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# The Artificial Cell, the Semipermeable Membrane, and the Life that Never Was, 1864–1901

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## ABSTRACT

Since the early nineteenth century, a membrane or wall has been central to the cell's identity as the elementary unit of life. Yet the literally and metaphorically marginal status of the cell membrane made it the site of clashes over the definition of life and the proper way to study it. In this article I show how the modern cell membrane was conceived of by analogy to the first "artificial cell," invented in 1864 by the chemist Moritz Traube (1826–1894), and reimagined by the plant physiologist Wilhelm Pfeffer (1845–1920) as a precision osmometer. Pfeffer's artificial cell osmometer became the conceptual and empirical basis for the law of dilute solutions in physical chemistry, but his use of an artificial analogue to theorize the existence of the plasma membrane as distinct from the cell wall prompted debate over whether biology ought to be more closely unified with the physical sciences, or whether it must remain independent as the science of life. By examining how the histories of plant physiology and physical chemistry intertwined through the artificial cell, I argue that modern biology relocated vitality from protoplasmic living matter to non-living chemical substances—or, in broader cultural terms, that the disenchantment of life was accompanied by the (re)enchantment of ordinary matter.

KEY WORDS: cell membrane, protoplasm, plant physiology, colloid chemistry, biophysics, physical chemistry, osmosis, materialism

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## INTRODUCTION

Since the 1950s it has been known that most cell membranes are 7–10 nm (70–100 Å) thick, about half of which is the iconic heads-out tails-in lipid

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bilayer, the membrane's primary structural element. An ordinary light microscope can theoretically resolve objects down to about 250 nm, and then only under ideal conditions.[1] In hindsight the cell membrane was essentially invisible until the 1930s, when x-ray diffraction and polarized light microscopy were used to provide indirect signs of its existence and structure. Even as the electron microscope's ångström-scale resolution reached down to the high double digits by the 1950s, the identification of the cell membrane was as much an epistemological and conceptual problem as it was one of optics and resolution: "Where does the cell membrane begin if indeed there is any sharp boundary?" one biologist asked in 1957. Showing an electron microgram with six pairs of arrows, indicating the range of opinion on where and what the membrane is, he added, "Most electron microscopists have avoided the question by adopting the practice of light microscopists of calling the thinnest line they could see next to the cytoplasm the cell membrane . . . the outer arrow is placed as close to the inner arrow as possible, or is simply erased and forgotten."[2]

Although this sharp boundary is now one of the defining characteristics of the cell, in the cell theory's first century the membrane led a more dubious life, held together by a mix of sheer conviction, haphazard terminology, and analogizing across scientific domains. Nevertheless, a microscopically visible membrane, "envelope," or boundary around the cell was already a central feature of its individuality very early in the history of cell theory. In 1802, Jean Pierre Vaucher (1763–1841) shook apart filamentous algae into its constituent cellular parts: "Each compartment in the [algal filament] is itself a plant which does not communicate with the others contained in the same [filament]," wrote Vaucher. "Each has its own envelope, its spirals, its particles, in a word, everything that constitutes a plant."[3] In 1838, Matthias Schleiden (1804–1881) cast the nucleus and the *Zellenmembran* as the essential constituents of cells

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[1] For comparison, an *E. coli* bacterium is about 600 nm long, and the influenza virus is 80–120 nm in diameter. On the Abbe diffraction limit, see David Cahan, "The Zeiss Werke and the Ultramicroscope: The Creation of a Scientific Instrument in Context," in *Scientific Credibility and Technical Standards in 19th and Early 20th Century Germany and Britain*, ed. Jed Z. Buchwald, Archimedes 1 (Dordrecht: Kluwer, 1996), 67–115.

[2] J. D. Robertson, "The Ultrastructure of Cell Membranes and Its Derivatives," in *The Structure and Function of Subcellular Components*, ed. E. M. Crook, Biochemical Society Symposium 16 (Cambridge: Cambridge University Press, 1959), 3–43, on 5.

[3] Jean Pierre Vaucher, *Histoire des conferves d'eau douce* (Geneva: J. J. Paschoud, 1803), 41–42; translation from Henry Harris, *The Birth of the Cell* (New Haven, CT: Yale University Press, 1999), 69–70. Earlier historians cited G. R. Treviranus' 1805 *Biologie, oder Philosophie der lebenden Natur*, Bd. 3 (Göttingen: Röwer) as the earliest demonstration of cellular individuality. When

*qua* "universal elementary organ of vegetables."[4] When Theodor Schwann (1810–1882) generalized Schleiden's theory to make the cell the universal organ of all plant *and* animal life, he simultaneously made the cell membrane a universal structure across all living organisms. 1838 was important in the history of the cell membrane in other ways as well: that December, the French chemist Anselme Payen (1795–1871) identified "*la substance membranéiforme naissante*" of plant cells, which was christened *cellulose* the following month.[5]

Of course, Payen's identification of cellulose with the cell membrane mixes up the distinction we make today between the lipo-protein cell membrane and the cellulosic cell wall, the latter being found exclusively in plants. In the mid-nineteenth century, however, "cell membrane," *Zellenmembran*, *Zellhaut*, and *membrane cellulaire* were used interchangeably with variations on "wall," *Wand*, *paroi*, "hyaline layer," and even "ectoplasm," all indicating the singular outer boundary of the cell.[6] Biologists' insistence that cells did not need to have membranes in order to be cells compounded this empirical and terminological confusion. In the second half of the nineteenth century, biologists came to the consensus that the cell was an individuated unit of living matter or "protoplasm"—in the same way that an ice cube requires only space to individuate it from other ice cubes.[7] The protoplasm concept originated from debates over the cell's microscopic anatomy, but it quickly became synonymous with "living matter," as biologists sought to define vitality *vis-à-vis*

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possible, I will refer to published English translations of the German and French texts cited; all other translations are my own.

[4] Matthias Schleiden, "Contributions to Our Knowledge of Phytogenesis," trans. William Francis, *Taylor's Scientific Memoirs* 2, no. 6 (1841): 281–312, on 283; German, "Beiträge zur Phytogenesis," *Archiv für Anatomie, Physiologie und wissenschaftliche Medicin* 5 (1838): 137–76, on 139.

[5] Anselme Payen, "Mémoire sur la composition du tissu propre des plantes et du ligneux," *Comptes rendus hebdomadaires de l'Académie des Sciences* 7, no. 7 (17 Dec 1838): 1052–56. The name "cellulose" was given in the report conforming Payen's discovery by Alexandre Brongniart, Théophile-Jules Pelouze, and Jean-Baptiste Dumas, "Rapport sur un Mémoire de M. Payen, relatif à la composition de la matière ligneuse," *Comptes rendus hebdomadaires de l'Académie des Sciences* 8, no. 2 (14 Jan 1839): 51–53.

[6] For example, Schwann used the terms "cell wall" (*Zellenwand*) and "cell membrane" (*Zellenmembran*) indiscriminately; see *Mikroskopische Untersuchungen* (Berlin: Sanders'chen Buchhandlung, 1839), 209–11. Julius Sachs printed "Zellhaut (Zellwand)" in his textbooks to indicate the synonymy, in his *Lehrbuch der Botanik: Nach dem gegenwärtigen Stand der Wissenschaft*, 1st ed. (Leipzig: Wilhelm Engelmann, 1868), 2.

[7] On the debates over the boundedness of cells, see Andrew S. Reynolds, *The Third Lens: Metaphor and the Creation of Modern Cell Biology* (Chicago: University of Chicago Press, 2018), 30–34; Daniel Liu, "The Cell and Protoplasm as Container, Object, and Substance, 1835–1861," *Journal of the History of Biology* 50, no. 4 (Nov 2017): 889–925.

a material substance.[8] As Gerald Geison, Andrew Reynolds, Robert Brain, and Trevor Pearce have shown, protoplasm theory developed as biologists' desires to move away from immaterial "vital forces" aligned with a diffuse materialism in a broader European scientific culture.[9] But naturalizing "life" into an undifferentiated "living matter" also meant that any wall or membrane was auxiliary equipment, a protoplasmic secretion rather than an essential part of the cell.[10] So strong was the injunction against the notion of a cell's membrane that in the 1890s the cytologist Oscar Hertwig (1849–1922) could follow the letter and not the spirit of protoplasm theory by rejecting the cell membrane's necessity, while at the same time accepting that a "thin outer zone" of the protoplasm is "a specially differentiated organ of the cell and is endowed with special functions."[11]

In this article I will show how the modern cell membrane was conceived of by analogy to the first so-called "artificial cell" or *künstliche Zelle*, invented in 1864 by the German chemist Moritz Traube (1826–1894) and redesigned and reimagined in 1877 as a precision instrument for measuring osmotic pressure by the plant physiologist Wilhelm Pfeffer (1845–1920). In 1877, Pfeffer became the first biologist to identify an osmotically active "plasma membrane" as a distinct organ, separate from the rigid, inert plant cell wall. In 1887, the Dutch physical chemist Jacobus van 't Hoff (1852–1911) generalized Traube and Pfeffer's artificial cells as "semipermeable membranes" in his formulation

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8. Robert Kohler has argued that in the history of biochemistry, "The very success of the protoplasm theory tended at first to discourage more searching questions as to how protoplasm caused vital reactions to occur"; "The Enzyme Theory and the Origin of Biochemistry," *Isis* 64, no. 2 (Jun 1973): 181–96, on 185.

9. Gerald L. Geison, "The Protoplasmic Theory of Life and the Vitalist-Mechanist Debate," *Isis* 60, no. 3 (Oct 1969): 273–92; Andrew Reynolds, "Amoebae as Exemplary Cells: The Protean Nature of an Elementary Organism," *Journal of the History of Biology* 41, no. 2 (Jul 2008): 307–37; Robert Brain, *The Pulse of Modernism: Physiological Aesthetics in Fin-de-Siècle Europe* (Seattle: University of Washington Press, 2015); Trevor Pearce, "'Protoplasm Feels': The Role of Physiology in Charles Sanders Peirce's Evolutionary Metaphysics," *HOPOS: The Journal of the International Society for the History of Philosophy of Science* 8, no. 1 (Mar 2018): 28–61.

10. Max Schultze articulated the argument that membranes were not necessary for cells, in "Ueber Muskelkörperchen und das, was man eine Zelle zu nennen habe," *Archiv für Anatomie, Physiologie, und wissenschaftliche Medicin* 27 (1861), 1–27; this was quickly accepted by Ernst Brücke in his influential essay "Die Elementarorganismen," *Sitzungsberichte der kaiserlichen Akademie der Wissenschaften, mathematisch-naturwissenschaftliche Classe, 2. Abtheilung* 44, no. 23 (17 Oct 1861): 381–406.

11. Oscar Hertwig, *The Cell: Outlines of General Anatomy and Physiology*, trans. M. Campbell (London: Swan Sonnenschein, 1895), 7–10, 14–15; German, *Die Zelle und die Gewebe* (Jena: Gustav Fischer, 1893), 7–9, 13–14.

of his law of dilute solutions.[12] Van 't Hoff's law is better known for its daring analogy between the thermodynamics of gases and solutions, but as I will show here, his synthesis of osmotic pressure and kinetic theory created an equivalency across all membranes, living and non-living. Although biologists were skeptical of Pfeffer's use of an artificial analogue to generate an anatomical and physiological theory, their concerns were ignored as physical chemists enthusiastically embraced the artificial cell as a model membrane. Consequently, the artificial cell, with its dual role in the histories of biology and physical chemistry, destabilized the distinction between the living and the non-living, and even upended the assumption that biologists study living things.[13]

Any theory of the necessity of a cell's membrane posed a threat to a protoplasm-centric cell theory by insisting that anatomical spatialization was more critical to understanding the cell than its material composition.[14] That Pfeffer based his plasma membrane theory on an analogy to his artificial cell only

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[12] Van 't Hoff's analogy between gases and dilute solutions goes by several names in different languages: the "law of dilute solutions," the "theory of dilute solutions," the simpler "theory of solutions," and occasionally "van 't Hoff's law" and the "law(s) of osmotic pressure."

[13] I use "biology" to broadly mean "science of life" in a way that would have been anachronistic until the 1890s; the "biologists" I discuss preferred to think of themselves primarily as plant physiologists. I have two reasons. First, following the suggestion by Cécilia Bognon-Küss and Charles T. Wolfe, eds., *Philosophy of Biology Before Biology* (Abingdon, UK: Routledge, 2019), the development of "biology" as part of an evolving system of disciplines in the nineteenth century only incompletely captured the development of "life" as a conceptual or metaphysical domain. Second, physiologists, anatomists, and naturalists in the late nineteenth century were dissolving the form-function dichotomy that had structured the disciplinary separation of physiology from anatomy, natural history, etc. The weakening or dissolution of this dichotomy, along with the rise of experimental studies of genetics, development, and evolution in the early twentieth century, led to a fragmentation and reorganization of physiology—as an intellectual tradition, monopoly on technique, and social structure—into the more capacious categories of "biology" and "the life sciences." On this disciplinary terminology, see Joseph A. Caron, "'Biology' in the Life Sciences: A Historiographical Contribution," *History of Science* 26, no. 3 (1988): 223–68; Kai Torsten Kanz, "Biologie: Die Wissenschaft vom Leben?" in *Lebenswissen: Eine Einführung in die Geschichte der Biologie*, ed. Ekkehard Höxtermann (Rangsdorf: Natur & Text, 2007), 100–121; and Lynn K. Nyhart, *Biology Takes Form: Animal Morphology and the German Universities, 1800–1900* (Chicago: University of Chicago Press, 1995). On the independence of physiology, see Richard L. Kremer, "Physiology," in *Modern Biological and Earth Sciences*, ed. Peter J. Bowler and John V. Pickstone, vol. 6 of *The Cambridge History of Science* (Cambridge: Cambridge University Press, 2009), 342–66.

[14] On a later conflict between the spatialization versus the biochemistry of the cell, see Mathias Grote's study of Peter Mitchell's (1920–1992) analogy between biological cells and hydrogen fuel cells, in "Surfaces of Action: Cells and Membranes in Electrochemistry and the Life Sciences," *Studies in History and Philosophy of Biological and Biomedical Sciences* 41, no. 3 (Sep 2010): 183–93.

intensified the destabilization of the distinctions between life and non-life, and of protoplasmic living matter from its non-living constituents. As I will demonstrate, the cell membrane made the leap from an analogy grounded in artifice to second nature by means of physical chemistry, a domain outside of biology as traditionally construed.[15] This essay is thus, in part, a response to Angela Creager's recent call to explore how biologists have used chemical ideas, tools, and practices to elucidate the secrets of life.[16] In the first two sections of this article I show how botanists instrumentally adapted mechanical and colloid chemical concepts to study plants' unique physiology.

But I also want to go a few steps further. By exploring the intertwined histories of the artificial cell, the cell membrane, and van 't Hoff's law of dilute solutions, I argue that the history of modern biology can be seen as a relocation of vitality from protoplasmic living matter to non-living chemical substances—or, to put it in broader cultural terms, that the disenchantment of life was accompanied by the (re)enchantment of ordinary matter.[17] From the middle of the nineteenth century onward a conception of "brute matter," or matter deprived of all agency, was replaced by theories of matter that emphasized the unique agency, capacities, even the vitality of specific "lifeless" substances. Ursula Klein has shown that this shift began in chemistry in the 1830s: as organic chemists synthesized and analyzed organic substances that were not found in living plants or animals, the chemical categories of the organic, life, and artifice ceased to be mutually exclusive.[18] In biology, it was only by

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[15] On the concepts of first and second nature, see William Cronon, *Nature's Metropolis: Chicago and the Great West* (New York: Norton, 1991).

[16] Angela N. H. Creager, "A Chemical Reaction to the Historiography of Biology," *Ambix* 64, no. 4 (Nov 2017): 343–59.

[17] Mathias Grote, *Membranes to Molecular Machines: Active Matter and the Remaking of Life* (Chicago: University of Chicago Press, 2019); Grote, "Surfaces of Action" (ref. 14). See also Bernadette Bensaude-Vincent, "Biomimetic Chemistry and Synthetic Biology: A Two-Way Traffic across the Borders," *Hyle: International Journal for Philosophy of Chemistry* 15, no. 1 (Jul 2009): 31–46; Bernadette Bensaude-Vincent, "Materials as Machines," in *Science in the Context of Application*, ed. Martin Carrier and Alfred Nordmann, Boston Studies in the Philosophy of Science 274 (Dordrecht: Springer Netherlands, 2011), 101–11; cf. Evelyn Fox Keller, "Active Matter, Then and Now," *History and Philosophy of the Life Sciences* 38, no. 3 (Sep 2016). On the standard formulation of vitalism as a reenchantment of a mechanistic and disenchanted science in the Weberian sense, see Anne Harrington, *Reenchanted Science: Holism in German Culture from Wilhelm II to Hitler* (Princeton, NJ: Princeton University Press, 1996); on recent reassessments of the disenchantment thesis, see Michael Saler, "Modernity and Enchantment: A Historiographic Review," *American Historical Review* 111, no. 3 (Jun 2006): 692–716.

[18] Ursula Klein, *Experiments, Models, Paper Tools: Cultures of Organic Chemistry in the Nineteenth Century* (Stanford, CA: Stanford University Press, 2003), chap. 2.

continuing and extending this relocation of vitality that a thoroughgoing mechanistic materialism could make sense as the foundation for a modern biology. Whereas Jessica Riskin has recently claimed that the mechanistic view of life from its origins in the seventeenth century is premised on smuggling a supernatural, animist, or theological source of vital agency into the living machine, I argue that this is definitely *not* the case from the mid-nineteenth century onward.[19] Rather, scientists broadened their conceptions of what matter is capable of, trading a metaphysical opposition of life and matter for what Laura Dassow Walls, borrowing from Alexander von Humboldt, refers to as a dynamic and integrative "rational empiricism." Following Walls' lead, I want to turn the history of the vitalist-mechanist debate on its head and suggest that the oppositional character of the vitalist-mechanist and active-versus-passive-matter debates is premised on a flattening of matter theory, a historical misunderstanding that persists to this day.[20]

Van 't Hoff's use of Pfeffer's experimental results and his formulation of the analogy between gases and solutions was already recognized as historically significant before he received the Nobel Prize in 1901, and outlines of this history have been a mainstay of the history of the physical sciences ever since.[21]

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19. Cf. Jessica Riskin, *The Restless Clock: A History of the Centuries-Long Argument Over What Makes Living Things Tick* (Chicago: University of Chicago Press, 2016). As early as 1965 Everett Mendelsohn cautioned historians against classifying biologists into strict vitalist or mechanist categories, in "Physical Models and Physiological Concepts: Explanation in Nineteenth-Century Biology," *The British Journal for the History of Science* 2, no. 3 (1965): 201–19.

20. Laura Dassow Walls, *Seeing New Worlds: Henry David Thoreau and Nineteenth-Century Natural Science* (Madison: University of Wisconsin Press, 1995). Walls specifically blames Coleridge's opposition of mechanism and organism and his insistence on the total passivity of matter, positions that were rooted in his conservative theology and politics.

21. Examples of the earlier historiography include Harry C. Jones, ed., *The Modern Theory of Solution: Memoirs by Pfeffer, Van't Hoff, Arrhenius, and Raoult* (New York: Harper & Brothers, 1899), v–xi; Ernst Cohen, *Jacobus Henricus van't Hoff: Sein Leben und Wirken*, Grosse Männer 3 (Leipzig: Akademische Verlagsgesellschaft, 1912); Alexander Findlay, *Osmotic Pressure*, 2nd ed. (London: Longmans, Green, 1919). From the more recent historiography, see Elisabeth T. Crawford, *The Beginnings of the Nobel Institution: The Science Prizes, 1901–1915* (Cambridge: Cambridge University Press, 1984), chap. 5; H. A. M. Snelders, "J. H. van 't Hoff's Research School in Amsterdam (1877–1895)," *Janus* 71 (1984): 1–30; H. A. M. Snelders, "J. H. van 't Hoffs theorie van de verdunde oplossingen," *Tijdschrift voor de geschiedenis der geneeskunde, natuurwetenschappen, wiskunde en techniek* 10, no. 1 (1987): 2–19; John W. Servos, *Physical Chemistry from Ostwald to Pauling: The Making of a Science in America* (Princeton, NJ: Princeton University Press, 1990), 31–33; Mary Jo Nye, *Before Big Science: The Pursuit of Modern Chemistry and Physics, 1800–1940* (New York: Twayne, 1996), 102–03; Patrick Coffey, *Cathedrals of Science: The Personalities and Rivalries That Made Modern Chemistry* (London: Oxford University Press, 2008).

Yet even if van 't Hoff's law of dilute solutions is occasionally mentioned in connection to Pfeffer or Traube, the deeper conceptual and experimental continuities between cell theory, botany, and physical chemistry have not been explored.[22] Despite the cell membrane's shared origins with the law of dilute solutions, the historiography of the cell membrane has been frustrated by a long list of technical, terminological, and even disciplinary difficulties, because it lies outside of a canonical historiography of medical and animal physiology.[23] By examining the history of the cell membrane in plant physiology, I seek to bridge a historiographical gap between the Berlin circle of "organic physics" of the mid-nineteenth century and the biophysics of the mid-twentieth, both of which use medical and animal physiology to frame the larger history of reductionism and scientific materialism.[24] In the first two parts of this article I will examine the debates over botanical mechanics from 1862 to 1877 between Wilhelm Hofmeister (1824–1877) and Julius Sachs' (1832–1897) school of plant physiology. In the middle sections I will evaluate the successes and failures of Traube and Pfeffer's artificial cells as an analogy for cellular mechanics, between Traube's invention of the artificial cell in 1864 and Pfeffer's publication of his *Osmotic Investigations* in 1877. In the concluding two sections, I will

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[22] A typical example is Joseph S. Fruton, *Molecules and Life: Historical Essays on the Interplay of Chemistry and Biology* (New York: Wiley-Interscience, 1972), 132–33.

[23] The best overviews of the history of the cell membrane are Arnošt Kleinzeller, *Exploring the Cell Membrane: Conceptual Developments*, Comprehensive Biochemistry, vol. 39 (Amsterdam: Elsevier, 1995), chap. 2; Jonathan Lombard, "Once upon a Time the Cell Membranes: 175 Years of Cell Boundary Research," *Biology Direct* 9, no. 32 (2014); and especially the post-1930 history, Grote, *Membranes to Molecular Machines* (ref. 17), chap. 1; see also Daniel Liu, "Heads and Tails: Molecular Imagination and the Lipid Bilayer, 1917–1941," in *Visions of Cell Biology: Reflections Inspired by Cowdry's General Cytology*, ed. Karl Matlin, Jane Maienschein, and Manfred Laubichler (Chicago: University of Chicago Press, 2018), 209–45.

[24] On "organic physics," the Berlin circle, and physicalist physiology, see Paul F. Cranefield, "The Organic Physics of 1847 and the Biophysics of Today," *Journal of the History of Medicine and Allied Sciences* 12, no. 10 (Oct 1957): 407–23; Charles A. Culotta, "German Biophysics, Objective Knowledge, and Romanticism," *Historical Studies in the Physical Sciences* 4 (Jan 1974): 3–38; Timothy Lenoir, "Social Interests and the Organic Physics of 1847," in *Science in Reflection*, ed. Edna Ullmann-Margalit, Boston Studies in the Philosophy of Science 110 (Dordrecht: Kluwer, 1988), 169–91; and Richard L. Kremer, *The Thermodynamics of Life and Experimental Physiology, 1770–1880* (New York: Garland, 1990). On the formation of the Berlin circle, see M. Norton Wise, *Aesthetics, Industry, and Science: Hermann von Helmholtz and the Berlin Physical Society* (Chicago: University of Chicago Press, 2018). On early twentieth century biophysics, see Nicolas Rasmussen, "The Mid-Century Biophysics Bubble: Hiroshima and the Biological Revolution in America, Revisited," *History of Science* 35, no. 109 (Sep 1997): 245–93; and Peter J. Westwick, "Abraded from Several Corners: Medical Physics and Biophysics at Berkeley," *Historical Studies in the Physical and Biological Sciences* 27, no. 1 (Jan 1996): 131–62.

show how the success of the artificial cell as both instrument and analogy after 1877 highlighted a growing disciplinary rift between conceptions of biology as an independent science of life and a biology that was increasingly aligned with physical chemistry.

## JULIUS SACHS' SCHOOL OF PLANT PHYSIOLOGY AND THE MECHANICAL LIVELINESS OF PLANTS

Foucault's claim in *The Order of Things* that "life" as a category was co-constructed with biology as an independent scientific domain is premised on the rearrangement of a "classical" episteme's tripartite classification of animal, vegetable, and mineral into a modern, dualistic classification of the living and the non-living.[25] Doubtless such a rearrangement did occur, but when Lamarck, Treviranus, and others began using the term "biology" around 1800, neither they nor their conceptions of life itself obliterated the old distinctions between the animal, vegetable, and mineral.[26] In fact, an era of *divergence* of the sciences of plant and animal life can be observed in the aftermath of Schwann's cell theory. If a specifically modern biology is characterized by a scientific interest in vitality—the interplay between anatomical structure and physiological function—then plant physiology came into its own in the mid-nineteenth century as scientists renewed their interest in a specific plant vitality. Indeed, both botanists at the time and later historians have agreed that in 1842, Matthias Schleiden inaugurated a new inductive period in botany with the publication of his *Grundzüge der wissenschaftlichen Botanik*, a work whose aim was to show how little botanists knew about the physiological processes that specifically characterized plant life.[27]

Seen in this light, we can interpret some of the more tedious debates in mid-nineteenth century botany as attempts to reestablish the definition of a "plant"

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[25] Michel Foucault, *The Order of Things: An Archaeology of the Human Sciences* (London: Routledge, 2007), 139, 175, 287–304. Foucault's claim for the co-construction of "life" and "biology" virtually ignores the existence of physiology as an endeavor separate from comparative anatomy.

[26] On the conceptual origins of "biology," see Bognon-Küss and Wolfe, eds., *Philosophy of Biology Before Biology* (ref. 13); and John H. Zammito, *The Gestation of German Biology: Philosophy and Physiology from Stahl to Schelling* (Chicago: University of Chicago Press, 2018).

[27] Matthias Schleiden, *Grundzüge der wissenschaftlichen Botanik* (Leipzig: Wilhelm Engelmann, 1842), 22–34.

through anatomical and physiological theory, rather than by morphology or taxonomic fiat.[28] In the 1850s, Wilhelm Hofmeister undertook a series of anatomical and physiological explorations of the relationship between water uptake and plant structure, demonstrating that young shoots bend as they grow because of the rigidity of the epidermal tissue relative to the turgescence of the large, softer parenchyma cells that sit beneath it.[29] Hofmeister sliced into the succulent parenchyma cells, popping them, and observed as the shoot suddenly curved, pulled to one side by the taut epidermal tissue, now freed from opposing mechanical tension of the parenchyma. By noting the curvature of sprouts before and after making these cuts, Hofmeister showed that the ability of some of the plant's cells to absorb much more water than others was mechanically responsible for the overall shape and growth of the plant.[30] Though it has never been a mystery that plants need water to grow, Hofmeister showed for the first time that plant structure and development could be studied as an exercise in cellular mechanics and hydraulics, rather than through Linnaean schemas or idealized *Baupläne* (archetypes).[31]

As other botanists began to sort out the causal relations among water, cells, tissues, and the overall life history of the plant, what began as a simple mechanical exercise escalated into a bitter argument over what "life" was in plants—or, more specifically, where their vital action was located. Initially, the most outspoken devotee of Hofmeister's research on "tissue tension" was Julius Sachs, who virtually republished Hofmeister's three articles on plant mechanics in his

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[28] The distinction between plant morphology and plant anatomy arose in the nineteenth century and was formalized in the twentieth—the former was the science of the broader macroscopic or organismal form, the latter the science of the internal cellular and histological structure of the plant. This distinction is rooted in disagreements among Nägeli, Hofmeister, Sachs, and de Bary, and continues in some corners of botany today; see, for example, the special issue, "Plant Structure: Concepts, Connection, and Challenges (Katharine Esau Symposium)" of *International Journal of Plant Sciences* 153, no. 3, pt. 2 (Sep 1992).

[29] On Hofmeister, see Donald R. Kaplan and Todd J. Cooke, "The Genius of Wilhelm Hofmeister: The Origin of Causal-Analytical Research in Plant Development," *American Journal of Botany* 83, no. 12 (Dec 1996): 1647–60.

[30] Wilhelm Hofmeister, "Über die Beugungen saftreicher Pflanzentheile nach Erschütterung," *Berichte über die Verhandlungen der königlich sächsischen Gesellschaft der Wissenschaften zu Leipzig, mathematisch-physische Klasse* 11 (13 Aug 1859): 175–204; "Über die durch Schwerkraft bestimmten Richtungen von Pflanzentheilen," *Berichte über die Verhandlungen der königlich sächsischen Gesellschaft der Wissenschaften zu Leipzig, mathematisch-physische Klasse* 12 (12 Dec 1860): 175–204.

[31] Karl Goebel, *Wilhelm Hofmeister: Arbeit und Leben eines Botanikers des 19. Jahrhunderts*, Grosse Männer 8 (Leipzig: Akademische Verlagsgesellschaft, 1924), chap. 7.

1865 textbook.[32] But Sachs' and Hofmeister's views diverged as they looked at tissue tension at ever smaller scales. Hofmeister came to believe that the cellulosic, "living cell membrane" (*die lebende pflanzliche Zellhaut*) selectively absorbed water and was ultimately responsible for transporting it into the cell and throughout the plant. In Hofmeister's eyes, this made the cell membrane the causal agent not only of tissue tension, but of plant structure and development more broadly.[33] Sachs, by contrast, believed that the protoplasm—the moving, metabolizing contents within the cell—transported or induced water to flow into the cell, developing a turgor pressure pressing outward against the cell membrane, conceptualized as a non-living protoplasmic secretion.[34] For Sachs the cellulosic cell membrane was an inert, dead structure, whereas the protoplasm was alive, moving, and the seat of vital activity in the plant as a whole. Only cells with protoplasm "can grow, develop new chemical combinations, and, under certain conditions, form new cells," Sachs argued. "Since then no further process of development can take place in the cells which no longer contain protoplasm, it may be concluded that the latter is the proximate cause of growth."[35]

This debate shaped a significant area of plant physiology for over a decade, as Sachs and his students studied protoplasm in living plant tissues to show how a relatively tiny proportion of the plant cell's mass could be responsible for the plant's growth, structure, and even movement. As Hofmeister's health and temperament declined in the 1870s, Sachs energetically recruited students to his new and lavishly appointed botanical institute at the University of Würzburg.[36] Wilhelm Pfeffer came to Würzburg in 1870 to work as Sachs'

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[32] Julius Sachs, *Handbuch der Experimental-Physiologie der Pflanzen: Untersuchungen über die allgemeinsten Lebensbedingungen der Pflanzen und die Functionen ihrer Organe*, Handbuch der physiologischen Botanik, 4. Band (Leipzig: Wilhelm Engelmann, 1865), chap. 13.

[33] Wilhelm Hofmeister, *Die Lehre von der Pflanzenzelle*, Handbuch der physiologischen Botanik, 1. Band, 1. Abt. (Leipzig: Wilhelm Engelmann, 1867), 267–72. Hofmeister's views about water movement through the cellulosic cell wall have been partially vindicated: today it is recognized that water moves through the plant through an extra-plasmatic or "apoplastic" pathway, as well as through the cytoplasmic or "symplastic" pathway.

[34] Sachs, *Lehrbuch der Botanik*, 1868 (ref. 6), 500–13, see esp. 502n.

[35] Julius Sachs, *Text-Book of Botany: Morphological and Physiological*, trans. Alfred W. Bennett, 1st English ed. (Oxford: Clarendon Press, 1875), 3; German, *Lehrbuch der Botanik: Nach dem gegenwärtigen Stand der Wissenschaft*, 3rd ed. (Leipzig: Wilhelm Engelmann, 1873), 3. The first English edition of Sachs' textbook corresponds to the third German edition, but this exact wording is also present in the first German edition of 1868 (ref. 6, p. 3).

[36] On Sachs' early career and the Würzburg institute, see Soraya de Chadarevian, "Laboratory Science versus Country-House Experiments: The Controversy between Julius Sachs

laboratory assistant, and the following year, the young Dutch botanist Hugo de Vries (1848–1935) became one of several to leave Hofmeister's laboratory in order to work with Sachs.[37] In Würzburg, Pfeffer began examining the cellular mechanics of the rapidly moving stamens found in knapweed (*Centaurea jacea*), artichoke (*Cynara scolymus*), and other plants in the *Cynareae* tribe of thistles. When Hofmeister had analyzed these rapid movements, he compared the plant cell membrane to animal muscle, with the active ability to contract and relax. In contrast, Pfeffer and the Sachsian school conceived of the cell as a protoplasmic, water-inflated balloon pressing outward on an elastic membrane. In this model, sudden plant movements were caused when a stimulus triggered the cell to rapidly expel excess water into an extracellular space, releasing the built-up elastic tension of the cell membrane.

In 1872, Pfeffer tried to measure the force exerted by contracting *Centaurea jacea* and *Cynara scolymus* stamens by tying small weights with silk thread to bundles of stamens, imitating animal muscle experiments.[38] Live, dead, and chloroformed stamens were tested for their capacity to contract, the weights serving to counteract the elastic and tensile forces exerted by the cells' membranes. Pfeffer was astonished by the "colossal" measurements he obtained, and much of his published commentary on the stamen experiments was devoted to deducing their mechanical and anatomical implications.[39] After comparing the elasticity of the dead stamens and the contractile force of stimulated live stamens, Pfeffer realized that the turgor pressure required simply to maintain a normal stamen in its pre-stimulated state was the equivalent of at least a 15-meter-tall water column (1,103 mmHg, or 1.45 atm).[40] Based on the anatomy of the stamen and the volume of a single cell, Pfeffer then suggested that each parenchyma cell in the stamen exerted at least double this

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and Charles Darwin," *The British Journal for the History of Science* 29, no. 1 (Mar 1996): 17–41; Hartmut Gimmler, ed., *Julius von Sachs in Briefen und Dokumenten, Teil 1: 1832–1868* (Würzburg: Schmitt & Meyer, 2003); and Ernst G. Pringsheim, *Julius Sachs: Der Begründer der neueren Pflanzenphysiologie, 1832–1897* (Jena: Gustav Fischer, 1932), 23–24.

[37] The best biographical sources for Pfeffer and de Vries are, respectively, Erwin Bünning, *Ahead of His Time: Wilhelm Pfeffer, Early Advances in Plant Biology*, trans. Helmut William Pfeffer (Ottawa: Carleton University Press, 1989); and Erik Zevenhuizen, "Vast in het spoor van Darwin: Biografie van Hugo de Vries" (PhD dissertation, University of Amsterdam, 2008), https://pure.uva.nl/ws/files/4287262/144074_Thesis.pdf.

[38] Wilhelm Pfeffer, *Physiologische Untersuchungen* (Leipzig: Wilhelm Engelmann, 1873), 105–16.

[39] Ibid., 120.

[40] Ibid., 119.

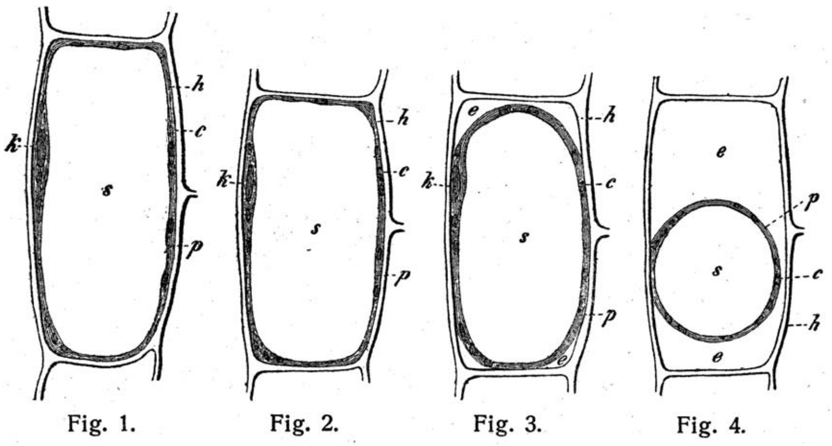

**FIG. 1.** Hugo de Vries' 1877 schematic of a plant cell and plasmolysis, showing, from left to right, a healthy cell (parenchyma cell of *Cephalaria leucantha* peduncle), and cells in 4%, 6%, and 10% potassium nitrate solutions. Today such figures are also used to explain hypo-, iso-, and hypertonic solutions, corresponding (in plant cells) to the turgid, flaccid, and plasmolyzed states. *h.* cell wall (*Zellhaut*); *p.* "protoplasmic wall-covering"; *k.* cell nucleus; *c.* chloroplast; *s.* cell sap (central vacuole); *e.* permeated salt solution. De Vries' original caption reads: "Fig. 1 and 4 after nature, Fig. 2 and 3 schematic." *Source*: de Vries, *Mechanischen Ursachen der Zellstreckung* (ref. 42), 35.

turgor pressure simply to maintain its normal state, with the cell membrane applying an equal amount of compressive tension on the cell's contents.

Hugo de Vries worked in parallel with Pfeffer to determine how the same elastic and hydraulic forces might affect the overall shape and development of a plant. Beginning in 1871 and working each summer through 1876, de Vries elaborated on the Sachsian model of the plant cell, emphasizing the spatial orientation of the cell, and showing how the protoplasm could control the relationship between the cell's interior and exterior environments (Fig. 1).[41] This image is still used in introductory biology textbooks today in some fashion, though with different terminology: an elastic shell (*h*), within which sits the living protoplasm (*p*), which itself encloses the cell sap (*s*, or in modern parlance, the central vacuole). De Vries' diagram literally illustrated life as protoplasm (*p*), discrete from the rest of the cell. What we would now clearly

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[41] On the cell as an oriented spatial field, see Grote, "Surfaces of Action" (ref. 14); Liu, "Cell and Protoplasm" (ref. 7). On the ontology of orientational metaphors more generally, see George Lakoff and Mark Johnson, *Metaphors We Live By*, 2nd ed. (Chicago: University of Chicago Press, 2003).

refer to as the cell wall, however, de Vries called the *Zellhaut* (*h*), *Zellwand*, or *Zellenmembran*, with little distinction between these terms; likewise, the inner living body was simply protoplasm, with no membranes of its own. In de Vries' model, the living protoplasm creates "resistance to filtration" by sealing off the cell sap and preventing the sugars, salts, and dyes stored within from escaping. If the protoplasm is killed, no such filtration resistance develops. Thus regulated and contained, the cell sap draws water through the *Zellhaut* and the protoplasm by osmosis, increasing its volume and causing the protoplasm to press outward against the elastic *Zellhaut*, thus creating cell turgor.[42] This spatial model also suggested a method of measuring the effect of turgor pressure on the overall growth and shape of the plant: if the osmotic flow could be neutralized or reversed, then the cell would enter into a turgorless or "plasmolytic" state, and the protoplasm would no longer stretch out the *Zellhaut* (Fig. 1, second from the left).[43] In his 1876 "cell-stretching" experiments, de Vries immersed "thin, vigorously growing organs" in salt and sugar solutions, shrinking a 10 cm shoot by 8.8 mm, and thus showing that passive water pressure alone accounted for nearly 9% of the plant's structure. In this way, de Vries was able to translate the plant's morphology through the protoplasm's physiological role in regulating the cell's spatial field.

At the time, de Vries viewed cell stretching as a mechanistic approach to a strictly biological problem, designed to reveal the relationship between water and plant vitality. As he said years later, "My main focus was always the protoplasm as the bearer of life and growth. I would often ponder well into the night how a thin, runny mass could induce and endure such pressures in the cell."[44] Five years after his cell-stretching experiments, he realized that he had nearly found a method for determining the osmotic equivalents of different solutions, if only he had paid closer attention to precisely what solute concentrations led to the isotonic state, that is to say, the border between turgid and turgorless states. In fact, de Vries' early cell-stretching experiments were so simple that they could easily have been performed a century earlier: he had hardly used the microscope, knew relatively little chemistry, and

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[42] Hugo de Vries, *Untersuchungen über die mechanischen Ursachen der Zellstreckung* (Leipzig: Wilhelm Engelmann, 1877), 28–29.

[43] Ibid., 6.

[44] Vladimir Úlehla, "Erde und Sohn: Ein Besuch bei Hugo de Vries," *Prager Presse* 15, no. 149 (2 Jun 1935): 5.

performed measurements no more granular than at the millimeter scale.[45] His only microscopic investigation was meant to show that the minimum concentration of salt or potassium nitrate solution needed to induce plasmolysis was about 4–5%, whereas for sugar solutions the minimum concentration needed to induce plasmolysis ranged from 20 to 30%.[46] But in 1876, de Vries did not bother to determine this physico-chemical minimum more exactly, because he assumed that the biological variability of living cells imposed a different set of experimental requirements:

> It is clear that for my method, only those solutions may be chosen in which all growing cells of the experimental objects become plasmolytic. It is not enough that most of them lose their turgor; turgor must be neutralized down to the very last cell. Only then will the shoot be fully tensionless, and its length correspond to the plasmolytic state. From this it follows that 5% solutions of saltpeter or table salt are usually too dilute, and that one must choose a concentration at least a few degrees higher. How much higher the concentration must be cannot be decided microscopically.[47]

For de Vries in 1876, working "a few degrees higher" than his established 5% floor was merely a way of adjusting to the natural variability and unpredictability of live plant tissues, while ensuring the salt concentrations he used were not so high as to pickle and permanently alter the sample. He believed the boundary between a plasmolyzed and turgescent cell was hazy, and depended on the species, tissue type, and even age of the plant: "The cited differences show that the border is not sharp."[48]

Nor does it seem to have occurred to de Vries in 1876 to explore why a 4–5% potassium nitrate solution and a 20–30% sugar solution would have the same effect on cells. This chemical problem had nothing to do with the natural existence of the living plant, and to de Vries it was therefore beyond the scope of a biological experiment. He only returned to osmosis research and plasmolysis in the early 1880s, after belatedly realizing that his method could be used to explore not only plant structure, but also the fundamental molecular dynamics of chemical solutions.

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[45] de Vries, *Mechanische Ursachen der Zellstreckung* (ref. 42), 36.

[46] Ibid., 49.

[47] Ibid., 51–52.

[48] Ibid., 51.

## WILHELM HOFMEISTER'S LIVING CELL MEMBRANE AND THE ARRIVAL OF COLLOID CHEMISTRY IN BIOLOGY

From the mid-nineteenth century onward, some of the most interesting debates within physiology centered not on arguments of vitalism versus mechanism per se, but rather what *kinds* of mechanisms might be found beyond the visible realm. Although Hofmeister and Sachs shared a desire to align plant physiology with contemporary physics and chemistry, deciding on *which* theories and how to apply them was a more open question than naïve reductionism would suggest. Whether one believed with Sachs that the protoplasm was the living matter, or with Hofmeister that the "living cell membrane" was the primary agent of plant growth, these positions were bound up together with developments in matter theory more broadly. Hofmeister's peculiar notion of the "living cell membrane" had its origins in his embrace of the idea of the colloidal state, developed by the Scottish chemist Thomas Graham (1805–1865) in his 1861 paper, "Liquid Diffusion Applied to Analysis."[49] Graham was already famous for showing that the rate of diffusion of a gas is inversely proportional to the square root of its molecular weight, and "Graham's law" was influential in animal respiration physiology in the 1840s.[50] In the 1840s and '50s, he tried to repeat that success in liquids, only to be lost in what his biographer called a "wilderness of facts" about fluids, diffusion, and osmosis.[51] Attempting to move forward, Graham set up a simple experiment, whereby "[a] sheet of very thin and well-sized letter paper, of French manufacture" was laid on top of a basin of water, and a solution of 5% each of sugar and gum arabic was gently poured on top of the paper. After twenty-four hours, the gum solution increased in volume by drawing water up through the paper, whereas the sugar moved down into the water below. Graham referred to the procedure as "dialysis"—"the method of separation by diffusion through a septum of gelatinous matter"—and the paper filter as a "dialyzer" (likely from the Greek διάλυσις, separation or dissolution).[52] Based on these experiments, Graham

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[49] Thomas Graham, "Liquid Diffusion Applied to Analysis," *Philosophical Transactions* 151 (1861): 183–224.

[50] Culotta, "German Biophysics" (ref. 24); Alan J. Rocke, *Image and Reality: Kekulé, Kopp, and the Scientific Imagination* (Chicago: University of Chicago Press, 2010), 14–21; Michael Stanley, "The Chemical Work of Thomas Graham" (PhD dissertation, The Open University, 1979).

[51] Michael Stanley, "Graham, Thomas (1805–1869), chemist," *Oxford Dictionary of National Biography*, online ed. (Oxford: Oxford University Press, 2008).

[52] Graham, "Liquid Diffusion" (ref. 49), 186.

operationally defined "colloids" as a broad class of materials such as "starch, dextrin and the gums, caramel, tannin, albumen, gelatine, vegetable and animal extractive matters," which sat on top of the filter and absorbed water upward through it.[53] Everything else, the "crystalloids" (e.g., salts, cane sugar, hydrochloric acid), would diffuse downward through the filter and into the water below.

The "sizing" Graham mentions does not refer to the linear dimensions of his French letter paper, but rather to the gelatinous coating applied by the manufacturer to make it suitable for writing or painting. It was the size, a "film of gelatinous starch"—not the paper's fibers—that he referred to as a "septum" and a "membrane":

> The jelly of starch, that of animal mucus, of pectin, of the vegetable gelose of Payen [i.e., cellulose], and other solid colloidal hydrates, all of which are, strictly speaking, insoluble in cold water, are themselves permeable when in mass, as water is, by the more highly diffusive of substances. But such jellies greatly resist the passage of the less diffusive substances, and cut off entirely other colloid substances like themselves that may be in solution. They resemble animal membrane in this respect.[54]

Graham's examination of the paper filter as a membrane, made by explicit analogy to animal membrane, assumed that colloids would not mix with one another: the paper filter in the dialysis experiment resists the passage of the gum arabic because both are colloids.

In addition, Graham conceived of this thin membrane as an active, catalyzing agent of osmosis. He described the membrane as a meso-mechanical pump: "The inner surface of the membrane of the osmometer contracts by contact with the saline solution, while the outer surface dilates by contact with pure water."[55] Graham ascribed this contracting and dilating action to colloids more generally, moreover stating that "the colloidal is, in fact, a dynamical

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[53] Ibid., 185. Stanley notes that Graham never explained why he chose the word "colloid," though later chemists believed Graham had derived it from the Greek *κολλα*, for glue; Stanley, "Chemical Work" (ref. 50), 330n.137. Terms like "colloid," "colloid corpuscles," or "colloidal cancer" had previously been used in pathology to describe the translucent, granular, and sickly material produced when tissues decomposed.

[54] Graham, "Liquid Diffusion" (ref. 49), 185. After the food industry, the paper industry today is the leading consumer of manufactured starch.

[55] Ibid., 223. I am using the term "meso-mechanical" here to differentiate between this and a truly micro-mechanical description based on the billiard-ball movements of atoms or molecules. Graham, a committed atomist, provided both in the "Liquid Diffusion" paper.

state of matter, the crystalloidal being the statical condition." He added a vitalist flourish, "The colloid possesses ENERGIA. It may be looked upon as the probable primary source of the force appearing in the phenomena of vitality."[56] In other words, Graham argued that colloids could move water and crystalloids of their own accord, without significantly changing their own composition.

Graham's theory of colloids was read before the Royal Society in London on June 13, 1861, and it was translated and published in Wöhler and Liebig's *Annalen der Chemie und Pharmacie* in January 1862.[57] Within months Graham's paper was noticed by the German plant physiologists: first by Sachs, who wrote a very short summary for the February 28th issue of the general botanical journal *Flora*, and by Hofmeister in the November 10th and 20th issues.[58] (By contrast, the animal physiologists barely gave the paper notice.[59]) Whereas Sachs noted that the distinction between crystalloids and colloids might be useful for describing assimilation and nutrition, Hofmeister believed that Graham provided a basis to add physical detail to his theory of tissue tensions and cell turgor. Hofmeister associated Graham's colloidal "membrane" filter with the "membrane" of plant cells, and then redefined plant cell membranes as colloids. Echoing Graham's meso-mechanical description of osmosis as a catalytic process, he described plant cell membranes as actively absorbing, constituting, and pumping water from one side to the other.

> The living plant membrane [*die lebende pflanzliche Zellhaut*] is able to expel a portion of the water which constitutes it when acted upon by minor outside influences, and also to absorb a corresponding amount of water when left undisturbed for some time—both phenomena accompanied by a corresponding increase or decrease in volume. This ability is not an

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[56] Ibid., 184. I have not found any contemporary biologist who explicitly endorsed or adopted this particular idea until the early 1900s; this passage is quoted without further comment in Wilhelm Hofmeister, "Ueber die Mechanik der Reizbewegungen von Pflanzentheilen," *Flora, oder allgemeine botanische Zeitung* 45, nos. 32–33 (10 & 20 Nov 1862): 497–503, 513–17, on 500.

[57] Thomas Graham, "Anwendung der Diffusion der Flüssigkeiten zur Analyse," *Annalen der Chemie und Pharmacie* 121, no. 1 (Jan 1862): 1–77.

[58] Julius Sachs, "Ergebnisse einiger neueren Untersuchungen über die in Pflanzen enthaltene Kieselsäure," *Flora, oder allgemeine botanische Zeitung* 45, no. 5 (28 Feb 1862): 65–71; Hofmeister, "Die Mechanik der Reizbewegungen" (ref. 56).

[59] The first mention of either colloids in general or Graham's paper in particular did not appear in Müller's *Archiv* until 1886, and then only as a glancing reference in Friedrich Bidder, "Experimentelle und anatomische Untersuchungen über die Nerven der Glandula submaxillaris," *Archiv für Anatomie, Physiologie und wissenschaftliche Medicin*, 1886, 321–58.

> isolated quality of the vegetable membrane, but rather one which can be attributed very generally to colloidal substances.[60]

This equation of the colloids and the "living plant membrane"—again, what we now call the cell wall—led Hofmeister to reconceptualize the membrane as an active agent in plant life rather than a passive one. Most other botanists had thought of the cell wall as a dead structure merely secreted by the protoplasm: indeed for Sachs and many others, the solidity and immobility of the cell wall was what defined plant against animal life.[61] Hofmeister's treatment of the cell wall as a *living* part of the plant cell promised to keep botany up-to-date with the latest in chemical theory, but it also threatened to destabilize one of the most important recent developments in plant cell and protoplasm theory.

Hofmeister's idiosyncratic view of the plant cell membrane culminated in his controversial 1867 monograph *Die Lehre von der Pflanzenzelle*—the book that infuriated Sachs and prompted him to assign Pfeffer and de Vries their early research projects. Hofmeister's membrane-centric view of cell turgor was a scaled-down vision of the processes he observed in tissue tension, with one elastic, water-saturated membrane bound to a more rigid, drier one. "Because of their stronger water absorption, the inner layers expand more forcefully in tangential and radial directions than the outer layers . . . which creates tension in the cell membrane [*Zellmembran*]," Hofmeister argued. "This relationship causes turgor of the cell membrane, independent of the endosmotic force of the cell contents."[62] For Sachs, Pfeffer, and de Vries, a vital phenomenon like growth had to be explained through the proximate mechanisms of protoplasmic action. For Hofmeister, however, a botanist had to use the whole plant to explain the activities of its cells and protoplasm: in other words, Sachs, Pfeffer, and de Vries had it backwards. "The formation of new cells," Hofmeister insisted, "is a function of general growth, not its cause."[63] By placing greater

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[60] Hofmeister, "Die Mechanik der Reizbewegungen" (ref. 56), 503.

[61] Liu, "Cell and Protoplasm" (ref. 7), 919.

[62] Hofmeister, *Lehre von der Pflanzenzelle* (ref. 33), 267. In *Die Lehre von der Pflanzenzelle* Hofmeister did not repeat his 1862 suggestion that the living plant cell membrane was a colloid, and instead used the awkward term "capacity for water" (*Wassercapacität* or *Capacität für Wasser*) in an attempt to quantify the forces at work within the membrane. As a result, Hofmeister was known for having applied Graham's colloid theory to protoplasm theory, and not cell membrane theory; see Goebel, *Wilhelm Hofmeister* (ref. 31), 102–03, 120; A. G. Morton, *History of Botanical Science* (London: Academic Press, 1981), 421.

[63] Hofmeister, *Lehre von der Pflanzenzelle* (ref. 33), 129. By the late 1870s, the view that the plant creates its cells became widely held as a consequence of protoplasm theory. Many botanists credited Hofmeister for this crucial reversal, e.g., in Anton de Bary, review of *Lehrbuch der*

emphasis on a living cell membrane that was continuously reticulated throughout the plant, Hofmeister could make the plant's cells subordinate to a theory of plant life as a whole. Graham's theory of colloids had given him the vocabulary and imagery to make it work.

## MORITZ TRAUBE'S ARTIFICIAL AND INORGANIC CELLS

Although Hofmeister and the Sachsian school vehemently disagreed about the causal relations between the parts of plant tissues, they agreed on three crucial points: that the plant cell had a single, cellulosic membrane; that plant physiologists applied physical laws and methods *to* living plants; and that the living part of the cell, whether it was protoplasm or living membrane, was responsible for cell turgor. Likewise, Graham theorized and experimented extensively on the nature of physical processes, but made only speculative gestures as to how his physical chemistry might be applied in other domains. This disciplinary divide has always been difficult to cross, which made it all the more remarkable when in 1864, the chemist Moritz Traube announced he had invented an "artificial cellular formation" (*künstlichen Zellenbildung*), argued that nonliving matter could generate cell turgor, and fully committed himself to creating biological theories from chemical experiments—even before he renamed his object an "artificial cell" (*künstliche Zelle*) in 1866 and an "inorganic cell" (*anorganische Zelle*) in 1874. Whereas plant physiologists had been coaxing living specimens into displaying osmotic phenomena, from the beginning Traube intended his artificial cell to demonstrate the broader physical workings of a stable colloidal membrane, one that separated an interior from an exterior chemical environment. Traube never claimed to have actually created life, though his artificial cell arguably represents a chapter in the long history of attempts to do so. Instead, Traube claimed that real living cells and his artificial cell exhibited identical molecular mechanics, and he did so through the Berlin circle's now-common argument that physical and chemical principles necessarily hold true in biology. But the historical riddle of Traube's artificial cell is why it never became a legitimate biological object, despite his experiments,

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*Botanik für mittlere und höhere Lehranstalten*, by Karl Prantl, *Botanische Zeitung* 37, no. 14 (4 Apr 1879): 221–23. Even Sachs came around to this view by the time of Hofmeister's death in 1877; Julius Sachs, "Ueber die Anordnung der Zellen in jüngsten Pflanzentheilen," in *Arbeiten des botanischen Instituts in Würzburg*, 2. Band (Leipzig: Wilhelm Engelmann, 1884), 46–104; and *Vorlesungen über Pflanzen-Physiologie*, 1st ed. (Leipzig: Wilhelm Engelmann, 1882), chap. 27.

arguments, and rhetorical incantations. Although Traube hoped to breach the category of "life" through his theory of invisible molecular mechanics, he lost the ensuing debate with the plant physiologists over the legitimacy of a *comparison* between artificial cells and living cells. The botanists, against Traube, continued to insist on the genetic, taxonomic, and physiological distinctions between living protoplasm and non-living matter—and, eventually, the disciplinary line that divided biology from everything else.

Traube was the second son of a family of Jewish wine merchants in Ratibor (in Prussian Silesia, now Racibórz, Poland), and in 1842 his father sent him to Berlin, to follow in the steps of his elder brother Ludwig (1818–1876) and pursue a medical education. Moritz quickly abandoned medicine, traveling instead to Giessen to study chemistry with Justus Liebig, then returned to Berlin in 1847, where he and his brother both joined the Berlin Physical Society, the institutional home of the Berlin circle of physiological reductionists. In 1849, Moritz took up the family business in Ratibor, where he set up a small chemistry laboratory in his attic and became one of the leading interlocutors in mid-century biological chemistry.[64] Traube invented what would become the artificial cell in 1864, while exploring Thomas Graham's "Liquid Diffusion" paper. Graham had argued that colloids do not diffuse into one another, though he only reported exploring the mutual diffusion of colloids of similar concentration (2% gelatin, 5% gum arabic, etc.). Traube's initial experiment was to place a 50% "solution" of gelatin (really more of a sticky lump) in a 5% solution of tannic acid.[65] Upon dropping the gelatin ball into the tannic acid, Traube was surprised to discover that

> The ball, with a weight of 1.8 g and a diameter of 14.5 mm, coated itself with a dirty-grey, nearly opaque coating of gelatin-tannate, within which the jelly

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[64] On Traube's theory of fermentation, see Fruton, *Molecules and Life* (ref. 22), 81–02, 291–94; and Theodore L. Sourkes, "Moritz Traube, 1826–1894: His Contribution to Biochemistry," *Journal of the History of Medicine and Allied Sciences* 10, no. 4 (1955): 379–91. Biographical details can be found in Henrik Franke, *Moritz Traube (1826–1894): Vom Weinkaufmann zum Akademiemitglied, der aussergewöhnliche Weg des jüdischen Privatgelehrten und Pioniers der physiologischen Chemie*, Studien und Quellen zur Geschichte der Chemie, Bd. 9 (Berlin: Verlag für Wissenschafts- und Regionalgeschichte, 1998); and Guido Bodländer, "Moritz Traube," *Berichte der deutschen chemischen Gesellschaft* 28, no. 4 (1895): 1085–1108. On the Traube brothers' membership in the Berlin Physical Society, see Annett Fiedler, *Die Physikalische Gesellschaft zu Berlin: Vom lokalen naturwissenschaftlichen Verein zur nationalen Deutschen Physikalischen Gesellschaft (1845–1900)* (Aachen: Shaker, 1998), 38; and Wise, *Aesthetics, Industry, and Science* (ref. 24), chap. 6.

[65] Traube used the German word *Leim*, which today simply means "glue." The closest equivalent is hide glue used for traditional woodworking.

> swelled, while maintaining its consistency, such that after 13 days the ball had a weight of 6.5 g and a diameter of 22.5 mm.[66]

Traube had expected that the ball of gelatin would simply sit, either refusing to diffuse, or diffusing out into the solution only very slowly, as Graham had predicted a few years earlier. Instead, its newly formed coating effectively protected the gelatin, allowing it to absorb water from the tannic acid solution, while also preventing the gelatin itself from diffusing out into its more dilute environment. Whereas the laboratory ideal in ordinary chemical synthesis and analysis was to completely transform reactants into a product, Traube had created a semi-stable system that lasted for weeks, one whose reactants produced a barrier that prevented further reaction or mixing.

Traube quickly perceived that the coating behaved like the paper "membranes" that Graham had used in his dialyzer experiments, despite that "the matte, opaque skin that formed had no resemblance to the transparent, homogenous membranes seen in young animal and plant cells."[67] Sensing that he was mere steps away from creating something more visually suggestive, his subsequent experiments were designed to mimic the transparency and tenacity of real cells, while also using materials that had a runniness similar to the slimy protoplasm found in cells. Working intuitively with varying mixtures of gelatin, tannic acid, and salt, Traube mixed, cooked, dried, diluted, and stirred his materials, trying to generate imitation cells essentially by trial and error, through texture and appearance rather than any obvious chemical or physical reasoning.

When Traube published his first artificial cell paper in 1864, he already believed he had discovered the basic process by which living cells formed their membranes. Just as gelatin would precipitate a membrane upon contact with tannic acid, Traube argued that protoplasm must precipitate a membrane upon contact with water, or whatever other fluid surrounded the protoplasm. Solely from his experiments with artificial cells, Traube felt confident in declaring that "membrane-less" cells consisting only of protoplasm could not exist: if living protoplasm was anything like his non-living membrane-formers, then it would always exist in a membrane-bound state, with the membrane acting as the catalyst for growth by osmosis. After all, Traube reasoned, since

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[66] Moritz Traube, "Experimente zur Theorie der Zellenbildung," *Centralblatt für die medicinischen Wissenschaften* 2, no. 39 (10 Sep 1864): 609–15, on 610. Traube referred to the unexpectedness of this first experiment again in 1874; see note 86.

[67] Ibid., 611.

protoplasm was a slimy, gelatinous substance, then it must be a colloid, and behave much like his colloidal gelatin, forming membranes and individuating itself upon contact with other substances. Traube thus argued that the process by which his gelatin ball created its own cell was identical to the way protoplasm individuated itself into cells: "On the one hand, the protoplasm serves to establish the cell space through its endosmotic force, on the other hand it contributes to the formation of the cell membrane. In turn, by circumscribing the contents of the cell without completely excluding it, it makes it a small chemical workshop and enables the cell to live a life distinctly different from that of other adjacent cells."[68] Just as living cells grew by bringing in water through their membranes and into their protoplasm, so too did Traube's artificial cells grow by bringing in water from the environment, through the colloidal membrane, and into the body of the gelatinous drop. "As soon as a new particle of the protoplasm, which is expanding through endosmose, comes into contact with the surrounding fluid, it will immediately become solid and transform into membrane substance," Traube wrote, directly following the sentence with the unambiguous if parenthetical remark, "(Intussusception)."[69]

By referring to the artificial cell's method of growth as intussusception, Traube attacked the old concepts that divided organic from mineral growth, the distinction between growth by apposition—the addition of layers of material to the outside surface of a crystal—and growth by intussusception, or the intercalation and assimilation of new material from within an organic body.[70] By 1866, Traube called his objects "artificial cells." "Intussusception" lost its parentheses, and he began referring to the colloidal solutions he was using as "membrane formers."[71] In doing so, Traube tried to close the conceptual space between his precipitation membranes and real living cells, relocating vital agency to non-living matter while also de-vitalizing the living cell. The distinction between intussusception and apposition had long made intuitive

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[68] Ibid., 614–15. On the mechanistic metaphor of the cell as a chemical laboratory, workshop, or factory, see Reynolds, *The Third Lens* (ref. 7), chap. 2,

[69] Traube, "Experimente zur Theorie der Zellenbildung" (ref. 66), 614.

[70] Boris Demarest and Charles Wolfe argue that the distinction between organic growth by intussusception and mineral or crystalline growth by apposition was first made in 1720 by Louis Bourget, and quickly picked up by Buffon, Linnaeus, Lamarck, and others as a firm line between the living and the non-living; "The Organism as Reality or as Fiction: Buffon and Beyond," *History and Philosophy of the Life Sciences* 39, no. 1 (Mar 2017): 6n.5.

[71] Moritz Traube, "Ueber homogene Membranen und deren Einfluss auf die Endosmose," *Centralblatt für die medicinischen Wissenschaften* 4, nos. 7–8 (10 & 17 Feb 1866): 97–100, 113–15.

sense: minerals grow by exterior accretion in a way a child does not. For Traube, the fact that his artificial cells grew without visibly thinning their membranes proved that they grew by intussusception. Chemists from Lavoisier to Liebig had used relatively simple in vitro experiments to make inferences about physiological phenomena, and these in vitro inferences were often combined with quantitative intake-output experiments on whole organisms, or at least were used to develop methods of chemical experimentation on living specimens.[72] Yet in the 1860s Traube's experiments were highly unusual, and likely entirely novel, in that the evidence that his artificial cells grew by intussusception was their superficial, visual imitation of cellular growth. This novelty was compounded by the fact that Traube never reported any observations of nor experiments on living cells in order to test, or even make comparisons between the two.

Instead of relying on visual comparison, Traube imagined a molecular mechanism at work in his membranes, one which echoed the mechanical processes Carl Nägeli (1817–1891) had described in the 1850s in starch granules.[73] Modifying Graham's description of a dilating colloidal membrane, Traube hypothesized that membranes allowed water in by osmosis through invisible pores, which stretched wider as the contents of the (artificial) cell increased and pressed outward; as soon as the pores were large enough to fit them, molecules of membrane formers would rush in from both the inside and the outside of the cell, creating new membrane substance within the pore. Traube insisted that this internal deposition and growth by intercalating particles "is that which the physiologists call 'intussusception,' the hitherto enigmatic growth process of cell membranes, which through our experiments finds a physical explanation that is as complete as it is simple."[74] Equipped with

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[72] Frederic L. Holmes, "Elementary Analysis and the Origins of Physiological Chemistry," *Isis* 54, no. 1 (Mar 1963): 50–81; Frederic L. Holmes, "The Intake-Output Method of Quantification in Physiology," *Historical Studies in the Physical and Biological Sciences* 17, no. 2 (1987): 235–70.

[73] Carl Nägeli, *Die Stärkekörner: Morphologische, physiologische, chemisch-physicalische und systematisch-botanische Monographie* (Zürich: Friedrich Schulthess, 1858). On Nägeli's micellar theory, see J. S. Wilkie, "Nägeli's Work on the Fine Structure of Living Matter," *Annals of Science* 16–17 (1960–61): 11–42, 171–207, 209–38, 27–62; and Brigitte Hoppe, "Die 'mechanische Molekularphysiologie' der Stärkekörner, eine Erörterung zwischen C. W. Nägeli und S. Schwendener, 1881/1882," in *Biology Integrating Scientific Fundamentals: Contributions to the History of Interrelations Between Biology, Chemistry, and Physics from the 18th to the 20th centuries*, ed. Brigitte Hoppe, Algorismus 21 (Munich: Institut für Geschichte der Naturwissenschaften, 1997), 331–53.

[74] Moritz Traube, "Experimente zur Theorie der Zellenbildung und Endosmose," *Archiv für Anatomie, Physiologie, und wissenschaftliche Medicin*, 1867, 87–165, on 110.

a micro-mechanical process, Traube argued that all membranes grew by intussusception, not only the ones formed by his artificial (albeit organic) gelatin tannate cells, but those of living cells as well. Though he never claimed his artificial cells were alive—they obviously lacked nuclei, did not metabolize nutrients, and did not reproduce—Traube argued that they, like living cells, "grew" by intussusception.

In short, Traube argued that his artificial cells followed the same molecular-mechanical process that living cells did. "Until now, no one knew of any physical process that displayed even a distant similarity to this vital phenomenon," Traube wrote in 1867; "It is hardly to be expected that a second physical process will be found that will be able to show in its entirety a similarity with organic cell formation."[75] He began to add to the list of substances that could create membranes: besides gelatin, Traube succeeded in making membranes using inorganic, metallic compounds of mercury, potassium, copper, and barium.[76] Of the inorganic artificial cells, those made of copper ferrocyanide were the most convincing. These were produced by a mixture of copper chloride and potassium ferrocyanide ("yellow prussiate of potash"), the well-known ingredients for the colloidal pigment Prussian blue.[77] Though he believed that the colloidal, membrane-forming substances themselves worked to build both the membranes and the cell-like structures, his rhetoric belied the fact that he was increasingly interventionist in the creation and arrangement of his experiments, as he tried to improve his ability to mimic and imitate the appearance of real cells. For example, the copper ferrocyanide cells tended to "erupt" upward quickly, in an un-lifelike way.[78] Traube had to develop a "*Kunstgriff*"—an artifice or trick, though the word was originally used to

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[75] Ibid., 158–59.

[76] Traube, "Ueber homogene Membranen" (ref. 71) 98–99.

[77] Cf. Laura M. Barge et al., "From Chemical Gardens to Chemobrionics," *Chemical Reviews* 115, no. 16 (26 Aug 2015): 8652–8703. Barge et al. link Traube's use of copper salts to seventeenth-century alchemical "chemical gardens," admired by Robert Boyle, Isaac Newton, and other alchemists as imitations of living forms. However, Traube never mentions Newton or alchemy. It therefore seems more likely that the commonplace production of the pigment Prussian blue—with its precursor stage as a gummy, colloidal mass—was the inspiration for Traube's inorganic cells.

[78] So-called Traube cells of erupting copper ferrocyanide columns are sometimes used in classroom chemistry demonstrations today, e.g., "How to grow an artificial cell from water and salts ('Traube Cell' experiment)," MEL Science, 23 Aug 2017, YouTube video, 1:22, https://youtu.be/n5O549CM3Kk.

describe wrestling moves—of lowering and raising pipettes containing membrane-formers to make them grow as cell-like bubbles.[79]

Traube published the broadest exploration of his artificial cell experiments in 1867, in Reichert and du Bois-Reymond's *Archiv für Anatomie, Physiologie und wissenschaftliche Medicin*, at the time the most important German-language animal physiology journal.[80] It moldered in the pages of the *Archiv* until 1872, when Julius Sachs wrote a lengthy summary of it in the third edition of his *Text-Book of Botany.*[81] Sachs' generally positive appraisal of Traube's artificial cell experiments was in keeping with his own apparatus-driven approach.[82] He particularly praised Traube's experiments with gelatin artificial cells for shedding light on the molecular structure of the cellulosic cell membrane, and his theory of osmosis via the membrane's invisible pores. "These researches," Sachs wrote, "are of extreme importance in reference to vegetable physiology," and he was particularly glad that Traube had connected Nägeli's theory of growth by intussusception to Graham's theory of colloids.[83] For Sachs, Traube's experiments provided additional ammunition in his running argument against Hofmeister, showing that pressure from within the cell caused cell wall growth—i.e., that fluid flowing into the artificial cell meets its contents and forms new membrane as the existing membrane stretches to accommodate its greater volume.[84]

But Sachs did not believe that Traube's copper ferrocyanide cells displayed intussusception, and he denied that such inorganic cells had any biological relevance. Moreover, he did not believe Traube's "trick" for preventing the copper ferrocyanide membranes from erupting had made them more cell-like. Sachs repeated Traube's trick, but then he pricked the membrane, observing as the green copper chloride flowed out, immediately becoming "coated with a pellicular precipitate which appears either as an intercalated piece of the previous one, or as an excrescence or branch of it." Sachs then drew a sharp

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[79] Traube, "Zellenbildung und Endosmose" (ref. 74), 137.

[80] Traube's treatise was noticed by animal physiologists in the early 1870s, but their commentary was minimal. Exceptionally, the physiologist Alfred Gruenhagen used Traube's precipitation membrane to illustrate why purely physico-chemical models had to date failed to explain physiological phenomena: *Die electromotorischen Wirkungen lebender Gewebe* (Berlin: Otto Müller, 1873), 2.

[81] On the importance of Sachs' textbook, see Anton de Bary, review of *Lehrbuch der Botanik, zweite Auflage*, *Botanische Zeitung* 28, no. 45 (11 Nov 1870): 724–25. The first French and English editions were translated from the third German edition in 1874 and 1875, respectively; see note 35.

[82] de Chadarevian, "Laboratory Science versus Country-House" (ref. 36).

[83] Sachs, *Text-Book of Botany*, 597 (ref. 35); German, *Lehrbuch der Botanik*, 1873, 583.

[84] Ibid., 729–30; German, 718.

distinction between the copper ferrocyanide cell on the one hand, and the gelatin cell and living plant cells on the other: "We cannot therefore in this case conclude that deposition of fresh molecules of the pellicle takes place in between those already in existence. These cells cannot, so to speak, be injured."[85] For Sachs injury, growth, and regeneration were related vital phenomena, sharing the same mechanical-molecular processes, i.e. growth by intussusception; since the inorganic copper ferrocyanide membrane did not grow by intussusception, it could not speak to issues of plant vitality.

In the years following, what began as a minor disagreement over a technical problem escalated into an argument over the artificiality and vitality of Traube's artificial cells more generally. Although Sachs had given Traube's artificial cells a prominent and mostly complimentary platform, Traube was frustrated that Sachs had construed his theory so narrowly: Traube believed his copper ferrocyanide experiments were crucial in showing that his mechanical theory of intussusception was truly universal across all organic and inorganic chemical domains. Following the publication of the fourth edition of Sachs' textbook in the middle of 1874, Traube sought to secure ever broader claims for his artificial cells, pressing his case that September at the meeting of the Gesellschaft Deutscher Naturforscher und Ärzte (GDNÄ; Society of German Natural Scientists and Physicians) in Breslau. Ten years after creating his first "artificial cells," Traube renamed his objects *anorganische Zellen*, or "inorganic cells." Abandoning his earlier terminology, Traube now stated, "They are not artificial cells, as they have been called, but rather structures occurring under certain conditions which make growth possible, developing into different forms depending on the composition of the precipitation, the influence of their coherence, and various agents, e.g. gravity and light."[86] He forcefully argued that "the formation of membrane-bound cells, endosmosis, growth, and the capacity for intussusception are not just peculiar to the organic world, but occur in the interaction of inorganic masses as well."[87] He believed his theory represented "the simple and complete explanation of the hitherto mysterious vital process of intussusception, which was long considered to be the characteristic feature of the growth of

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[85] Ibid., 597–98; German, 583–84. *Niederschlagsmembran* was translated as "pellicle" in the English edition, hence the odd phrase "pellicular precipitate."

[86] Moritz Traube, "Experimente zur physikalischen Erklärung der Bildung der Zellhaut, ihres Wachsthums durch Intussusception und des Aufwärtswachsens der Pflanzen," in *Tageblatt der 47. Versammlung deutscher Naturforscher und Aerzte in Breslau, vom 18. bis 24. Sep 1874* (Breslau: E. Morgenstern, 1874), 191–99, on 192.

[87] Ibid.

organisms, versus the growth of inorganic crystals, which increase by apposition."[88] He performed a demonstration of the copper ferrocyanide membrane at the GDNÄ meeting, precipitating a copper ferrocyanide cell and tilting its glass container to show how it could grow in a way that evoked young bean shoots.[89] Reiterating that the living and the non-living obeyed the same physical and chemical laws, Traube ended his lecture with a flourish: "The ropes that Bramante used to lift and move the enormous obelisk in Rome were, in the last, nothing more than chemical precipitations in the form of bast cells."[90]

Traube's performance at the GDNÄ and his rhetorical shift of vitality away from "life" found at least one sympathetic ear in Karl Marx, and artificial cells made a cameo appearance in Frederich Engels' *Anti-Dühring* (1878) as an example of materialist scientific practice triumphing over the "meaningless gibberish" of Eugen Dühring's philosophical definition of life.[91] Traube himself was even more explicit in claiming to have collapsed the distinction between living and non-living matter in a letter he wrote to Charles Darwin, which he sent along with copies of his artificial cell papers in 1875. Linking Darwin's rejection of special creation to his own rejection of the separation between the organic and the inorganic, Traube wrote:

> Your successful endeavour to free the complexity of organic nature from the miracle of many particular creations and to trace it back to natural causes is clearly closely related to that school of natural science that endeavours to demonstrate that processes considered to be specific to life are simply physico-chemical processes . . . In this sense one could conclude from my investigations that the organisms which first appeared with cells surrounded by a membrane did not receive this ability to form cells as a new power, but rather borrowed it from inorganic nature.[92]

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[88] Ibid., 195.

[89] Ibid., 198.

[90] Ibid., 199. Traube was referring to the obelisk in St. Peter's Square, relocated and raised by the architect Domenico Fontana in 1585–66, which he recounted in *Della trasportatione dell'obelisco Vaticano* (Rome: Domenico Basa, 1590). Donato Bramante was the architect of St. Peter's Basilica but had nothing to do with the obelisk.

[91] See letters from Marx to Pyotr Lavrov, London, 18 Jun 1875, and Marx to Wilhelm Alexander Freund, London, 21 Jan 1877, in *Marx & Engels Collected Works*, vol. 45 (Moscow: Progress Publishers, 1991), 78, 191–92; Friedrich Engels, *Anti-Dühring: Herr Eugen Dühring's Revolution in Science*, trans. Emile Burns (New York: International Publishers, 1939), 90–91.

[92] Traube to Charles Darwin, Breslau, 2 Mar 1875 (Letter no. 9878), in *The Correspondence of Charles Darwin*, vol. 23, ed. Frederick Burckhardt et al. (Cambridge: Cambridge University Press, 2015), 93–95, 528–29.

Traube did not claim any particular credit for mastering an art of creating cells. Instead, he argued that the vital phenomena of growth and membrane formation could be found in matter generally and not only in living matter, granting to copper ferrocyanide and all other colloids a capacity that had previously been given only to living—or at least organic—matter. In the language of mid-nineteenth-century natural science, Traube thus claimed to have discovered the mechanical law of cell growth, the "process of growth of the cell membrane [*Zellhaut*] by intussusception, as well as the growth of organic cells in general."[93]

But such generalizing from chemical or physical theory to botanical fact required rhetorical, experimental, and disciplinary resources that Traube did not fully possess. In 1878, Traube tried to launch a priority dispute against Sachs and de Vries, after de Vries had credited Sachs for a theory of cell membrane growth in his cell-stretching monograph. Traube insisted that he had understood the physiological importance of cell turgor as early as 1867, and that Sachs and de Vries needed to credit him for discovering the physiological significance of, as Traube put it, "osmotic swelling of the cell contents (of turgor)," for providing a physical explanation of intussusception, and "the intertwining of both processes [osmosis and growth by intussusception] as the cause of cellular growth."[94] (Traube had never used the word "turgor" before 1878.)

Traube's most interesting claim against Sachs was that, with the inorganic (*née* artificial) cell, physicists and chemists like himself had surpassed the professional "*Botaniker von Fach*" in their knowledge of osmosis, chemical precipitations, and micro-mechanics.[95] Physics and chemistry, Traube argued, could legitimately supply the "general mechanical laws of cellular growth," and moreover "it would be unnecessary, indeed wrong, and offends the universally valid principles of natural science to seek another explanation for these vital phenomena."[96] In other words, the botanists had to accept his conclusions because the mechanical laws he discovered as a physicist and chemist extended to biology as well. Traube mocked Sachs' inability to create cells that were

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93. Moritz Traube, "Zur Geschichte der mechanischen Theorie des Wachsthums der organischen Zellen," *Botanische Zeitung* 36, no. 16 (19 Apr 1878): 241–46, on 242.

94. Ibid., 244.

95. Moritz Traube, "Zur mechanischen Theorie des Zellwachsthums und zur Geschichte dieser Lehre," *Botanische Zeitung* 36, nos. 42–44 (18 Oct–1 Nov 1878): 657–63, 673–85, 689–99, on 659.

96. Ibid., 690, 691.

strong enough to resemble turgid plant cells, noting the challenge of mastering the technique.[97] At the same time, Traube insisted that his inorganic cell was evidence of "living forces" (*lebendige Kräfte*) operating universally across biological and chemical domains, and that the existence of such forces obviated any tricks or devices that the experimenter needed to deploy to reveal the fundamental phenomenon. Writing entirely unironically, Traube declared that "in the production of inorganic cellular vesicles [*anorganischer Zellbläschen*] the experimenter is not active, as in the production of artificial instruments, but rather only living forces, which emanate from and are generated by substances acting upon each other."[98]

If Traube hoped to win an argument based on his theory of molecular mechanics, then Sachs' derisive response aimed to assert the vast distance that separated living and artificial cells, and the analogous distance between biology and chemistry. Sachs noted that Traube had not made an artificial cell using cellulose or any other botanically related materials (an argument that also, in hindsight, highlights the historical ambiguity of the term "membrane"). Even if one construed plant cells as being bound by a precipitation membrane, Sachs noted that cellulose membranes like those in plants were demonstrably too porous to withstand any turgor pressure without a living protoplasmic lining, as de Vries had just shown.[99] Had Traube been a real botanist, Sachs insinuated, such a basic fact would have been obvious. Real plant cells had as much in common with Traube's artificial cells "as artificial [*gemachte*] flowers have with real ones . . . Plant cells do not only grow in surface area, but in thickness, they develop pits, spiral bands, etc.," Sachs wrote. "What little Traube can say about them is based on a mere analogy with 'inorganic cells,' an analogy whose scientific validity is both doubtful and unproven by Traube. In any case Traube probably cannot be the judge, since his writings suggest that real plant cells are only superficially known to him."[100]

[97] Traube, "Geschichte der mechanischen Theorie des Wachsthums" (ref. 93), 243.

[98] Traube, "Zur mechanischen Theorie des Zellwachsthums" (ref. 95), 673–74. Traube's "living forces" were "1) the affinity of the two membrane builders [*i.e.*, the gelatin and tannic acid] for one another, 2) through the prevailing affinity of the inner membrane builder for water."

[99] Julius Sachs, "Zur Geschichte der mechanischen Theorie des Wachsthums der organischen Zellen," *Botanische Zeitung* 36, no. 20 (17 May 1878): 308–16.

[100] Ibid., 309–10. On Sachs' frequent criticisms of "unprofessional" botanists, see de Chadarevian, "Laboratory Science versus Country-House Experiments" (ref. 36); and "Zur Konstruktion des Amateurs in der Botanik des 19. Jahrhunderts: Julius Sachs versus Charles Darwin," in *Dilettanten und Wissenschaft: Zur Geschichte und Aktualität eines wechselvollen Verhältnisses*, ed. Elisabeth Strauß (Amsterdam: Rodopi, 1996), 95–122.

These debates—about skills, the distinction between "growth" and "eruption," and invisible molecular processes—were ones Traube would not win with his preferred style of argument. He had never undertaken any particularly detailed comparison of real cells to his artificial ones to, as Sachs put it, validate the analogy. It is hard to say if any experiment could have shown that living and artificial cells "grew" by the same process: in hindsight, no molecular-mechanical theory of growth was empirically accessible. In his fight with Sachs, all that remained was each man's force of will and their disciplinary authority, which Sachs had and Traube did not. Traube had asserted that his mechanical law prevailed across living and non-living matter, making any comparison between living and artificial cells unnecessary. But biologists and physical chemists would soon discover that the artificial cell's success was to be found precisely in comparison and analogy.

## WILHELM PFEFFER, THE PLASMA MEMBRANE, AND THE MAKING OF VAN 'T HOFF'S LAW OF DILUTE SOLUTIONS

From 1873 to 1877, Wilhelm Pfeffer refashioned Traube's artificial cell into a highly sensitive osmometer, imitating the structure and behavior of living plant cells by precipitating Traube's cell into a porcelain pot. For roughly thirty years Pfeffer's adaptation of Traube's artificial cell would remain the standard method for direct determination of osmotic pressure.[101] Pfeffer's artificial cell osmometer effectively reproduced with non-living copper ferrocyanide what he had previously hoped to measure in live plant specimens. In early 1872, Pfeffer had concluded that rapid plant movements were due to the mechanical relationship between hydrostatic pressure within the cell and the high tensile force exerted by the cell membrane/wall. But he was unsatisfied with the wide range of measurements he obtained with live *Cynareae* stamens, and after leaving Sachs' laboratory in 1872 for a professorship in Marburg, he began looking for a way to make a more precise determination of cell turgor pressure. Of the "many atmospheres" of turgor pressure at work in the plant cell, Pfeffer wanted to know what proportion was due to the active intervention of the living protoplasm and what portion might be due to passive, physical osmotic

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[101] Findlay, *Osmotic Pressure* (ref. 21), chap. 3. Later improvements to Pfeffer's copper ferrocyanide artificial cell osmometer increased its physical rigidity and temperature resistance (>60°C).

forces.[102] Despite the centrality of turgor pressure in the debates between Hofmeister, Sachs, and later Traube, nobody had attempted to measure the pressures involved: the benchmark measurements of osmotic pressure up to the 1870s had been performed by Henri Dutrochet (1776–1847) in the 1820s and '30s, using an animal bladder stretched across the end of a funnel. The resulting low measurement of 1238 mmHg (1.6 atm) osmotic pressure for a 33% sugar solution is now understood to have been caused by the porosity and elasticity of the bladder.[103] Since the cell sap's concentration was understood to be weaker than a 33% sugar solution, a measurement of turgor pressure above "many atmospheres" would have suggested that the living protoplasm played a direct and active role in regulating cell turgor. Instead, using the artificial cell as a precision osmometer, Pfeffer found that the surprisingly high osmotic pressure in living cells could be generated by weak sugar solutions—a discovery that changed perceptions of what even highly diluted, simple substances could do.

Whereas Traube and Sachs had entered into an intractable argument about the precise nature of plant life and the invisible mechanics of growth, Pfeffer produced a technological method through which the cell's mechanics could be analogically grasped—and with "mechanics" defined by measurable forces, rather than Traube's imaginary molecular movements. To make the artificial cell osmometer relevant to biology, Pfeffer developed an analogy that linked the structure and function of the artificial cell to the structure and function of the real cell: both, he argued, consisted of a soft, osmotically active membrane, and an inert rigid wall. Ironically, Pfeffer succeeded in generating this analogy because he found ways to further isolate the physical function of osmosis from notions of living matter and the protoplasmic basis of life: he accessed the secrets of life by distancing his practice from the strictures of the living.

Pfeffer discovered Traube's articles on the artificial cell sometime in mid-1872, around the same time as Sachs.[104] Whereas Sachs, Pfeffer, and de Vries

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[102] Wilhelm Pfeffer, "Über die Entstehung hoher, hydrostatischer Druckkräfte in Pflanzenzellen," in *Tageblatt der 48. Versammlung deutscher Naturforscher und Aerzte in Graz vom 18. bis 24. Sep 1875* (Graz: Leuschner & Lubensky, 1875), 59–60.

[103] Henri Dutrochet, *Mémoires pour servir à l'histoire anatomique et physiologique des végétaux et des animaux*, vol. 1 (Paris: J.-B. Baillière, 1837), 38–39.

[104] Wilhelm Pfeffer, "Untersuchungen über Reizbewegung," *Sitzungsberichte der Gesellschaft zur Beförderung der gesammten Naturwissenschaften in Marburg* Jahrgang 1872, no. 9 (30 Oct 1872): 129–35. This is probably the earliest published use of the term *Niederschlagsmembran* by someone besides Traube.

had earlier been convinced that a living, impermeable layer of protoplasm was required to develop cell turgor, Traube had provided both an argument and an experimental system demonstrating that some hydrostatic pressure could develop with a precipitation membrane alone. Traube had also suggested that many substances ought to be impermeable through membranes generally—a point that had been central to Graham's theory, and which Traube had subsequently ignored as he poured his energies into his molecular theory of growth. For Pfeffer, however, if artificial cells were genuinely impermeable to dissolved substances, then he could compare the impermeability of artificial cells to living protoplasm's so-called "resistance to filtration." In other words, Pfeffer saw an opportunity to disaggregate the purely physical features of osmosis from the role the living protoplasm played in creating the 1.5–3 atmospheres of turgor pressure he had measured in *Cynareae* stamens. But Traube's free-floating artificial/inorganic cells could not withstand the pressures that Pfeffer believed were present in real plant cells: they would tear or burst before reaching anywhere near one atmosphere of internal pressure, and besides, Traube had never devised a way to measure the pressure in his artificial cells to begin with.

To build an artificial cell that could resist high hydrostatic pressure, Pfeffer turned to the plant cell for inspiration:

> To render [measurements of osmotic action] possible the membranes must be placed against a support, which can offer resistance to ordinary pressure, but which is relatively easily permeable to water and salts. The plant cells furnish us with the model desired for imitation. In these, the plasma membrane [*Plasmamembran*] which, in its diosmotic properties, is similar to the artificial precipitation membranes, is pressed against the cell wall [*Zellhaut*].[105]

Pfeffer's first artificial cells, constructed between 1873 and late 1875, consisted of a "suspended" copper ferrocyanide cell loosely precipitated inside of a glass tube, and sealed on one end with either linen, silk, or parchment paper. This tube was then filled with a 2% sucrose solution, fitted with an air manometer on the other end of the tube, and dipped into a container of water; the manometer measured the compression of the air as water

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[105] Wilhelm Pfeffer, *Osmotic Investigations: Studies on Cell Mechanics*, trans. Eduard Stadelmann and Gordon R. Kepner (New York: Van Nostrand Reinhold, 1985), 2; German, *Osmotische Untersuchungen: Studien zur Zellmechanik* (Leipzig: Wilhelm Engelmann, 1877), 4.

flowed through the linen plug and then through the copper ferrocyanide membrane.[106]

But imitating the plant cell so closely proved to be a liability when actually measuring osmotic pressure. The copper ferrocyanide membrane leaked out of the pores of most of the materials Pfeffer tried; the small bubbles that formed on the outside of the cell altered the artificial cell's volume and surface area, spoiling the precision of the experiment. Pfeffer's second version of the suspended membrane cell, likely developed in early 1875, used a copper ferrocyanide membrane precipitated inside a porous, unglazed porcelain pot, of the type used in wet-cell battery construction, 46 × ø16 mm with walls 1.5 mm thick.[107] Here too, the membrane leaked out. In late 1875 or early 1876, Pfeffer created the third and final version of his artificial cell, with the copper ferrocyanide membrane precipitated *within the wall* of the porcelain pot: by dipping the pot in copper sulfate while injecting it with potassium ferrocyanide, the copper ferrocyanide membrane would precipitate as a thin, reddish-brown line longitudinally down the middle of the porcelain.[108]

This third artificial cell, though a little less cell-like with its "internal membrane," nonetheless resisted the high pressures that developed: all of the pressure exerted by water flowing into the cell was directed at the 200–250 cm tall mercury manometer attached to it, and the measurement did not require arbitrary compensatory factors to accommodate the cell's flex or expansion. Once filled with a dilute solution, the entire apparatus was plunged into a water bath with two thermometers attached (Fig. 2), and water would begin to osmotically flow into the cell. Pfeffer to claimed that his rigid artificial cell osmometer had a precision down to 1 mmHg (0.001 atm), and was sensitive enough to temperature that he would only tolerate a 0.2°C change over 10 minutes. At last, Pfeffer had an instrument that could solve the problem of what physical and chemical forces were proximately responsible for cell turgor. Using his artificial cell osmometer, Pfeffer found that a 1% sucrose solution developed an osmotic pressure of 538 mmHg (0.71 atm), whereas a 6% sucrose solution in the cell developed an astonishing 3075 mmHg (4.05 atm) of osmotic pressure.[109] Such

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[106] Wilhelm Pfeffer, "Über Zustandekommen eines hohen hydrostatischen Druckes durch endosmotische Wirkung," *Verhandlungen des Naturhistorischen Vereins der preussischen Rheinlande und Westphalens* 32 (2 Aug 1875): 276–79.

[107] On mid-nineteenth century battery construction and its other implications in cell theory, see Grote, "Surfaces of Action" (ref. 14)

[108] Pfeffer, *Osmotic Investigations* (ref. 105), 2; German, *Osmotische Untersuchungen*, 4–5.

[109] Ibid., 82, 112; German, 81, 110.

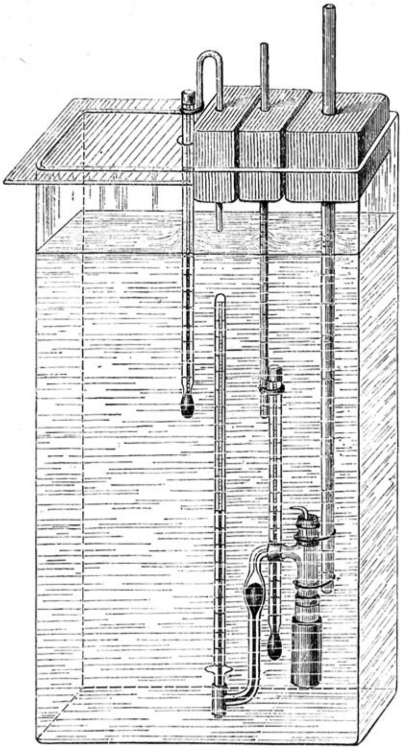

**FIG. 2.** Wilhelm Pfeffer's artificial cell manometer in use in 1877; the artificial cell itself is the thicker, dark cylinder on the lower right. One thermometer, clamped to a glass tube, is placed close to the cell, and a second placed in the middle of the tank. *Source*: Pfeffer, *Osmotische Untersuchungen* (ref. 105), 22.

high osmotic pressures due to solute concentration alone demonstrated that the large mechanical forces Pfeffer had found in his *Cynareae* experiments could be attributed purely to physical and chemical causes: no additional contractile or metabolic activity by the living protoplasm was necessary to develop such high osmotic pressures.

The discovery that a crucial aspect of plant cell life could be accounted for by a strictly physico-chemical mechanism also translated back to the biology of the plant cell. If the structure of the plant cell initially inspired Pfeffer's development of the artificial cell osmometer, now the artificial cell osmometer inspired Pfeffer to think of a soft, precipitated cell membrane or "plasma

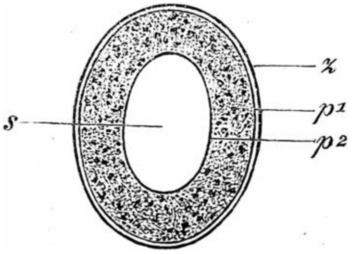

**FIG. 3.** Wilhelm Pfeffer's 1881 schematic of the plant cell, with the cell wall (*z*) and plasma membranes ($p^1$ and $p^2$) marked. *Source*: Pfeffer, *Pflanzenphysiologie* (ref. 112), 34.

membrane" as a structure distinct from a rigid cell wall, analogous to the soft copper ferrocyanide membrane precipitated within or against the rigid porcelain battery cell. "There is most probably only an outer zone that is decisive for the diosmotic processes, which we observe in the protoplasm. To express this, I have decided to call this diosmotically decisive layer 'plasma membrane' [*als Plasmahaut oder Plasmamembran zu bezeichnen*]."[110] Just as the copper ferrocyanide membrane precipitated through the mixture of iron chloride and potassium ferrocyanide, or Traube's gelatin membranes were precipitated with tannic acid, Pfeffer suggested that the plasma membrane was precipitated when membrane-forming proteins were secreted by the protoplasm, both into its surrounding aqueous environment and into the cell sap.[111] His osmometer was, in effect, a fulfillment of Traube's claim to render in inorganic matter what had previously been known only in living protoplasm. Pfeffer illustrated the plasma membrane for the first time in 1881 (Fig. 3), showing the cell wall (*Zellhaut* or *Zellwand*, *z*), one plasma membrane ($p^1$) enclosing the protoplasm, and a second membrane ($p^2$) separating the protoplasm from the cell sap.[112] Unlike in de Vries' illustration from 1877 (Fig. 1), Pfeffer did not explicitly label the living protoplasm.

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[110] Ibid., 139; German, 123.

[111] Ibid., 145–47; German, 132–34.

[112] Pfeffer's habitual terminological equivocation led him to call $p^2$ the "hyaloplasmic cuticle" (*Hyaloplasmahäutchen*) in 1881, an unfortunate attempt to reconcile the older term "hyaloplasm" with his new theory of a clearly distinct membrane. Wilhelm Pfeffer, *Pflanzenphysiologie: Ein Handbuch des Stoffwechsels und Kraftwechsels in der Pflanze*, 1st ed., vol. 1, Stoffwechsel (Leipzig: Wilhelm Engelmann, 1881), 34.

Pfeffer's *Osmotic Investigations* and de Vries' monograph on cell stretching were published within weeks of each other early in 1877, and a quiet rivalry ensued.[113] Both had stayed largely within Sachs' theory of cell and protoplasm structure, and both sought mechanical explanations for a set of plant physiological phenomena first grouped together by Hofmeister: movement, growth, and anatomical structure. But the shared origins could not mask the relative shortcomings of de Vries' project, as he could make only a modest argument about the structural effect of turgor pressure: his was not a study of the physics of turgor as such, but only its effects in living tissue. Pfeffer not only showed that an anatomically distinct plasma membrane was responsible for developing turgor pressure, he also gave a clear physical measurement of the mechanical forces involved. That he had done so by performing experiments on a strictly non-living, artificial, and even inorganic object was a departure not only in botany, but in biology as a whole. Pfeffer's artificial cell research demonstrated that major discoveries in anatomy and physiology need not be made by studying living cells or even formerly living specimens, but could occur through an entirely artificial construction. Pfeffer's interpretive interplay between the artificial and living cell was what Ernst Cassirer described as a moment when the traditional relationship between theory and praxis is reversed, with a scientific conception of life becoming increasingly defined through technological utility rather than through philosophy or metaphysics.[114] Whereas Traube had relied on visual similarity and rhetorical bombast, Pfeffer assumed that the similarity of *measurements* between *Cynareae* stamens and the artificial cell would legitimate the comparison.

Pfeffer's work on the artificial cell then passed into legend. Various sources agree that, likely in the first half of 1885, the physical chemist Jacobus van 't Hoff was walking near his laboratory in Amsterdam when he ran into Hugo de Vries, who was out on a stroll with his wife. The most colorful version of this story was recorded in the 1980s by George Wald (1906–1997), who had heard the story from one of de Vries' friends, the American plant physiologist W. J. V. Osterhout (1871–1964):

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[113] Notices for de Vries' *Untersuchungen über die mechanischen Ursachen der Zellstreckung* and Pfeffer's *Osmotische Untersuchungen* appeared in the *Botanische Zeitung* on 23 Feb and 6 Apr (vol. 35, nos. 8 and 14), respectively.

[114] Ernst Cassirer, "Form and Technology," in *Ernst Cassirer on Form and Technology: Contemporary Readings*, ed. Aud Sissel Hoel and Ingvild Folkvord, trans. Wilson McClelland Dunlavey and John Michael Krois (Basingstoke: Palgrave Macmillan, 2012), 15–53.

> Finally de Vries ventured, "The other day I had a letter from Pfeffer." To the desultory Dutch equivalent of "Oh, yeah? What's he up to?" de Vries replied, "He says he's measuring the effect of temperature on osmotic pressure." "What does he get?" asked van 't Hoff. "Well," said de Vries, "he writes that for each degree rise in temperature the osmotic pressure goes up by about 1/270."[115]

In 1877, Pfeffer had regarded this 1:270 ratio to be of little relevance: a 10°C change in temperature is physiologically significant, but the change in pressure accompanying the change in temperature would be physiologically insignificant.[116] But what Pfeffer regarded as a physiologically insignificant ratio of 1:270, van 't Hoff realized was a physically significant ratio of 1:1 between pressure and *absolute* temperature.[117] After his outdoor meeting with de Vries, van 't Hoff began writing a series of papers in the summer of 1885, culminating in "The Function of Osmotic Pressure in the Analogy between Solutions and Gases," published in the inaugural volume of the *Zeitschrift für physikalische Chemie* in 1887.[118] Relying on Pfeffer's osmotic pressure and temperature measurements, van 't Hoff was able to show that physical laws relating gas pressure and temperature also apply to the relationship between osmotic pressure and temperature in fluid solutions. The kinetic theory of gases was, by this argument, analogous to the behavior of solute molecules in a solution. Pressure, temperature, and solute concentration were directly proportional in both gases and liquid solutions, such that $PV = iRT$, in a clear parallel of Gay-

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[115] George Wald, "Origin of the Theory of Solutions," *Science* 217, no. 4565 (1982): 1084. This is essentially the same story that van 't Hoff himself like to tell; see J. H. van 't Hoff, "Wie die Theorie der Lösungen entstand," *Berichte der deutschen chemischen Gesellschaft* 27, no. 1 (1894): 6–19.

[116] Pfeffer, *Osmotic Investigations* (ref. 105), 95, 133n.; German, *Osmotische Untersuchungen*, 95. Years later Pfeffer offered a different explanation in private: the physicist Rudolf Clausius (1822–1888), his then-colleague at Bonn, had dismissed his osmometric findings as being too high. Pfeffer sourly recalled to a friend, "I spoke of the matter with Clausius, who at first declared such high osmotic pressures were impossible, and who only unwillingly acknowledged the fact after I demonstrated the pressure experiments to him. So it can be understood why Clausius never dealt with the matter, even though I repeatedly mentioned to him that there had to be some obvious relationship between osmotic performance on the one hand, and the size and number of molecules on the other." Ernst Cohen, "Wilhelm Pfeffer und die physikalische Chemie," *Die Naturwissenschaften* 3, no. 10 (1915): 118–20.

[117] George Wald, "How the Theory of Solutions Arose," *Journal of Chemical Education* 63, no. 8 (Aug 1986): 658–59.

[118] Cohen, *Jacobus Henricus van 't Hoff*, 225 (ref. 21); Snelders, "J. H. van 't Hoffs theorie van de verdunde oplossingen" (ref. 21).

Lussac's law relating gas pressure $P$, to volume $V$, and absolute temperature $T$, with the ideal gas constant $R$ working identically in both.[119]

The resulting theory of solutions represented a broad extension of thermodynamics, translating the rarefied physics of kinetics and heat engines down to practical problems of wet chemistry. "The great practical advantage arising from this method of regarding the behaviour of solutions, which leads at once to quantitative conclusions, consists in the fact that the application of the second law of thermodynamics to liquids is rendered exceedingly easy," van 't Hoff wrote in 1887.[120] For this "easy" synthesis of thermodynamics, Avogadro's law, osmosis, and chemical equilibrium, van 't Hoff was awarded the first Nobel Prize in chemistry in 1901.[121]

## LIFE'S ANALOGIES AND LIFE'S DIVISIONS

Pfeffer's plasma membrane was never fully embraced by biologists in his lifetime. His analogical argument not only ran against the grain of protoplasm theory, but also the classical form of physiological reasoning used by de Vries that relied on a combination of experimentation and anatomical analysis.[122] Several failed attempts to dissect the plasma membrane from the cell led one botanist to write in 1909 that Pfeffer's theories "could hardly be said to have maintained their ground in the opinion of many physiologists."[123] The reality of the cell membrane as an essential constituent of living cells was not secured within biology alone, but instead by a set of interlocking analogies and measurements across both physical chemistry and biology. Just as Pfeffer had used the artificial cell to conceptualize his plasma membrane, so too did van 't Hoff

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119. $i$ was the foundation for Svante Arrhenius' (1859–1927) demonstration that the anomalous osmotic properties of electrolytic solutions are related to their electrical conductivity; this formed the basis of Arrhenius' theory of ionic dissociation in solutions. See Servos, *Physical Chemistry* (ref. 21), 36–37.

120. J. H. van 't Hoff, "The Function of Osmotic Pressure in the Analogy between Solutions and Gases," trans. William Ramsay, *Proceedings of the Physical Society of London* 9 (Jul 1888): 307–34, on 309; German, "Die Rolle des osmotischen Druckes in der Analogie zwischen Lösungen und Gasen," *Zeitschrift für physikalische Chemie* 1, no. 9 (21 Oct 1887): 481–508, on 483.

121. On the circumstances of van 't Hoff's selection for the first Nobel Prize in chemistry, see Crawford, *The Beginnings of the Nobel Institution* (ref. 21), 116–19.

122. William Coleman and Frederic L. Holmes, eds., *The Investigative Enterprise: Experimental Physiology in Nineteenth-Century Medicine* (Berkeley: University of California Press, 1988).

123. J. Reynolds Green, *A History of Botany, 1860–1900: Being a Continuation of Sachs "History of Botany, 1530–1860"* (Oxford: Clarendon Press, 1909), 174.

rely on living cells to conceptualize the "semipermeable membrane," the generalized class of which the cell membrane has been an exemplary member since 1887. The kinds of analogies that were used to create the theory of dilute solutions and the cell and semipermeable membranes were not necessarily more powerful than more implicit metaphors ubiquitous in science.[124] Yet their very explicitness indicated the risk inherent in crossing the greater perceived distance between domains: biology and chemistry, gases and solutions, crystals and organisms, organic and inorganic, living and non-living.[125] The cell membrane and the theory of solutions alike could work as theories only if one assumed that a high degree of unity of prevailed across the biological and physical sciences.[126] Traube had believed that an *a priori* hegemony of physical

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124. Andrew Reynolds argues further that, not only do biologists use metaphors as cognitive instruments to understand cells, but that biologists use many overlapping, hybrid, and sometimes contradictory metaphors simultaneously, in order to capture the diversity and complexity of cells; Reynolds, *The Third Lens* (ref. 7), 135, 140, 145.

125. In this article I am examining the use of analogies to cross conceptual and disciplinary domains in the sciences, drawing on Devin Griffiths, *The Age of Analogy: Science and Literature Between the Darwins* (Baltimore: Johns Hopkins University Press, 2016); Victor Hilts, "Towards the Social Organism: Herbert Spencer and William B. Carpenter on the Analogical Method," in *The Natural Sciences and the Social Sciences*, ed. I. Bernard Cohen, Boston Studies in the Philosophy of Science 150 (Dordrecht: Springer Netherlands, 1994), 275–303; in the same volume, Camille Limoges, "Milne-Edwards, Darwin, Durkheim and the Division of Labour: A Case Study in Reciprocal Conceptual Exchanges between the Social and the Natural Sciences," 317–43; and Culotta, "German Biophysics" (ref. 24). Culotta notes that the physiologists of the 1847 Berlin circle were very cautious in their application of physical analogies to biology. Much of the classical literature on analogies in science examines the use of analogies in the construction of scientific models (e.g., the analogy between billiard balls and gas molecules), often within a single domain of inquiry; a systematic philosophical analysis of the artificial cell as a model system is not my focus here, though this would be a fruitful exercise. For overviews on analogies in scientific modeling, see Rebecca Mertens, *The Construction of Analogy-Based Research Programs: The Lock-and-Key Analogy in 20th Century Biochemistry* (Bielefeld: Transcipt Verlag, 2019); Daniela M. Bailer-Jones, "Models, Metaphors and Analogies," in *The Blackwell Guide to the Philosophy of Science*, ed. Peter Machamer and Michael Silberstein (Malden, MA: Blackwell, 2002), 108–27; Dedre Gentner and Michael Jeziorski, "The Shift from Metaphor to Analogy in Western Science," in *Metaphor and Thought*, 2nd ed., ed. Andrew Ortony (Cambridge: Cambridge University Press, 1993), 447–80; and Nancy Leys Stepan, "Race and Gender: The Role of Analogy in Science," *Isis* 77, no. 2 (Jun 1986): 261–277. For two different types of exchange across scientific domains, see Lindley Darden and Nancy Maull, "Interfield Theories," *Philosophy of Science* 44, no. 1 (Mar 1977): 43–64; and Kärin Nickelsen, "Physicochemical Biology and Knowledge Transfer: The Study of the Mechanism of Photosynthesis Between the Two World Wars," *Journal of the History of Biology* (Apr 2019): 1–29.

126. Ironically, some of the better attempts at categorizing types of arguments for the unity of science are found in Peter Galison and David J. Stump, eds., *The Disunity of Science: Boundaries, Contexts, and Power* (Stanford, CA: Stanford University Press, 1996).

chemistry over biology made it unnecessary to make an explicit analogy or systematic comparison between living cells and his artificial cells, insisting instead that the universality of his mechanical-molecular theory of growth should prevail. In contrast, van 't Hoff frequently acknowledged both his conceptual indebtedness to biologists and the instrumental usefulness of physical chemistry to biology.[127] Both Pfeffer and van 't Hoff explicitly used analogies to move horizontally across domains, rather than using laws or reduction to move vertically down a disciplinary hierarchy. But the analogical reasoning that made Pfeffer and van 't Hoff so successful resulted in a very peculiar conception of "life," one that was comprehensible only within the techno-scientific paradigm constructed around the artificial cell.

Van 't Hoff conceived of the "semipermeable membrane" in his famous 1887 paper, using the German terms *halbdurchlässige Membran* (once) and *halbdurchlässige Wand* (eleven times). His English translator, William Ramsay (1852–1916), used "semipermeable membrane" (twice) along with "semipermeable wall" (six times) and "semipermeable diaphragm" (four times); earlier versions of the paper in French used *parois semi-perméable* almost exclusively.[128] Under protest, the semipermeable membrane began life in van 't Hoff's 1887 paper as something of a fiction:

> The porous membrane, such as that described, will be termed in the following pages a "semipermeable membrane" [*halbdurchlässige Wand*] and the conception will be made use of even where experimental verification is lacking. The behaviour of solutions may thus be studied in a manner strikingly analogous [*die grösste Ähnlichkeit*] to that employed in the study of gases, inasmuch as what is known as "osmotic pressure" corresponds to pressure . . . of a gas. It is right to mention that this is no fanciful analogy [*nicht . . . eine künstlich aufgezwungene Analogie*], but a fundamental one; the mechanism which, according to our present views, controls the pressure of gases and the osmotic pressure of liquids is substantially the same.[129]

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127. J. H. van 't Hoff, *Physical Chemistry in the Service of the Sciences*, trans. Alexander Smith (Chicago: University of Chicago Press, 1903).

128. See J. H. van 't Hoff, "L'équilibre chimique dans les systèmes gazeux ou dissous à l'état dilué," *Archives néerlandaises des sciences exactes et naturelles* 20, no. 3 (1886): 239–302.

129. van 't Hoff, "Analogy between Solutions and Gases" (ref. 120), 309; German, "Analogie zwischen Lösungen und Gasen," 483. Ramsay's choice of "fanciful analogy" is better translated as "artificially imposed analogy," and his phrasing of "strikingly analogous" is actually "the greatest similarity."

Once one accepted an analogy between the kinetics of gases and dilute solutions, the physico-chemical, semipermeable membrane became quite real, despite the fact that many of the biologists whose research van 't Hoff relied upon remained skeptical of the cell membrane's biological existence. Pfeffer's artificial cell was the most important, but not the only biological source for van 't Hoff's analogy. In the early 1880s, de Vries, realizing the inadequacy of his cell-stretching research in comparison to Pfeffer's artificial cell experiments, began to observe plant cells under low microscopic magnification to identify "isotonic" concentrations of different solutes—concentrations that would eliminate cell turgor, defined as the moment plasmolysis began.[130] These measurements were indexed to the osmotic performance of potassium nitrate, resulting in relative isotonic coefficients. De Vries' research was then repeated by the Dutch physiologists H. J. Hamburger (1859–1924) and F. C. Donders (1818–1889) using red blood cells, and the three Dutch scientists together succeeded in using living cells as physico-chemical instruments for determining the relative molecular weights and osmotic potentials of a wide range of chemical compounds.[131]

The biological cell became the archetype for van 't Hoff's semipermeable membrane, even though his analogy between gases and fluids relied on a creative misreading of Pfeffer and de Vries' research on plant cell turgor. Just as gas pressure can be conceptualized as molecules of a gas impacting the walls of a container, van 't Hoff's analogy suggested that molecules of a dissolved substance collided against a semipermeable membrane to produce osmotic pressure (Fig. 4). Responding to Lothar Meyer's criticism that any observer of Pfeffer's experiments could see that osmotic pressure was the flow of water into the artificial cell and not the impact of solute molecules on the manometer attached to it, van 't Hoff retreated somewhat. Van 't Hoff noted that his comparison between gases and dilute solutions was not an *a priori* definition of osmosis, but a "practical" one, a "means of gaining insight into the analogy" that was needed to connect disparate empirical studies and measurements.[132] Counting Pfeffer's artificial cell, water flowing into or out of cells accounted for

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[130] Hugo de Vries, "Eine Methode zur Analyse der Turgorkraft," *Jahrbücher für wissenschaftliche Botanik* 14 (1884): 427–601.

[131] H. J. Hamburger, "De invloed van scheikundige verbindingen op bloedlichaampjes in verband met hare moleculair-gewichten," *Onderzoekingen gedaan in het physiologisch laboratorium der Utrechtsche Hoogeschool*, 3, 9 (1884): 26–42.

[132] J. H. van 't Hoff, "Über das Wesen des osmotischen Drucks (Antwort an Herrn Lothar Meyer)," *Zeitschrift für physikalische Chemie* 5, no. 2 (6 Mar 1890): 174–76.

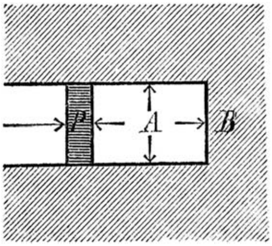

**FIG. 4.** J. H. van 't Hoff's 1887 interpretation of Pfeffer's artificial cell as a piston (*P*) and a vessel (*A*) whose walls are semi-permeable. The piston/manometer measures the pressure exerted by the sugar solution (*B*), and can be (conceptually) used to adjust the concentration of the sugar solution of *A* by compressing or expanding the vessel. *Source*: van 't Hoff, "Analogie zwischen Lösungen und Gasen" (ref. 120), 482.

three of his five experimental examples, and they were the only sources of van 't Hoff's conception of semipermeable membranes in his 1880s papers on osmosis. The other two experimental cases, François-Marie Raoult's (1830–1901) vapor-pressure depression experiments and Charles Soret's (1854–1904) experiments with thermal diffusion, linked Pfeffer's temperature measurements with the isotonic coefficients of de Vries, Hamburger, and Donders. In other words, he *needed* an analogy with cells and membranes—living and artificial—in order to make Avogadro's law relating the volume and quantity of gas molecules generalizable to solutions as well. The material details of osmosis were less important than the way the analogy allowed van 't Hoff to move smoothly from fluid solutions to the piston-equipped ideal engines familiar in the Carnot cycle and most subsequent exercises in thermodynamics.[133] This "hypothetical conception" of the semipermeable membrane soon fell away as the easy familiarity of thermodynamic models became more closely associated with living cells.[134]

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133. This analogy was also contested by dissenters from the "Ionist" school of van 't Hoff, Arrhenius, and Wilhelm Ostwald (1853–1952); see R. G. A. Dolby, "Debates over the Theory of Solution: A Study of Dissent in Physical Chemistry in the English-Speaking World in the Late Nineteenth and Early Twentieth Centuries," *Historical Studies in the Physical Sciences* 7 (Jan 1976): 297–404; H. A. M. Snelders, "The Dutch Physical Chemist J. J. van Laar (1860–1938) Versus J. H. van 't Hoff's 'Osmotic School,'" *Centaurus* 29, no. 1 (Mar 1986): 53–71; Helge Kragh and Stephen J. Weininger, "Sooner Silence than Confusion: The Tortuous Entry of Entropy into Chemistry," *Historical Studies in the Physical and Biological Sciences* 27, no. 1 (1996): 91–130, on 106–08.

134. J. H. van 't Hoff, "Osmotic Pressure and Chemical Equilibrium," in *Nobel Lectures in Chemistry, 1901–1921* (Amsterdam: Elsevier, 1966), 5–10, on 7; "Nobel-Vorlesung von Prof. J. H. van 't Hoff, 13. Dez. 1901," in *Les Prix Nobel en 1901* (Stockholm: P.-A. Norstedt & Fils, 1904), 1–7, on 3.

Van ’t Hoff reinforced this sense of physical chemistry’s dependency on biology in his Nobel lecture in 1901. Though the first of its kind and awkwardly truncated, he divided his time into three parts: beginning with Pfeffer and de Vries, proceeding to theoretical chemistry, and ending with remarks about “the problem of life” (*Lebensfrage*) and praise for Jacques Loeb’s (1859–1924) discovery of artificial parthenogenesis.[135] As he synthesized the chemistry, physics, and biology of osmotic pressure, van ’t Hoff drew a mental image of the cell that resembled Pfeffer’s artificial cell. The dominant biological conception of life-as-protoplasm fell by the wayside in van ’t Hoff’s papers on dilute solutions: the material composition of the membrane/wall/diaphragm was unimportant, so long as it was semipermeable and thus created the conditions for osmosis. In his most specific statement on the structure of living plant cells, van ’t Hoff even conflated Pfeffer and de Vries’ views on the matter: “the membrane of [the] protoplast is semipermeable, and when immersed in solutions with high osmotic pressure the protoplast withdraws, and the so-called plasmolysis occurs.”[136]

Such a statement would have upset de Vries in particular, who not only rejected Pfeffer’s plasma membrane but became committed to a vision of biology that had Pfeffer and van ’t Hoff as its main foils. In 1878, as Sachs and Traube were attacking each other in the *Botanische Zeitung*, de Vries wrote in a regional Dutch journal that “the supposed analogy [*la prétendue analogie*] between precipitation membranes and living protoplasm is limited to a simple appearance, devoid of any meaning.” Although he accepted that modern biology needed tools and concepts from physical chemistry, for de Vries, accepting the legitimacy of the artificial cell would mean that “the recognized property of protoplasm would no longer be the exclusive preserve of living or organized membranes, but would also belong to artificial, unorganized films.”[137] In other words, de Vries categorically denied the validity of Traube and Pfeffer’s relocation of the vital phenomenon of cell turgor from living to non-living matter. So soon after critiquing Hofmeister’s “living cell membranes,” de Vries in the 1880s found himself invested in “living membranes” of a different sort. De Vries published his own paper in the *Zeitschrift für physikalische Chemie* in 1888 with the pointed title, “Osmotic Experiments with

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[135] Ibid.

[136] van ’t Hoff, “Wie die Theorie der Lösungen entstand” (ref. 115), 11.

[137] Hugo de Vries, “Sur la pérmeabilité des membranes précipitées,” *Archives néerlandaises des sciences exactes et naturelles* 13, no. 4 (1878): 344–55, on 355.

Living Membranes," reiterating that "the osmotic membrane in these cells is the living protoplast, the almost immeasurably fine bubble enclosing the cell sap."[138] Even his famous *Intracellular Pangenesis* (1889) featured an extended digression on "*die fragliche Autonomie der Hautschicht*"—literally, the questionable autonomy of the skin layer, though his English translator translated de Vries' *Hautschicht* into a more Pfeffer-esque "plasmatic membrane."[139] Tracing a disciplinary division between physics and biology, as well as an analogous divide between artifice and nature, de Vries argued that, although physical chemistry was instrumentally useful to biology, it could not constitute a science of life as such. There are, de Vries wrote,

> two kinds of processes [that] occur in the living body. In the first place, those that are separable from living substance, *and can therefore be artificially imitated*, or even exactly duplicated. In the second place, those that are inseparable from that substratum, and which indeed find their existence in the processes of life of that very substratum. The former processes are purely physical or chemical; in a word, they are aplasmatic processes; the latter ones we must designate as plasmatic; that is, as taking place in the molecules of the living protoplasm itself. The former belong to physiological chemistry and physics, the latter form the proper subject of physiology.[140]

Thus, de Vries not only rejected Pfeffer's analogy between living and artificial cells as biologically unwarranted, he insisted on the separation of biology and physics as independent domains—a division marked by the difference between protoplasm and non-living matter. Even as de Vries enjoyed praise and attention through his association with van 't Hoff's theory of solutions, he nonetheless argued throughout the 1880s that simple physical theories of vital phenomena were constantly being thwarted by biologists who could demonstrate the complexity of what living organisms do: "If the progress of our science in the last decades is attentively followed, then one will note that countless phenomena that earlier could only be explained in a purely physical way have now turned out to come about only under the direct involvement of life."[141]

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[138] Hugo de Vries, "Osmotische Versuche mit lebenden Membranen," *Zeitschrift für physikalische Chemie* 2, no. 6 (5 Jun 1888): 415–32, on 418.

[139] Hugo de Vries, *Intracellular Pangenesis*, trans. Charles Stuart Gager (Chicago: Open Court, 1910), 160; German, *Intracellulare Pangenesis* (Jena: Gustav Fischer, 1889), 159.

[140] Ibid., 39–40, emphasis added; German, 36–37.

[141] Hugo de Vries, "Plasmolytische Studien über die Wand der Vacuolen," *Jahrbücher für wissenschaftliche Botanik* 16, no. 4 (1885): 465–598, on 499.

Even Pfeffer shared some of de Vries' anxieties about his analogies between nature and artifice, and living and non-living matter. In his 1877 *Osmotic Investigations*, Pfeffer repeatedly undermined his own theory of the plasma membrane by pointing out the many ways the analogy between it and the artificial cell ought to fail. Despite declaring that the term "plasma membrane" was a way of pointing to the "diosmotically decisive" layer, Pfeffer also suggested it was "morphologically unnecessary," writing that, "I regard even the term 'plasma membrane' as a stopgap measure, and would be glad to stop using it as soon as knowledge of the structure and properties of the hyaloplasm [N.B., the glassy, outer layer of the protoplasm] would allow me to. Besides, it is not likely that the plasma membrane is clearly delineated against the inner layers of the hyaloplasm."[142] Thus, having elaborately constructed a novel analogy between his artificial cell and the membrane of living cells, Pfeffer nearly abandoned it on the grounds that it did not conform to classical anatomical and morphological technique, which demanded clear identification by dissection. His reliance on the artificial cell came at the expense of the physiological traditions of vivisection and autonomic measurement, traditions that Sachs had brought from animal physiology into plant physiology.[143] But Pfeffer was also suspicious of scientific analogies more generally: he preferred the positivistic certainty of exact measurement. Of his pivotal analogy between living cells and his artificial cell osmometer, Pfeffer wrote that it "essentially recalls the alchemists centuries ago marveling at the so-called metallic trees, which were also, in part, inorganic cells." Doubling-down on his concerns about analogical reasoning, he agonized, "History will judge our efforts as we judge analogous efforts by the alchemists."[144]

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[142] Pfeffer, *Osmotic Investigations* (ref. 105), 139; German, *Osmotische Untersuchungen*, 123–24. Pfeffer was infamous for his prevaricating prose; in his memoirs Gottlieb Haberlandt complained that "the countless ifs and buts in his [textbooks] nearly brought me to despair," while Karl Goebel reportedly scribbled, "o, Herr, ist das noch deutsch?" (Oh Lord, is this really German?) in the margin of his copy of Pfeffer's *Pflanzenphysiologie*. Gottlieb Haberlandt, *Erinnerungen, Bekenntnisse und Betrachtungen* (Berlin: Julius Springer, 1933), 95; Bünning, *Ahead of His Time* (ref. 37), 97.

[143] Sachs thought Pfeffer was conceited and delusional ("*Selbstüberhebung*") for straying from botany and "getting himself mixed up in a purely physical issue"; letter from Sachs to Hugo Thiel, 21 May 1876, in Pringsheim, *Julius Sachs* (ref. 36), 278–79. On Sachs' laboratory methods, see de Chadarevian, "Laboratory Science versus Country-House Experiments" (ref. 36); and de Chadarevian, "Graphical Method and Discipline: Self-Recording Instruments in Nineteenth-Century Physiology," *Studies in History and Philosophy of Science Part A* 24, no. 2 (Jun 1993): 267–91. On physiological method see Holmes, "Elementary Analysis" (ref. 72); and Holmes and Coleman, eds., *Investigative Enterprise* (ref. 122).

[144] Pfeffer, *Osmotic Investigations* (ref. 105), 252; German, *Osmotische Untersuchungen*, 219. On alchemical trees, see Lawrence Principe, "Apparatus and Reproducibility in Alchemy," in

History has judged Pfeffer and de Vries very well, along with van 't Hoff, Sachs, and every other scientist mentioned thus far in this essay. Yet the division that the artificial cell bridged, and which de Vries insisted upon, continued to divide biology; it even divides the historiography of biology up to today. For de Vries, the self-evident nature of the organism's liveliness and protoplasm's vitality formed a backstop against which biology was defined as the science of life. By the end of the 1880s, de Vries decided to give up osmosis research, turning instead to experimental evolution and what would later become his mutation theory. Bert Theunissen has suggested that de Vries was squeezed out of osmosis research in Amsterdam by van 't Hoff, and Erik Zevenhuizen has argued that, with a growing family and increasing teaching duties, de Vries was seeking ways of becoming less a creature of the laboratory, preferring work in the field and botanical garden.[145] To these I would add that de Vries' shift from osmosis to evolutionary research was not only the result of local politics and personal desires, but was also a way of moving away from a biology whose approach to life looked beyond the study of living organisms.

Indeed, by the beginning of the twentieth century it was not hard to find physiology textbooks that opened with a discussion of osmosis, van 't Hoff's law, and Pfeffer's *Osmotic Investigations* as a foundation for all that followed.[146] There were even those who believed that science had a firm grasp on molecules, solutions, and colloids, but a very poor understanding of life: hence, the breathless twentieth-century argument that life is not understood until scientists can create it.[147] In the immediate aftermath of van 't Hoff's synthesis, a sudden enthusiasm for osmosis nearly left several biologists on the wrong side of scientific respectability and historical judgement. The most high-profile case was Jacques Loeb's development of artificial parthenogenesis: van 't Hoff had seen it as demonstrating physical chemistry's reach, and Loeb himself believed

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*Instruments and Experimentation in the History of Chemistry*, ed. Frederic L. Holmes and Trevor Levere (Cambridge, MA: MIT Press, 2000), 55–74; see also note 77.

[145] Bert Theunissen, "De beheersing van mutaties: Hugo de Vries' werdegang van fysioloog tot geneticus," *Gewina, Tijdschrift voor de Geschiedenis der Geneeskunde, Natuurwetenschappen, Wiskunde en Techniek* 15 (1992): 97–115; Zevenhuizen, "Vast in het spoor van Darwin" (ref. 37), 193–96.

[146] For example, Rudolf Höber, *Physikalische Chemie der Zelle und der Gewebe*, 1st ed. (Leipzig: Wilhelm Engelmann, 1902); and Ludwig Jost, *Vorlesungen über Pflanzenphysiologie* (Jena: Gustav Fischer, 1904).

[147] Luis A. Campos, "That Was the Synthetic Biology That Was," in *Synthetic Biology: The Technoscience and Its Societal Consequences*, ed. Markus Schmidt et al. (Dordrecht: Springer Netherlands, 2009), 5–21.

his research to be proof of the importance of van 't Hoff's theory of dilute solutions in physiology.[148] But Loeb's hopes to use van 't Hoff's theory to achieve an "artificial transformation of dead into living matter" was only a rhetorical flourish, and his accomplishment of artificial parthenogenesis would be overshadowed by later and more medically successful work in *in vitro* fertilization.[149] Daniel Trembley MacDougal (1865–1958), an exponent of de Vries' mutation theory in the United States, attempted to artificially induce mutations in plants by manipulating cell turgor.[150] Likewise, Stéphane Leduc's (1853–1929) outlandish claims to have created lifelike "osmotic growths" liberally borrowed from Traube's combinations of copper ferrocyanide and gelatin. Even more remarkable than Leduc's uncanny imitations of cell division was his fantasy that physical chemistry had matured enough to completely collapse the distinction between living and non-living matter: his "synthetic biology" explicitly rested upon the foundation of van 't Hoff's theory of dilute solutions, Pfeffer's copper ferrocyanide artificial cell, and Graham's theory of colloids.[151]

## CONCLUSION: THE DIVISION OF LIFE AND THE UNITY OF SCIENCE

The so-called meaninglessness and the undoing of life have been recurring themes in philosophical and critical commentary around biology since the *fin-de-siècle*, as have various attempts to salvage or rebuild the concept of "life" out of its physico-chemical parts.[152] I have argued that, in one sense, these discourses of

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[148] Jacques Loeb, *Studies in General Physiology* (Chicago: University of Chicago Press, 1905), 471–72; German, "Physiologische Untersuchungen über Ionenwirkungen," *Pfluger's Archiv für die gesammte Physiologie des Menschen und der Thiere* 69, no. 1 (9 Nov 1897): 1–27.

[149] Jacques Loeb, *The Dynamics of Living Matter* (New York: Columbia University Press, 1906), 223. On the fate of artificial parthenogenesis, see Philip J. Pauly, *Controlling Life: Jacques Loeb and the Engineering Ideal in Biology* (New York: Oxford University Press, 1987), chap. 8.

[150] See Luis A. Campos, *Radium and the Secret of Life* (Chicago: University of Chicago Press, 2015), 107, 121.

[151] On Leduc, see Evelyn Fox Keller, *Making Sense of Life: Explaining Biological Development with Models, Metaphors, and Machines* (Cambridge, MA: Harvard University Press, 2002), chap. 1; Stéphane Leduc, *Théorie physico-chimique de la vie et générations spontanées* (Paris: A. Poinat, 1910).

[152] The "undoing" of life in the late twentieth and early twenty-first centuries has been a theme in the work of Stefan Helmreich's school of the anthropology of biology; see Stefan Helmreich, *Sounding the Limits of Life: Essays in the Anthropology of Biology and Beyond*

the de- and re-construction of life were part of a single, larger phenomenon: the gradual transfer of vitality from living to non-living matter, one which coordinated the practices and theories of biologists, chemists, and physicists alike. A new definition of life evolved from Traube and Pfeffer's artificial cells, one that had its home exclusively in the bio-physical-chemical laboratory. With their artificial cells, Traube and Pfeffer relocated activities and capacities for organization that were once thought to be solely in the province of living organisms, finding them in ordinary matter.

Their success was not founded on a dramatic creation or re-creation of life itself: indeed, the history of the artificial cell is far from exhausted by the historiography of the natural and the artificial, or of the history of attempts to imitate life.[153] Rather, the success of the artificial cell, Pfeffer's cell membrane theory, and physico-chemical biology more generally has rested on a synthesis of ideas across disciplines, shifting the notion of life into new territories and reframing its terms and questions. Pfeffer and van 't Hoff's research became the foundation of cell membrane biophysics—a field that depends on creating artificial membranes to study membrane proteins—and since the beginning of the twentieth century it has been normal to do biochemical and biophysical research on individual processes of life by studying the specific capacities of molecular entities without ever thinking about what, philosophically, makes a thing "alive" or not.[154] By the 1870s, biologists could choose to emphasize the organized nature of the living organism and its parts, or the formless protoplasm as living matter—or even both together, as Claude Bernard did near the end of his life.[155] By the end of the nineteenth century, the success of the artificial cell in plant physiology and physical chemistry created a third (or fourth) option: the reconstruction of certain living processes from their many non-living material elements, each characterized by particular chemical composition and physical behavior. Traube rather caustically argued in 1867 that the old biology, concerned only with living things, could never

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(Princeton, NJ: Princeton University Press, 2015); Natasha Myers, *Rendering Life Molecular* (Durham, NC: Duke University Press, 2015); Sophia Roosth, *Synthetic: How Life Got Made* (Chicago: University of Chicago Press, 2017).

[153] Bernadette Bensaude-Vincent and William R. Newman, eds., *The Artificial and the Natural: An Evolving Polarity* (Cambridge, MA: MIT Press, 2007); Hans Blumenberg, "'Imitation of Nature': Toward a Prehistory of the Idea of the Creative Being," trans. Anna Wertz, *Qui Parle* 12, no. 1 (2000): 17–54.

[154] Grote, *Membranes and Molecular Machines* (ref. 17).

[155] See the eighth and ninth lectures of Claude Bernard, *Leçons sur les phénomènes de la vie communs aux animaux et aux végétaux*, vol. 1 (Paris: J.-B. Baillière, 1878).

penetrate the inner workings of life. "There is a kind of criticism that sees its task in making objections, blind to the tools that offer new facts of research," Traube wrote; "Questions of the significance of the cell membrane cannot be resolved through comparative anatomy and embryology, but only through direct experiment"—even if such experiments were directed toward preparations of gelatin and copper ferrocyanide.[156] Through such experiments, by the early twentieth century it became imaginable that life could be reconstructed through its material parts, and this was precisely due to the specific capacities biologists endowed to objects and materials that, by themselves, are not alive, or at least not obviously so.

*Pace* Jane Bennett and recent scholarship in "new materialism," vital materialism was the historical creation of a mechanistic approach to biology, and it lies at the heart of scientific modernity.[157] As I have sought to demonstrate, the materialism and mechanism of modern biology since the middle of the nineteenth century no longer rested on early modern notions of clockwork machines, but on explorations of matter in action. Yet attempts to seek a more profound philosophy of life after its late-nineteenth-century disassembly have often ignored the historical specificity as well as the specific scientific contexts in which this disassembly took place.[158] The relocation of vitality from living protoplasm to ordinary, non-living matter could happen in Traube or Pfeffer's laboratories, but it makes less sense outside of such spaces. After all, "life" is not only defined by biologists, much less one group of them.[159] By any more common or intuitive understanding, "life" has as its counterpart in "death," and along with life we commonly experience birth, sickness, thought, prosperity, reflex, etc. Modern life has a split personality, and the distance between common and scientific conceptions of life has waxed and waned as biological concepts and institutions of biology have developed historically, as is true of many concepts that exist both inside and outside of scientific milieus. By the same token, contemporary philosophers and theorists of biopolitics who

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156. Traube, "Zellenbildung und Endosmose" (ref. 74), 157, 160.

157. Cf. Jane Bennett, *Vibrant Matter: A Political Ecology of Things* (Durham, NC: Duke University Press, 2010).

158. Harrington, *Reenchanted Science* (ref. 17).

159. Cf. "Life," *Encyclopedia Britannica*, 1948, which states only, "see Biology." A genuinely radical statement of this formulation is Michel Morange, *Life Explained*, trans. Matthew Cobb and Malcom DeBevoise (New Haven, CT: Yale University Press, 2008), which offers a reconstruction of "life" from physico-chemical, evolutionary, and informational principles.

construe life and biology as monolithic or hegemonic categories ignore the fragmentary nature of both concepts at their own peril.[160]

While scientific knowledge is a product of its cultural context, scientific ideas and their cultural contexts are often at odds, and if we are interested in the crossings-over between the social and the scientific (or between the humanities and the sciences) then measuring this distance might help us to traverse it. In this article, I have suggested that there was not a single scientific conception of life, nor was there ever a single conception of how biology should encompass it. The contests and shifts over these conceptions of the life-biology matrix provide rich starting points for historical investigation without needing to deploy monolithic conceptions of either life or biology. Biology consists of more than probing the inner workings of life: de Vries could easily escape, so to speak, to research in evolution and descent, while Pfeffer's subsequent research on plant metabolism and transport looked well beyond the cell and its membrane. De Vries sensed in Traube and Pfeffer's artificial cell research a lingering problem of propriety, becoming increasingly critical of physical chemistry as his mutation research made him a leading public figure in the Netherlands.[161] Gone were the more philosophical concerns with the definition and uniqueness of life. From this point, many biologists were interested in studying the individual processes that happen inside of cells and also elsewhere, but they frequently lost the ability to address life as a broader phenomenon outside of the laboratory.

In 1972, the biochemist Albert Szent-Györgi (1893–1986) acknowledged the difference between a common and a scientific conception of life when he wrote bitterly of his failure to save his wife, who was dying of cancer:

> My own scientific career was a descent from higher to lower dimension, led by the desire to understand life. I went from animals to cells, from cells to bacteria, from bacteria to molecules, from molecules to electrons. The story had its irony, for molecules and electrons have no life at all. On my way life ran out between my fingers.[162]

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160. Alastair Hunt and Stephanie Youngblood, eds., introduction to *Against Life* (Evanston, IL: Northwestern University Press, 2016); Maurizio Meloni, *Political Biology: Science and Social Values in Human Heredity from Eugenics to Epigenetics* (Basingstoke, UK: Palgrave Macmillan, 2016); cf. Thomas Lemke, *Biopolitics: An Advanced Introduction*, trans. Eric Frederick Trump (New York: New York University Press, 2011).

161. Bert Theunissen, "Knowledge Is Power: Hugo de Vries on Science, Heredity and Social Progress," *The British Journal for the History of Science* 27, no. 3 (1994): 291–311.

162. Albert Szent-Györgyi, *The Living State, with Observations on Cancer* (New York: Academic Press, 1972), 7.

Szent-Györgi's book, *The Living State*, is one of many that have tried to reassemble life from its biochemical and biophysical parts, and the rest of the book has none of the emotional, human impact of these four sentences. Szent-Györgi's paradox is analogous to one Theodore Porter has linked to science in the early twentieth century more generally: fully confident in its technical abilities, science began to withdraw from morality and politics as it became increasingly identified only with technicalities.[163] The histories of the artificial cell and matter in action lead us to biologists' increasing technical virtuosity and estrangement from commonsense notions of life, and provide a new viewpoint from which to analyze how scientifically inflected ideas of life have proliferated.

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[163] Theodore M. Porter, "How Science Became Technical," *Isis* 100, no. 2 (Jun 2009): 292–309. Porter's call to understand how and why science disengaged with public reason is something of an inversion of Paul Forman's 1971 thesis that science retreated under broad cultural criticism; see Richard Staley, "The Fin de Siècle Thesis," *Berichte zur Wissenschaftsgeschichte* 31, no. 4 (Dec 2008): 311–30.