielding insights into the processes at play in the cell. The pioneering biochemist Frederick Gowland Hopkins was a leading turn-of-the-century critic of what he saw as the ''vague notion of a protoplasmic complex within which occurred pseudo-chemical events, mysterious and undecipherable'' (Stephenson, 1949). Usage of the term 'protoplasm' itself began to decline in the early 20th Century, due not only to its vitalistic baggage, but, more significantly, to the increasingly reductionistic focus on the intricacies of cellular (nay protoplasmic) composition.

Looking backward 100 years or so ago with a diachronic historiographic eye, one can perhaps grasp why it was that the cell theory, not the protoplasmic theory, survived the ideological melting pot of the 19th Century. The cell – albeit simply the 'housing' of life's basic physical, chemical, and genetic processes – was a concrete and easily identifiable physical entity, readily visible with light microscopy, and common to all living beings. At the time, the 'cell' proved to be a more objectifiable (and safer) philosophical construct than 'protoplasm,' with the ambiguities in defining the 'living substance' and the attendance to such holistic queries as 'What is life?' related to the latter concept. Most certainly, the cell biologists of the day recognized that much of the cellular operation was a 'black box,' but there was great faith that advances in physicochemical analysis would eventually clarify the picture. Today, it goes without saying that we know far more about the structure and function of cells than a century ago, but there remain tantalizing questions regarding the ultimate submicroscopic form of cellular ultrastructure that harken back to the time of the protoplasmic theory (Welch and Clegg, 2010).

2. E. B. Wilson's vision

To commemorate the dawn of the new millennium in 2000, Heilbron and Bynum (2000) presented a panoramic 'Millennial Highlights' synopsis of the history of science. Citing the authority of the eminent biologist E. B. Wilson, these authors chronicled that, in 1900 ''the cell was positioned squarely at the centre of development, heredity, function and much else besides.'' A

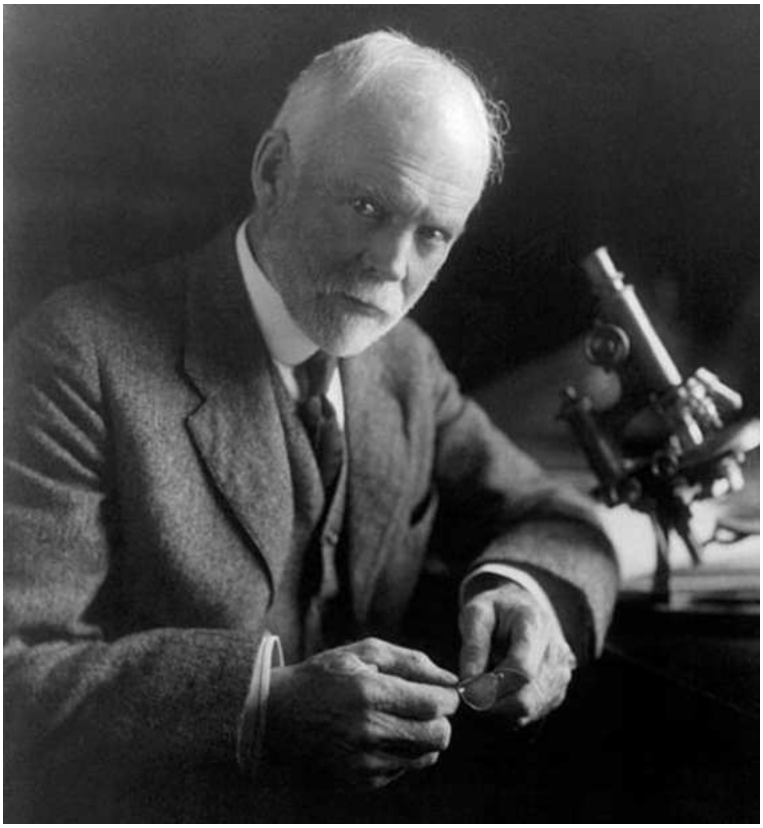

Figure 2 E.B. Wilson (1856–1939) (courtesy of The Marine Biological Laboratory Archives, Woods Hole, MA, U.S.A.)

legendary and farsighted scientist, Wilson has been hailed as 'America's first cell biologist' (Figure 2). His monumental text 'The Cell in Development and Heredity' went through three editions (Wilson, 1896, 1900, 1925), growing to 1000+ pages in length, and is considered by many as the single most influential treatise on the history of cell biology in the 20th Century. Wilson resolved the various views of protoplasmic structure from the late 19th Century with the new empirical realities of the field of cytology and prominently set the stage for the analysis of cell structure and function into the future. Each year, the American Society for Cell Biology recognizes a lifetime of achievement in cell biology by the presentation of its scientific highest honour, the E. B. Wilson Medal. It is, indeed, fitting that Wilson should be singled out historically in establishing how we think about the cell today.

Wilson's magnum opus 'The Cell in Development and Heredity' is, to be sure, a sweeping validation of the cell theory. Yet, in the opening pages, one finds the assertion that, ''It should from the outset be clearly recognized that the term 'cell' is a biological misnomer; for cells only rarely assume the form implied by the word of hollow chambers surrounded by solid walls. The term is merely an historical survival of a word casually employed by the botanists of the seventeenth century to designate the cells of certain plant-tissues, which give somewhat the appearance of a honeycomb…. Yet the word has become so firmly established that every effort to replace it by a better has failed, and it probably must be accepted as part of the established nomenclature of science'' (Wilson 1900). More specifically, the author maintains that, ''Essentially the cell is a minute mass of *protoplasm*… happily characterized by Huxley as the 'physical basis of life', and at the present time universally recognized as the immediate substratum of all vital activity.'' Wilson, from the start, directs the reader to protoplasm as the operational center of attention.

Wilson paid a more pointed tribute to Huxley in the First Sedgwick Memorial Lecture in 1922 in Boston, delivering a talk reminiscently entitled 'The Physical Basis of Life' (Wilson, 1923) – dedicated to his 'cherished friend,' William Thompson Sedgwick, whose ''lifelong habit was to think of the phenomena of life in terms of the activities of protoplasm.'' Wilson tells us how, as undergraduate students at Yale University, he and Sedgwick ''fell under the spell'' of Huxley's 1869 article; and he muses that ''the problems of protoplasm still hold us fast with a gripping interest that has lost nothing of its force with the flight of time,'' with the task at hand that of ''recasting in more modern terms'' the 19th Century precept. The profound and deeply personal impact of Huxley's work on Wilson's thinking is evident in the recollections of his students and colleagues. (Figure 3)

With Wilson's penchant for the role of complementarity as the 'secret of life,' one might speculate that the classic *form-function* biological dyad lay at the heart of his devotion to the reconciliation of the cell theory and the protoplasmic theory. Such conjecture aside, we dare say that this is a transcendent issue bearing upon the historical juxtaposition of these two doctrines today. Over time, discussions have tended to treat the cell theory and the protoplasmic theory, not as a complementary pair, but as a dominion

E. B. Wilson's Dream

"On the night before his oral examination for his doctoral degree at Columbia University in 1915, Hermann J. Muller, future Nobel laureate in Physiology and Medicine for his work on x-ray induced mutations in Drosophila, was confronted by his mentor, E. B. Wilson."

"Wilson was the head of the Columbia Biology Department at the time, and, although Muller had spent much of his time at Columbia working in Morgan's fly lab, it was to Wilson that he turned when he needed help… In an attempt to calm his nervous student, Wilson related a dream he had 34 years earlier, the night before his oral examination for his doctoral degree at Johns Hopkins University."

"As Wilson explained, his dream began with him standing at a podium before a blackboard and behind a set of curtains, anxiously awaiting his oral examination. As the curtains were drawn, his examiners were revealed to him. In the front row of the auditorium sat Thomas Huxley, Ernst Haeckel and Charles Darwin."

"Wilson began, 'I have a very simple thesis to present… I have the solution to the question *What is life?*'."

"He picked up a piece of chalk, walked up to the blackboard behind him, and drew a large triangle. He labeled the sides A, B, and C. He then drew a smaller triangle next to it, labeling its sides a, b, and c. He then turned around and exclaimed, 'That is the secret of life!' With that, Charles Darwin took off his hat, threw it in the air, and shouted, 'Huzzah! You've done it, my boy!' All three examiners proceeded to approach the podium to congratulate him."

"Muller remarked later that the most astounding thing to him was E.B. Wilson's intuitive understanding of the underlying importance of complementarity in life."

(Excerpt from "Reconstructing E. B. Wilson's Dream," by Anthony Dellureficio, the James D. Watson Special Collections Archivist at the Cold Spring Harbor Laboratory Library and Archives, Cold Spring Harbor, New York. See http://cshlarchives.blogspot.com/2007/12/e.html.)

Figure 3 E.B. Wilson's dream.

of one over the other. Framed in this light, one asks: does form dictate function, or does function drive form? Supremacy of the former stance is tantamount to a belief in the historical pre-eminence of the cell theory. With all due respect (and an apology) to proponents of this position, we would favour the latter posture and aver a revisionist history of science – suggesting that, on the biological macroscale, the 19th Century gave us the theory of evolution by natural selection, whereas on the microscale, it yielded the protoplasmic theory of life.

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