BJHS **52**(2): 345–352, June 2019. © British Society for the History of Science 2019
doi:10.1017/S0007087419000438

Essay Review

Metaphors and other slippery creatures

Karl Matlin, Jane Maienschein and **Manfred Laublicher** (eds.), *Visions of Cell Biology: Reflections Inspired by Cowdry's* General Cytology. Chicago and London: The University of Chicago Press, 2018. Pp. 400. ISBN: 978-0-2265-2048-3. $135.00 (cloth)

Andrew Reynolds, *The Third Lens: Metaphor and the Creation of Modern Cell Biology*. Chicago: The University of Chicago Press, 2018. Pp. 267. ISBN 978-0-2265-6312-1. $90.00 (cloth)

What are cells? How are they related to each other and to the organism as a whole? These questions have exercised biology since Schleiden and Schwann (1838–1839) first proposed cells as the key units of structure and function of all living things. But how do we try to understand them? Through new technologies like the achromatic microscope and the electron microscope. But just as importantly, through the metaphors our culture has made available to biologists in different periods and places. These two new volumes provide interesting history and philosophy of the development of cell biology. Reynolds surveys the field's changing conceptual structure by examining the varied panoply of changing metaphors used to conceptualize and explain cells – from cells as empty boxes, as building blocks, to individual organisms, to chemical factories, and through many succeeding metaphors up to one with great currency today: cells as social creatures in communication with others in their community. There is some of this approach in the *Visions* edited collection as well. But this collection also includes rich material on the technologies used to visualize cells and their dialectical relationship with the epistemology of the emerging distinct discipline of cell biology. This volume centres on, but is not limited to, 'reflections inspired by [E.V.] Cowdry's [1924 volume] *General Cytology*'; it benefits from a conference on the Cowdry volume as well as a 2011 Marine Biological Lab/Arizona State University workshop on the history of cell biology.

A common narrative, endorsed if not begun by modern cell biologists, states that the discipline of 'cell biology' first coalesced around cell fractionation techniques and electron microscopy in the years immediately after the Second World War. Jane Maienschein (*Visions*, p. 15) challenges this narrative, pointing out that the group working on Cowdry's *General Cytology* from 1922 to 1924 already 'clearly saw the beginning of a new field of cell biology emerging'. The editors of *Visions* further

https://doi.org/10.1017/S0007087419000438 Published online by Cambridge University Press

assert (p. 1) that 'the cellular conception of life emerged gradually within a rich context of cultural trends, philosophical claims, changing epistemologies and aesthetic preferences, political debates and institutional settings'. Thus both of these exciting new books survey changes in cell theory and in the organization of work to study cells, especially to use as a window into much broader issues in history and philosophy of science. Reynolds's book has slightly more overall emphasis on philosophical issues, but the two are in many ways excellent companion volumes. Reynolds's title nicely captures the dialectic both books explore: of how often metaphors and conceptual models serve as tools – lenses, in his own apt metaphor. Metaphors can magnify certain aspects of a phenomenon, though at the risk of blurring the resolution of other aspects of the cell. (Microscopists might wish each metaphor could be assigned a numerical aperture, to properly guide and caution their use.)

These books both describe the way that cytology, a largely morphological and observational discipline, by incorporating physiological and biochemical techniques and study of cells, transformed from *c.*1890–1950 into what 'cell biology' looks like today. They also detail a parallel movement away from the protoplasm theory that dominated from *c.*1861–1910, in which cells were often understood to be naked blobs of a homogeneous, jelly-like 'life-stuff' called protoplasm or sarcode.[1] Cowdry's 1924 volume – we learn from numerous *Visions* authors – takes stock of and endorses these changes. Indeed, the 1924 authors all argued that protoplasm is not a mere squishy, homogeneous substance; rather, they assert that the internal stuff of cells is spatially organized, structured into a 'cell architecture' – at least at the chemical level, even if not at the visible level, and even if little is yet known about how, physically, the cell's molecules can be spatially localized. Internal membranes are invoked to compartmentalize the cell interior, though few or none can be seen with the light microscopes of 1924. But here metaphors of the cell as a 'chemical laboratory', a 'factory', and a 'machine' – culturally ubiquitous and compelling metaphors in 1920s America and the industrialized West – deftly slip in to make the scientists convinced that, just as in a factory, the biochemical reaction chains must occur more or less in assembly-line fashion.

In his chapter in the *Visions* volume, Andrew Reynolds makes the interesting observation that the study of the cell began with solitary observers 'like Hooke and Leeuwenhoek, working in relative isolation in … private chambers', but evolved over time to the group that worked on *General Cytology* in 1924, 'a collaborative team or community working in communal spaces like the Marine Biological Laboratory … or a modern university of specialized workers requiring proper organization and communication in order to achieve desired results' (p. 66). In parallel, the scientists' views of the nature of the cell evolved from that of a simple empty chamber to a chemical lab/factory, to (by 1924) a highly organized, complex system. As Reynolds provocatively puts it, 'to the extent that the project of creating an integrated cellular biology has been successful, the science has become a metaphor for the organization within the cell (or is it the other way around?)' (p. 66). Using metaphors requires constant vigilance

1 Gerald Geison, 'The protoplasmic theory of life and the vitalist–mechanist debate', *Isis* (1969) 60, pp. 273–292.

https://doi.org/10.1017/S0007087419000438 Published online by Cambridge University Press

since the ever-present unconscious mechanism of projecting our own world onto nature is easy to slip into without noticing. To what extent did Darwin inductively see cutthroat, Adam Smith competitive capitalism leap out at him from nature, and to what extent did he project his Malthusian, Victorian industrializing worldview onto nature? Lest one think this a problem left behind by the more sophisticated research techniques and attitudes after the Second World War, one need only consult Nicolas Rasmussen's examination of the epistemology black-boxed into the electron microscope, or alternatively physiologist Stephen Rothman's *Lessons from the Living Cell*, a critique of modern cell biology's wilful blindness to its own preconceived assumptions behind the vesicle theory of secretion.[2] Harold Hillman mounted an even more extensive critique of this kind, as has Gerald Pollock.[3]

Cowdry and his colleagues did engage in robust critical debate over new biochemical and sectioning techniques, as well as specimen preparation and microscopy procedures, and the potential for artefact in all these – as Jutta Schickore admirably describes in Chapter 4 of *Visions*. William Bechtel has also written usefully on this, for the 1940s–1950s period.[4] Schickore gives a highly useful and engaging outline of the debates over microscope lighting, artefacts of staining, and the relative merits of higher magnifying powers from 1832–1900 or so. She makes clear that within microscopy, and even among biological microscopists, practitioners adopted a dizzying variety of stains, and an equally varied range of views flourished – as did spirited debate among biologists on these topics. One might point to Pierre LeComte du Noüy, Adrianus Pijper and Wilhelm Reich to show that, until the 1930s and 1940s, some chose to solve the artefact problem by prioritizing observations of cells and tissues in the living state.[5] The dramatic advantages of microscopic films made of live cells by Warren and Margaret Lewis, and by Ronald Canti at Strangeways Laboratory in the UK, underscored this approach.[6] More recently, cell biologist Lynn Margulis considered

2 Nicolas Rasmussen, *Picture Control*, Stanford: Stanford University Press, 1997; Stephen Rothman, *Lessons from the Living Cell*, New York: McGraw-Hill, 2002.

3 Gerald Pollock, *Cells, Gels and the Engines of Life: A New, Unifying Approach to Cell Function*, Seattle: Ebner and Sons, 2001; Harold Hillman, 'Biochemical cytology: has it advanced in the last 35 years?', *The Biologist* (1983) 65, pp. 1–16; Hillman, 'Some microscopic considerations about cell structure: light versus electron microscopy', *Microscopy* (1991) 36, pp. 557–576; Hillman, *The Case for New Paradigms in Cell Biology and in Neurobiology*, Lewiston, NY: Edwin Mellen Press, 1991; Hillman, *Evidence-Based Cell Biology*, Maastricht: Shaker Publications, 2008; Harold Hillman and Peter Sartory, *The Living Cell: A Re-examination of Its Fine Structure*, Chichester: Packard, 1980.

4 William Bechtel, *Discovering Cell Mechanisms*, Cambridge: Cambridge University Press, 2006.

5 Pierre LeComte DuNoüy, 'Tissue culture *in vitro*' (1931), in LeComte DuNoüy, *Between Knowing and Believing* (Paris: Hermann, 1966), pp. 21–38; LeComte DuNoüy, *Biological Time*, New York: Macmillan, 1937; James Strick, 'Adrianus Pijper and the debate over bacterial flagella, 1946–1956', *Isis* (1996) 87, pp. 274–305; Strick, *Wilhelm Reich, Biologist*, Cambridge, MA: Harvard University Press, 2015.

6 Ronald Canti, 'Cultivation of living tissue, part 3' (1933), at www.youtube.com/watch?v=OIhaaNeFgdE&t=48s, for example. For more on this see Brian M. Stramer and Graham A. Dunn, 'Cells on film: the past and future of cinemicroscopy', *Journal of Cell Science* (2015) 128, pp. 9–13, doi:10.1242/jcs.165019. On the Lewis films see Hannah Landecker, 'The Lewis films: tissue culture and "living anatomy", 1919–1940', in Jane Maienschein and Marie Glitz (eds.), *History of the Carnegie Institute Laboratory of Embryology*, Cambridge: Cambridge University Press, 2004, pp. 117–144; Landecker, 'Creeping, drinking, dying: the cinematic portal and the microscopic world of the twentieth-century cell',

https://doi.org/10.1017/S0007087419000438 Published online by Cambridge University Press

microcinematography of cells in the living state important enough that she archived many such films.[7]

The group around Cowdry in 1924 took a different approach to this conundrum, Schickore tells us (*Visions*, p. 96 n. 13), 'namely, the explicit acknowledgment of a diversity of approaches'. She contrasts this with yet another strategy, in this case one adopted by Victorian physics and microscopy communities and described by Graeme Gooday.[8] In that context, physicists attempted to re-engineer their laboratories to control the phenomena under study and impose more orderliness upon them. One wonders how much time, place and culture shape these responses to the study of nature. Another contrast along these lines can be drawn by comparing Viennese scientists from 1880 to 1920, as described by Deborah Coen. In biology, meteorology and even atmospheric physics, Coen describes an approach to science that characterized many of these scientists (particularly those from the tradition of Austrian liberalism) that embraced the variability of nature (and thus field studies) rather than trying to eliminate it by confining the objects of study to rigid laboratory conditions. 'In the field, physicists instead treated variations as further clues to the nature of the phenomenon under study.'[9]

Lijing Jiang's chapter on cell ageing and William Summers's chapter on cellular pathogenesis are complementary in interesting ways. Summers fills in the early part of Cowdry's career as professor of anatomy at the new Rockefeller Foundation-supported Peking Union Medical College in Beijing, China. Both stories describe the complexity of how Cowdry's work had to respond to, and largely push back against, Alexis Carrel's popular theory that in cell culture with ideal nutrients cells should be immortal.[10] Jiang (*Visions*, esp. pp. 121–123) sets research on cell ageing in the context of the emerging discipline of gerontology as a medical speciality and in the context of changing social policy towards older Americans. She shows that Cowdry was a leader in helping this new specialized field to coalesce. Cowdry invoked a new cross-cultural social metaphor: that ageing members of American society should be respected as elders were in China, and the vital role they played should be appreciated, just as ageing dead skin cells must be appreciated for performing the vital role of protecting the entire body. Additionally, he focused his research on a wide range of environmental and metabolic factors that might contribute to cell aging – eschewing notions that there might be some single factor that predetermined the process (e.g. what later was found to be the role of telomeres). As Summers puts it (*Visions*, p. 101), Cowdry 'committed to a holistic point of view: "Believing that the cell is a harmonious whole and that any

Science in Context (2011) 24, pp. 381–416. Adrianus Pijper's films are at the American Society for Microbiology archives at University of Maryland, Baltimore County, Catonsville, MD.

7 See, e.g., 'Forbidden Fertilization', at www.youtube.com/watch?v=ATQrxZSLia4.

8 Graeme Gooday, 'Instrumentation and interpretation', in Bernard Lightman (ed.), *Victorian Science in Context*, Chicago: The University of Chicago Press, 1997, pp. 409–437.

9 Deborah R. Coen, *Vienna in the Age of Uncertainty: Science, Liberalism and Private Life*, Chicago: The University of Chicago Press, 2007, p. 260.

10 Hannah Landecker, *Culturing Life: How Cells Became Technologies*, Cambridge, MA: Harvard University Press, 2007.

https://doi.org/10.1017/S0007087419000438 Published online by Cambridge University Press

attempt to dissociate its constituents is likely to result in error, the general viewpoint of synthesis has been adopted."'

Both Summers and Jiang remind us that while Cowdry 'turned out to be wrong' just prior to the 'molecular revolution' about many aspects of how to study viruses and mitochondria in cells, about the process of cell ageing, and so on, nonetheless much of his holistic approach, long overshadowed by the advances of molecular biology, appears relevant again in the more complicated twenty-first-century understanding of these phenomena. Further, says Summers (*Visions*, p. 109), 'Cowdry's cytopathological descriptions of [viral and Rickettsial] inclusions … became a central and persistent focus of diagnosis and investigation at least until the 1950s, and even today one finds his terminology still in use' (p. 109).

Regarding such protean terms as 'holistic', the *Visions* volume is helpful and nuanced because, when the term is used, the authors are careful to point out the sense in which it is being deployed. Reynolds in Chapter 3, for example, uses it in a different way from Summers. The Cowdry volume, as previously mentioned, aimed to understand the cell as having an organized 'architecture' that would allow its physical and chemical processes to be understood to operate in a manner analogous to a factory assembly line. Just as from a single screw or weld in that assembly line one could not infer the entire system, so, in that sense, 'This would be a holistic perspective, in the sense that it was the *organization* of the cell's microscopic and ultramicroscopic structures that made of it a system with the capacity for life' (*Visions*, p. 48, emphasis in original). This view is holistic relative to biochemists (*Visions*, p. 49), who would 'grind up cells so as to explore the chemical activity of their molecular components'. But this is still very much a project of physical–chemical reductionism, what Garland Allen dubbed 'holistic materialism'. Not in any sense does 'holistic' in this context mean 'vitalistic', though these terms are sometimes conflated by advocates of a more extreme mechanistic approach (e.g. Jacques Loeb) when attacking those who oppose that approach. Reynolds develops these distinctions about 'mechanism' and the 'machine metaphor' further in *The Third Lens*, especially pp. 73–84 of that book (on which, more below). This nuance is quite helpful given the ubiquitous, very generalized accounts circulating about the 'mechanism/vitalism controversy'.

This characteristic of the cell prompts further 'social-agential' metaphors from the Cowdry volume's authors: the cell is nothing but 'the co-ordinated sum of its parts … in a mechanism of differentiated and co-operative members they must all work together all the time' (*Visions*, p. 60). Reynolds astutely observes the tension between a machine metaphor and this cooperative social metaphor, again giving us a more nuanced view of how 'mechanism' is deployed: 'despite the implication of machine imagery, much mechanism talk assumes merely a regular causal arrangement within some system and is quite independent of any assumptions of a specific and concrete machine configuration' (*Visions*, p. 60). The machine metaphor was also complicated by the recognition that, without a rigid cell wall, 'the cell is in many instances a shape-shifter, a plastic speck of protoplasmic jelly (think of the changes it undergoes during division and the phenomenon of cell motility)' (*Visions*, p. 61). Contemplate the fact that most of us first learned that a cell was a static, two-dimensional 'typical cell' diagram in a textbook. It is this

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failure of basic biology education to convey one of the most striking and characteristic features of cells – their pulsation and motility – that motivated the likes of the Lewises, Pijper and Margulis to disseminate films of living, moving cells, as mentioned above. Rudolf Oldenbourg describes the polarized-light microscopy (and now imaging) developed at MBL by Shinya Inoué as one important effort made in this direction: to extend the resolution and magnification that had been previously possible while studying living cells, at first to be able to see clearly the process of mitosis in living cells.

Visions of Cell Biology contains many fascinating explorations of visual representations of cell structure (Steinert and MacCord's chapter) and how these visual representations merge into and dialectically interact with theoretical structures of cell biology (Dan Liu's chapter on the cell membrane as lipid bilayer, Matlin's and Bechtel's chapters). Fridolin Gross concludes the volume by analysing the use of models, bringing this up to present-day experimental and computational cell biology.

Turning to Reynolds's book-length treatment of metaphors in *The Third Lens*, the richness seen so far of exploring them – as heuristic tools, as instantiations of cell concepts in analogical and sometimes visual, pictorial form – is developed in still greater, more fascinating depth and over a longer span of time. Indeed, Reynolds examines cell metaphors from Hooke in the seventeenth century right up to modern cell-signalling research. We've had parts of this story before, in discussions of the 'cell-state' literature, or in Keller's *Making Sense of Life* (2002), for example. But Reynolds has synthesized here the grand overview of the history and philosophy of cell metaphors. The sheer number of different metaphors used is impressive when catalogued all in one place. As is their sometimes incompatibility, sometimes complementarity, and – always – situatedness in particular cultural and technological moments. Cells are (1) open spaces defined by solid walls for Hooke in the seventeenth century, (2) elementary organisms and/or (3) 'citizens of a cell-state' (the organism) throughout the nineteenth century, (4) 'chemical workshops or laboratories' in the 1830s–1840s, (5) 'factories' by the mid- to late nineteenth century, and/or (6) 'assembly lines' by 1913. Cells are at times (7) 'machines', at other times (8) 'lego blocks', (9) 'bags of enzymes' and most recently (10) 'social organisms.' After that I stopped counting.

Again, the strength of Reynolds's analysis is not merely cataloguing the range and variety of metaphors deployed. His greatest contribution is exploring at a deep level metaphors' ability to both enable and constrain the very conceptualizing of what a cell is – and how they point our attention to what cells can do for us. 'Metaphors are not only *descriptive* in nature, they can also be *prescriptive*', Reynolds shows us (*The Third Lens*, p. 61, original emphasis). If a one-celled amoeba is an elementary organism, then it can launch a field of research on the amoeba as a model organism, the simplest unit of animal behaviour, by Alfred Binet, among others.[11] 'Man is a complex amoeba!' declares one of Reynolds's subjects (*The Third Lens*, p. 38). This was also taken seriously by Sigmund Freud and others who saw the amoeba as a model for

11 Judy Johns Schloegel and Henning Schmidgen, 'General physiology, experimental psychology, and evolutionism: unicellular organisms as objects of psychophysiological research, 1877–1918', *Isis* (2002) 93, pp. 614–645.

https://doi.org/10.1017/S0007087419000438 Published online by Cambridge University Press

understanding basic forces such as libido.[12] If a cell is an organism, and an organism a cell-state, as Virchow and Haeckel would have it, then what kind of citizen in what kind of state? (*The Third Lens*, pp. 57, 72). There is division of labour, as in a modern state. But is it the Prussian authoritarian state sending out orders from the central brain (Berlin) to obedient subjects (cells and organs)? Or are the organs, and perhaps even cells, autonomous agents generating their own impulses without needing 'orders' from a centralized 'controlling agency'/brain – as Michael Foster and his students argued in the case of the source of the pulsation of the heart?[13] In that case, isn't the organism more like a natural cooperative – or as Wilhelm Reich would put it, like a work democracy – than like an authoritarian state?[14] Reynolds urges another closely related model: the 'anarcho-syndicalist cooperative' (pp. 133–137). This may seem a point long taken as established by historians and philosophers of science, so Reynolds gives us a salutary warning: in a biology curriculum developed by AAAS for sixth- to eighth-grade American students,

> children … are asked to think of ways that the cell is like a factory and … encouraged to create their own original analogies and metaphors for the cell. The chemist Theodore Brown recounts a colleague's confusion when confronted with the widespread use of the factory metaphor for talking about the cell. 'How else could you talk about it?' was the puzzled response. To make the point that the factory metaphor is not inevitable, Brown asked his colleague to consider how biologists unfamiliar with the existence of factories … might attempt to understand the cell. Why, for instance, aren't people talking about the cell as a kibbutz? (*The Third Lens*, p. 72)

But this is no mere semantic or academic word game. Thinking of cells as 'factories' and as 'machines' is no small part of what turned many scientists towards figuring out how to exploit them as technologies (as Hannah Landecker has pointed out) to produce fermentation products and to maximize production efficiency – from wine and beer for Pasteur, to acetone and butanol for Weitzmann, to antibiotics after 1940, to insulin and a host of other profitable products since the advent of recombinant DNA technology, spawning the enormous, consequential biotechnology industry. The CRISPR-cas9 technique will no doubt transform biotech still further toward control on a previously unimagined scale. Rather than being mere tools the researchers control, metaphors have agency inherent in them. Sometimes they start telling the researchers which questions to ask.

Reynolds traces the idea of 'cells as social organisms' from a 1923 discovery by Albert Fischer that cells will proliferate in culture 'only in the company of a minimal quantity of other cells' (*The Third Lens*, p. 91). Then it is deployed consciously in an article in *Science* in 1931 by Alexis Carrel, who calls for a new 'cell sociology', contrasting it with the morphological approach that long dominated cytology. This banner, we learn, was picked up and carried forward by Michael Abercrombie and Joan Heaysman in a 1953 article (*The Third Lens*, p. 90). Indeed, they found the usual social behaviour absent in some malignant tumour cells, rendering those cells true

12 Strick, *Wilhelm Reich*, op. cit. (5), pp. 26–27, 60–61.

13 Gerald Geison, *Michael Foster and the Cambridge School of Physiology*, Princeton, NJ: Princeton University Press, 1978.

14 Wilhelm Reich, *The Mass Psychology of Fascism*, New York: Farrar, Straus and Giroux, 1969; first published 1946, esp. Chapters 11–13.

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social deviants, sociopaths in the cellular community. Reynolds continues to trace the understanding of cell signalling and other features of social behaviour up to the present – a fascinating story in which I could only wish for one noticeable omission to be filled. He makes no mention at all of the related but branched-off discussion of the 'sociology within a single eukaryotic cell' that followed in the wake of Lynn Margulis's serial endosymbiosis theory. What kind of community is such a cell? A cozy commune of harmoniously cooperating organelles? Surely some exploration of this story would be appropriate in Reynolds's book, given what a major contribution it was to our understanding of the cell and to the history of evolution of life on Earth.[15] This is the only significant flaw I would note in an otherwise extremely useful and readable volume.

One of Reynolds's main objects is to argue for the importance of the question whether science seeks an account of the world that is literally true or one that is objectively true. This reviewer (a non-philosopher) benefited from being pressed on this distinction between two often conflated things. He argues persuasively that one need not be a radical relativist having understood how much metaphors dominate and even direct scientific research. He argues usefully that science can seek literal understanding of how the cell works and value the leverage this provides over manipulating and accurately predicting the behaviour of natural systems like cells, while still acknowledging the complex effect of metaphors – so often literally not true – and thus avoiding the 'metaphysical hubris' of thinking we have reached (or can reach) an objectively true account of what nature is like in its own terms, independent of our cognitive biases and limitations.

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15 See e.g. E.F. Keller, 'One woman and her theory', *New Scientist*, 3 July 1986, pp. 46–50, esp. the section 'A job for a woman'. Also James Strick, 'Exobiology at NASA: incubator for the Gaia and serial endosymbiosis theories', in Bruce Clarke (ed.), *Earth, Life, and System: Evolution and Ecology on a Gaian Planet*, New York: Fordham University Press, 2015, pp. 80–104, esp. 95–103.

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