100 years of virology: from vitalism via molecular biology to genetic engineering

Lute Bos

The identification of the causative agent of tobacco mosaic disease as a novel pathogen by the Dutch microbiologist Beijerinck is now acknowledged as being the foundation of virology as a discipline distinct from bacteriology. However, as this was contrary to the prevailing theories of the time, it took many years for virology to become firmly established as a separate discipline. The history of virology illustrates how accepted concepts in science evolve by trial and error and the need for a balanced approach when manipulating natural systems.

L. Bos is in the Research Institute for Plant Protection (IPO, Wageningen University and Research Centre), PO Box 9060, 6700 GW Wageningen, The Netherlands.
tel: +31 317 41 4682,
fax: +31 317 41 0113,
e-mail: lbos.jzn@wxs.nl

It is now just over 100 years since the famous Dutch microbiologist Beijerinck published his paper on the cause of tobacco mosaic[1–4]. In it, he described the agent as a '*contagium vivum fluidum*', contrary to the current theory at the time concerning the corpuscular (cellular) nature of the causes of infectious diseases. This paper marked the beginning of a far-reaching change in thinking in microbiology and led eventually to the development of virology, a new discipline distinct from the study of microorganisms.

Contagious disease

Contagious diseases of plants, animals and man himself have been long-standing puzzles in biology, and were originally ascribed to supernatural forces. Initially, microorganisms found to be associated with disease were considered to be a result of disease, rather than its cause. Life was thought to arise spontaneously (spontaneous generation) and was claimed to be more than mere physicochemistry (the concept of vitalism). However, by the middle of the 19th century, ideas had started to change. In agriculture, Albrecht Thaer's humus theory was replaced by Justus von Liebig's revolutionary theory concerning remineralization of organic matter and the central role of mineral elements in plant nutrition[5]. Agricultural chemistry boosted agricultural production and stimulated agricultural research. Louis Pasteur, when studying fermentation in 1860, demonstrated that 'life' does not originate spontaneously but develops from 'germs'[6]. In 1876, Robert Koch, while investigating anthrax in cattle, was the first to show convincingly that contagious disease results from infection by microorganisms[7], which could be cultivated in (or on) artificial media and be back-inoculated into disease-free specimens of the natural host to reproduce disease. This is how microbiology (or, more accurately, bacteriology) emerged as a new discipline.

Koch's successful *in vitro* cultivation of bacteria such as *Bacillus anthracis* (1876; Ref. 7), *Mycobacterium tuberculosis* (1882) and *Vibrio cholerae* (1883) stimulated the search for microorganisms. The development of solid media in 1880 was of great help in making pure cultures, and such successes soon led to the establishment of the Institut Pasteur in Paris (in 1888) and the Institut für Infektionkrankheiten in Berlin (in 1891), further promoting this new scientific field. However, Koch's successful methods became a pervasive theory known as Koch's Postulates, and bacteriology began to dominate the study of disease. Indeed, Koch's Postulates were accepted as dogma: according to Pasteur in 1890 (Ref. 8), viruses, a term previously used for any poisonous- or venomous-disease-inciting agent, 'are always microbes'. Towards the end of the 19th century, however, phenomena were observed that conflicted with these ideas.

Beijerinck's novel concept

On 26 November, 1898, during a meeting of the Academy of Sciences in Amsterdam, Martinus Willem Beijerinck (1851–1931; Fig. 1) presented a now-classical paper 'on a *contagium vivum fluidum* as the cause of the spot disease of tobacco leaves'. He had become familiar with tobacco mosaic disease when teaching botany at the Agricultural School (now University) at Wageningen, The Netherlands, at the beginning of his scientific career. In 1897, soon after becoming Professor of Microbiology at the Polytechnical School (now University) at Delft, The Netherlands, he established his own bacteriology laboratory and greenhouse, and immediately started to tackle the then-enigmatic disease, in the knowledge that Professor Adolf Eduard Mayer (1843–1942; Fig. 1) at Wageningen had been unable to find a bacterial or nutritional cause of the disorder, but had been able to prove its contagiousness.

0966-842X/00/$ - see front matter PII: S0966-842X(99)01678-9

Beijerinck's paper still makes fascinating reading owing to its clarity of writing and reasoning. A significant aspect was the application of unglazed filter candles (which had been developed 13 years before by Chamberland to obtain 'physiologically pure' water) for removing all visible microorganisms from expressed plant sap. Beijerinck concluded that infection is not caused by a microorganism (a *contagium fixum*), but by a non-corpuscular (i.e. non-cellular) entity, which he named *contagium vivum fluidum*. Within the originally poorly defined category 'viruses', filtration helped to define another subcategory, the filterable viruses. However, this was not Beijerinck's sole criterion for recognizing the tobacco-mosaic-disease-causing agent as something new, as throughout his text he refers to the 'contagium' or, more often, the 'virus'.

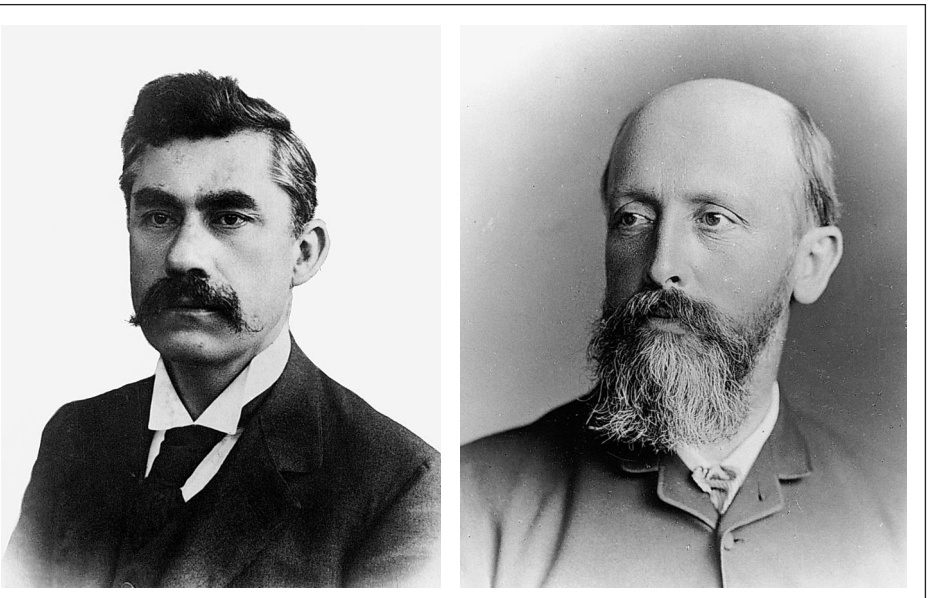

Fig. 1. Left: Martinus Willem Beijerinck (1851–1931). Right: Adolf Eduard Mayer (1843–1942). Photographs courtesy of the historical collection, Agricultural University, Wageningen, The Netherlands.

Beijerinck's virus was an entity fundamentally different from microorganisms, as it was present systemically in plants, passively moving, together with the plant's metabolites; it multiplied in growing tissue; and it retained infectivity in expressed sap after filtration and alcohol precipitation, as well as after storage in desiccated leaves and dry soil. Beijerinck clearly indicated that the virus became part of the cell's metabolism: 'Without being able to grow independently, it is drawn into the growth of the dividing cells and here increased to a great degree without losing in any way its own individuality in the process'. Beijerinck's awareness that the virus required an active host metabolism was crucial. Beijerinck's biographer stated that 'Throughout the paper, Beijerinck expresses a firm belief in the existence of an autonomous sub-microscopical (that is, subcellular) form of life'[9]. At the time, this was an entirely new concept. The prevailing theory that 'all viruses are microbes' was altered into 'a virus is not a microbe'. The word virus was acquiring an entirely new meaning, but would this revolutionize the study of infectious disease, or was it merely the threshold of change?

Forerunners and contemporaries of Beijerinck

Prior to Beijerinck's description of the *contagium vivum fluidum*, something had been 'in the air' already. In 1898, Beijerinck referred to observations made earlier by Mayer, an agricultural chemist trained in the School of Leibig, but also interested in fermentation[10]. In 1879, Mayer, like Beijerinck a teacher at the Agricultural School in Wageningen, and director of its Agricultural Experimental Station, was asked by farmers to study a tobacco disease then prevalent in the region. He called it mosaic disease (Fig. 2), and although he found no evidence of causal involvement of a visible organism, nutritional factors, humidity or temperature, he proved its infectious nature by transfer of the causal agent in expressed sap introduced into healthy plants by pricking with glass capillaries. In his 1882 paper, which is often overlooked, Mayer speculated on the existence of a 'soluble, possibly enzyme-like contagium, although almost any analogy for such a supposition is failing in science'[11]. However, in his 1886 paper, he gave up the idea of the possible involvement of an enzyme and adhered to the prevailing theory, with the interesting restriction that the mosaic disease 'is bacterial, but that the infectious forms have not yet been isolated, nor are their forms of life known'[12].

The way in which a theory can become dogma[13] is illustrated by the involvement of the Russian biologist Dimitrii Josifovič Ivanovsky (1864–1920; Fig. 3). In 1892, at the Academy of Sciences in St Petersburg, he read a short paper[14] on the tobacco mosaic disease, in which he stated without any further detail 'that the sap of leaves attacked by the mosaic disease retains its infectious qualities even after filtration through Chamberland filter candles'. From the outset, Ivanovsky insisted that he was dealing with a microorganism that could have passed through the pores of the bacteria-proof filter or that produced a filterable toxin, and he

Fig. 2. Symptoms of tobacco mosaic virus. (Photograph courtesy of the IPO, Wageningen, The Netherlands.)

Fig. 3. Postage stamp issued in Russia in 1964 on the occasion of the 100th birthday of Dimitrii Ivanovsky (1864–1920), claimed to be the founder of virology.

continued looking for cultivable bacteria. In reaction to Beijerinck's report, Ivanovsky later related that by 1892, he himself had already 'succeeded in evoking the disease by inoculation of a bacterial culture'[15], and in 1903, he claimed 'that the contagium of the mosaic disease is able to multiply in the artificial media'[16]. Obviously, Ivanovsky did not grasp the scope of his observations, and recent efforts to mark the year he published his results as the beginning of virology[17,18] have been renounced[19].

Also of interest are experiments performed at the same time as Beijerinck's investigations on tobacco mosaic disease by a German commission headed by Loeffler and Frosch on the cause of foot and mouth disease in cattle[20,21]. There is a remarkable parallel between Loeffler and Frosch's approach and conclusions and those of Beijerinck; however, Loeffler and Frosch did not refute the germ theory but ascribed the cattle disease to very small organisms. In fact, they speculated that 'the agents of numerous other infectious diseases of man and animals, such as smallpox, cowpox, scarlet fever, measles, typhus, and rinderpest etc., so far sought in vain, belong to the group of these minutest organisms'.

'Invisible' microbes

At the time of Beijerinck's, and Loeffler and Frosch's investigations, another line of research began at the Institut Pasteur in Paris. It concerned several infectious diseases of animals and man caused by filterable and 'invisible' agents, and included bovine pleuropneumonia, a cattle disease studied by Roux and others[22]. Initially, this disease seemed to defy Koch's Postulates, but eventually the causative agent was cultivated under very specific conditions, and could be visualized using the light microscope at high magnification, although they were 'so small that their form was difficult to define'. In 1903, in what was probably the first written review on 'viruses', Roux included Beijerinck's tobacco mosaic contagium as well as the agent of bovine pleuropneumonia and named them 'so-called "invisible" microbes'[23]. He then concluded that 'One cannot say that the microbe of pleuropneumonia is invisible, it is at the limit of visibility, it forms a transition between the ordinary bacteria and those which the microscope is incapable of showing'. The existence of sub-microscopic organisms, previously only a matter of speculation, was then viewed as a virtual certainty[24]. Pasteur's 'all viruses are microbes' continued to echo and Roux's 1903 paper haunted medical and animal virology for many years; indeed, these sub-disciplines still tend to regard viruses as microorganisms.

It was not until 1960 that electron microscopy revealed the involvement of a mycoplasma-like organism instead of non-cellular viruses in pleuropneumonia and of 'pleuropneumonia-like organisms' in aster-yellows-like plant diseases. They are now known as mollicutes, the smallest-known prokaryotic microorganisms, and are wall-less and bounded only by unit membranes; they are therefore pleomorphic, and able to pass through bacteria-retaining filters. Mollicutes found in plants resemble viruses in their relationships with plants (systemic infection) and insect vectors (persistent transmission). In these respects, they are virus-like agents, and have often confounded diagnosis of viral diseases.

Further evidence of the chemical, non-cellular nature of true viruses

At the time of Beijerinck, the methodologies and tools for experimentally testing his views were not yet available and, immediately after 1898, Beijerinck returned to bacteriology. When studying the etiology of graft-transmissible variegations, the German geneticist Erwin Baur (1876–1933) stated in 1904 that the agent of such disorders 'cannot be a living organism' but must be 'a nonorganized, let us say a pure chemical substance' and that 'the virus might function as a product of the metabolism of the infected plant'[25]. Mayer had earlier proposed an enzyme-like nature for the infectious agent of the tobacco mosaic disease[11]. Beijerinck later compared the infectious agent of tobacco mosaic disease with genes. In the early 1930s, experiments with collodion filters indicated that viruses range in size from ~300 nm to ~15 nm. This created further doubts as to the microbial nature of viruses, as it was argued that all the 'machinery' associated with a living organism could not be packed in a volume hardly larger than a protein molecule.

The advent of molecular biology

While Beijerinck stressed the non-organized, non-cellular but living nature of the new category of disease agents, Baur emphasized their mere chemical (i.e. non-living) quality. However, the true nature of viruses remained a matter of speculation for three more decades. Viruses were increasingly compared with enzymes, as already done by Mayer[11], or with genes, and Beijerinck had already ascribed the material base of heredity to enzymes[26,27]. However, prior to the advent of molecular biology, nobody knew the nature of either enzymes or genes, nor the relationships between them.

For the first three decades of the 20th century, viruses could only be studied for their transmissibility and host reaction, which are rather variable biological properties. However, the discovery of a rapidly increasing number of viral diseases, particularly during the 1920s, increased the need for information on the intrinsic properties of their causal agents. In 1927, James Johnson described 'physicochemical virus properties'[28] in plants, a challenging but now misleading term for nothing more than the persistence of the infectious agents in expressed sap on dilution, heating, chemical treatment and storage.

Real change only began in 1935 when the chemist Wendel M. Stanley (Fig. 4) was hired by the Rockefeller

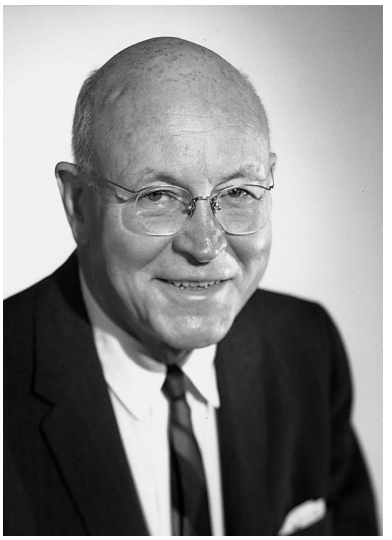

Fig. 4. Wendel M. Stanley (1904–1971). Photograph courtesy of the Virus Laboratory, University of California, Berkeley, CA, USA.

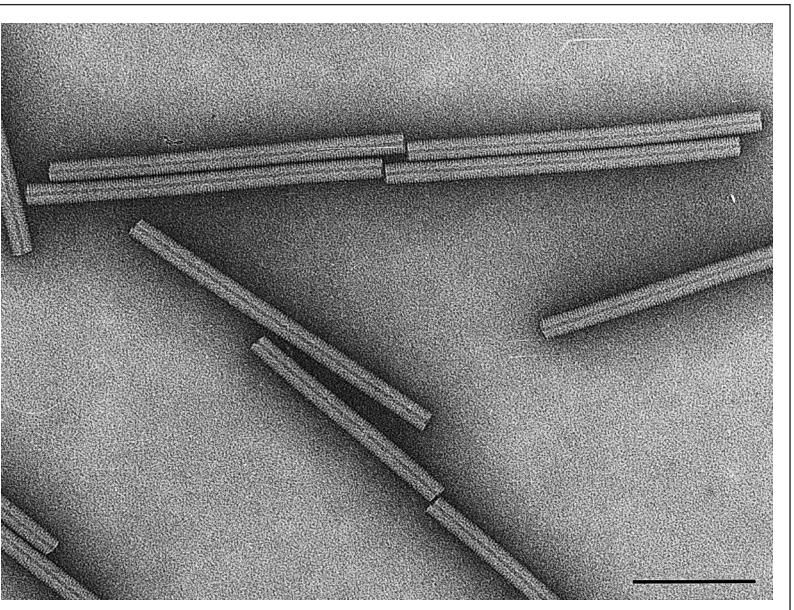

Fig. 5. Electron micrograph of particles of tobacco mosaic virus negatively stained with uranyl acetate. Scale bar represents 100 nm. Photograph courtesy of Dr J.T. Finch.

Institute to work on a more chemical approach to investigating the nature of viruses. Northrop had just successfully isolated and crystallized trypsin, pepsin and other enzymes, and soon after his arrival, Stanley succeeded in isolating 'a crystalline protein possessing the properties of tobacco mosaic virus' from diseased plants[29]. This later qualified him, together with Northrop and Sumner, for the 1946 Nobel prize for chemistry. Although erroneously describing tobacco mosaic virus (TMV) as an autocatalytic enzyme, this achievement, together with the characterization of the virus as a protein–nucleic acid complex by F.C. Bawden and N.W. Pirie in the UK soon afterwards[30], provided the crucial breakthrough in our understanding of viruses as truly physicochemical entities and their later description as genetic entities. These events signalled the advent of modern molecular biology and were a springboard for the development of the double helix model of genetic activity proposed by Watson and Crick in 1953 (Ref. 31).

Electron microscopy (Fig. 5), which had developed since the late 1930s, helped to eliminate much of the mystery shrouding the hitherto invisible disease agents that had long been 'beyond the microscope'. In the 1960s, it served as a key tool to solve the riddle of Roux's so-called 'invisible microbes'.

Viruses at the threshold of life

As described, after 1898 another 40 years were required for science to develop the methodology and technology required for unambiguous characterization of viruses. Several more years elapsed before the final description of their molecular nature as non-cellular, small packages of non-host genetic information, obligate parasites lacking any physiological machinery of their own; viruses live 'a borrowed life'[32]. Their study has much to say about the nature of life[33]. In their design and function, viruses really are at the threshold of life[34], and thus of utmost interest to biologists. They continue to play a key role in molecular biology.

When dying at the age of nearly 80 after a long and highly productive, mainly bacteriological career, Beijerinck had not lived long enough to witness the physical discovery of the agent, which he – as the 'Mendel of virology', far ahead of his time – had envisioned in 1898. The actual change of paradigm and general acceptance by the profession, and the subsequent change in technology turned out to be a time-consuming process. However, there is no doubt that conceptually, virology was conceived in 1898 when Beijerinck's classical paper was presented independently[1].

Back to Mayer

Soon after Beijerinck's paper was published, his former colleagues at Wageningen must have realized how close he and even Mayer were to the mark in their description of viruses. This is testified by the cartoon (Fig. 6) drawn in 1900 by Louis Raemaekers (A.M. De Ranitz, PhD thesis, University of Amsterdam, 1989). It depicts Mayer, while studying life *in vitro* as a student of Liebig's in a chemical laboratory, as Goethe's Dr Faust approaching the threshold of life with Mephistopheles, the symbol of temptation and evil, in the background.

The cartoon is highly visionary in that it represents the old dilemma between vitalism – that is, an awareness of something special in life, be it a vital factor or just natural complexity – and mechanicism – that is, the Cartesian, analytical, reductionist or physicochemical approach.

In agriculture, technological development was boosted by Leibig's agricultural chemistry (introduced to The Netherlands by Mayer). The beginning of virology, as conceived by Mayer but voiced by

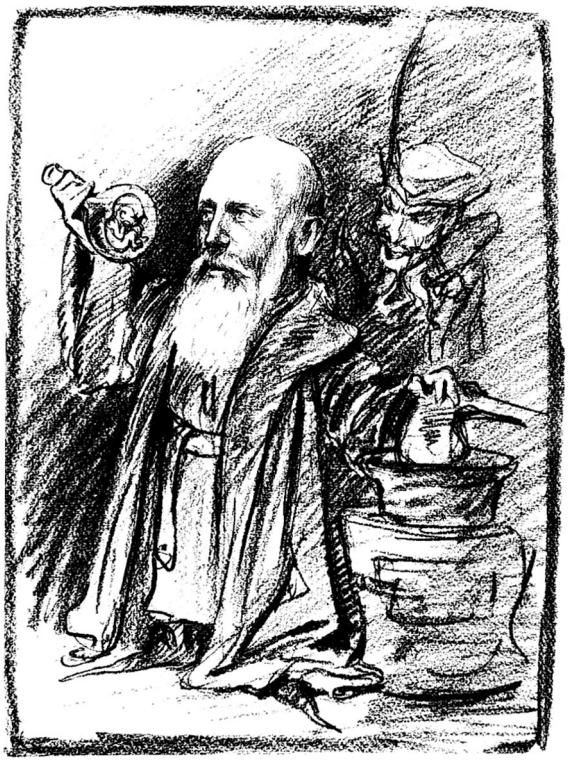

Fig. 6. Cartoon of Professor Adolf Mayer by Louis Raemaekers. Mayer is depicted as Goethe's Dr Faust with Mephistopheles as the symbol of evil in the background. It testifies the awareness of Mayer's (and Beijerinck's) involvement in phenomena at the threshold of life, and also symbolizes the beginning of virology. (Image courtesy of the historical collection, Agricultural University, Wageningen, The Netherlands.)

Beijerinck, was later followed by molecular biology, largely stimulated by the study of viruses and with the help of viruses as valuable and manageable tools of experimentation[31,34]. Biotechnology, including genetic engineering, reaching the threshold of life with outlooks towards engineering of life itself (as envisioned by Raemaekers) was, and still is, thought to be the final outcome.

Lessons to be learned

Keeping Raemaekers' Beijerinck-inspired cartoon in mind, there are lessons to be learned from the history of virology on its way from vitalism, via agricultural chemistry and molecular biology, to genetic engineering.

The first lesson is that progress in science requires human involvement. Progress in virology, as in science at large, involved human concepts of reality, which evolved by trial and error, with no one contribution independent from the others. In attempting to grasp reality, scientists are working with images in the same way as artists such as Raemaekers. The images are the concepts or the definitions of concepts (i.e. the ideas, theories or paradigms). Such images of reality, according to ancient Jewish teaching, should never grow into graven (carved) images, that is they should not become dogma. We must keep an open mind as to the unknown, and, like Beijerinck, be critical of current opinion. Definitions must be revised continually to accommodate the latest discoveries.

Holism, though much in vogue now, teaches that reality is so complex and multifactorial that our images or models will always fall short. This implies that we will never be able to manage nature as a whole, and could be why even so-called holistic approaches are doomed to fail. Any approach to disease control could, in the short term, help control one disease but it is likely to create new ecological niches that could allow other pathogens and pests to emerge. However, the consequences of reductionism – applying biotechnology and genetic engineering, thereby leading to science-based technological interference with natural complexity – are also uncertain. Practically any interference with natural systems that addresses single factors will almost certainly imbalance nature and create secondary problems, hence the increasing concern about newly emerging or re-emerging viral diseases[35,36].

Dealing with nature – including the control of viral diseases – therefore has to involve careful adjustment of natural equilibria rather than improvident exploitation. This requires seeking a balance between belief in the 'all-encompassing' approach on the one side and knowledge of detail on the other side, and prudent implementation of both approaches. The search for this balance can be nothing other than trial and error. Raemaekers' cartoon artistically represents the crucial question regarding the reliability of our images of reality and the scope of our technological interference with nature.

References

1 Bos, L. (1999) Beijerinck's work on tobacco mosaic virus: historical context and legacy. *Philos. Trans. R. Soc. London Ser. B* 354, 675–685

2 Calisher, C.H. and Horzinek, M.C. (eds) (1999) *100 Years of Virology: the Birth and Growth of a Discipline*, Springer-Verlag

3 Harrison, B.D. and Wilson, T.M.A. (eds) (1999) Tobacco mosaic virus: pioneering research for a century. *Philos. Trans. R. Soc. London Ser. B* 354, 517–685

4 Scholthof, K-B.G. *et al.* (eds) (1999) *Tobacco Mosaic Virus: One Hundred Years of Contributions to Virology*, American Phytopathological Society, St Paul, MN, USA

5 von Liebig, J. (1840) *Die Chemie in ihrer Anwendung auf Agrikultur und Physiologie*, Braunschweig

6 Pasteur, L. (1860) Expériences relatives aux générations dites spontanées. *C.R. Hebd. Séances Acad. Sci. Paris*, 303–307

7 Koch, R. (1876) Aetiologie der Milzbrandkrankeit begründet auf die Entwicklungsgeschichte des *Bacillus anthracis*. *Beitr. Biol. Pfl. Breslau* 2, 277–310

8 Pasteur, L. (1890) La rage. *La Lecture* 65, 449–465

9 Kluyver, A.J. (1940) Beijerinck, the microbiologist. In *Martinus Willem Beijerinck, His Life and His Work* (Van Iterson, G. *et al.*, eds), pp. 99–154, Nijhoff

10 Mayer, A. (1879) *Lehrbuch de Gärungschemie*, (3rd edn), Heidelberg

11 Mayer, A. (1882) Over de mozaikziekte van de tabak; voorloopige mededeeling. *Tijdschr. Landbouwk.* 2, 359–364

12 Mayer, A. (1886) Ueber die Mosaikkrankheit des Tabaks. *Landw. Vers. Stat.* 32, 451–467
English translation: Mayer, A. (1942) Concerning the mosaic disease of tobacco. *Phytopathol. Classics* 7, 11–24

13 Bos, L. (1981) Hundred years of Koch's Postulates and the history of etiology in plant virus research. *Neth. J. Plant Pathol.* 87, 91–110
14 Ivanovsky, D. (1892) Ueber die Mosaikkrankheit der Tabakspflanze. *St Petersb. Acad. Imp. Sci. Bull.* 35, 67–70
English translation: Ivanovsky, D. (1942) Concerning the mosaic disease of tobacco. *Phytopathol. Classics* 7, 25–30
15 Ivanovsky, D. (1899) Ueber die Mosaikkrankheit der Tabakspflanze. *Centbl. Bakteriol.* 5, 250–254
16 Ivanovsky, D. (1903) Ueber die Mosaikkrankheit der Tabakspflanze. *Z. PflKrankh.* 13, 1–4
17 Levine, A.J. *et al.* (1994) Foreword: 100 years of virology. In *Encyclopedia of Virology* (Vol. 1) (Webster, R.G. and Granoff, A., eds), pp. XLI–XLIII, Academic Press
18 Lustig, A. and Levine, J. (1992) One hundred years of virology. *J. Virol.* 66, 4629–4631
19 Bos, L. (1995) The embryonic beginning of virology: unbiased thinking and dogmatic stagnation. *Arch. Virol.* 140, 613–619
20 Loeffler (1898) Bericht (IV) der Kommission zur Erforschung der Maul-und Klauenseuche bei dem Institut für Infektionkrankheiten in Berlin. *Centrbl. Bakt. Parasitenk.* 24, 569–574
21 Loeffler and Frosch (1898) Berichte (I–III) der Kommission zur Erforschung der Maul-und Klauenseuche bei dem Institut für Infektionkrankheiten in Berlin. *Centrbl. Bakt. Parasitenk.* 23, 371–391
22 Nocard *et al.* (1898) Le microbe de la péripneumonie. *Ann. Inst. Pasteur* 12, 240–262
23 Roux, E. (1903) Sur les microbes dits 'invisibles'. *Bull. Inst. Pasteur* 1, 7–12, 49–65
24 Smith-Hughes, S. (1977) *The Virus. A History of the Concept.* Heinemann, London
25 Baur, E. (1904) Zur Aetiologie der infektiösen Panachierung. *Ber. dt. bot. Ges.* 22, 453–460
English translation: Baur, E. (1942) On the etiology of infectious variagation. *Phytopathol. Classics* 7, 53–62
26 Beijerinck, M.W. (1900) On different forms of hereditary variation of microbes. *Proc. Sect. Sci. Kon. Akad. Wetensch.* 3, 352–365
27 Beijerinck, M.W. (1917) The enzyme theory of heredity. *Proc. Sect. Sci. Kon. Akad. Wetensch.* 19, 1275–1289
28 Johnson, J. (1927) The classification of plant viruses. *Res. Bull. Wash. Agric. Exp. Stn.* 76, 1–16
29 Stanley, W.M. (1935) Isolation of a crystalline protein possessing the properties of tobacco mosaic virus. *Science* 81, 644–645
30 Bawden, F.C. and Pirie, N.W. (1937) The isolation and some properties of liquid crystalline substances from solanaceous plants infected with three strains of tobacco mosaic virus. *Proc. R. Soc. London Ser. B* 123, 274–320
31 Watson, J.D. and Crick, F.H.C. (1953) A structure for deoxyribose nucleic acid. *Nature* 171, 737–738
32 Laidlaw, P.P. (1938) *Virus Diseases and Viruses*, Cambridge University Press
33 Stanley, W.M. and Valens, E.G. (1961) *Viruses and the Nature of Life*, E.P. Dutton & Co. Inc., New York
34 Fraenkel-Conrat, H. (1986) The history of tobacco mosaic virus and the evolution of molecular biology. In *The Plant Viruses* (Vol. 2) (Van Regenmortel, M.H.V. and Fraenkel-Conrat, H., eds), pp. 5–17, Plenum Press
35 Bos, L. (1992) New virus problems in developing countries: a corollary of agricultural modernization. *Adv. Virus Res.* 41, 349–407
36 Morse, S. ed. (1993) *Emerging Viruses*, Oxford University Press

Bridging the gap

Cellular Microbiology: Bacteria–Host Interactions in Health and Disease
by B. Henderson, M. Wilson, R. McNab and A.J. Lax

John Wiley & Sons Ltd, 1999.
£75.00 hbk/£29.95 pbk
(xxv + 452 pages)
ISBN 0 471 98678 X/
ISBN 0 471 98681 X

Cellular microbiology is a field of research that describes prokaryotic–eukaryotic interactions. As an emerging and rather autonomous scientific discipline, cellular microbiology combines the ways of thinking and the experimental strategies of microbiology and cellular biology. In fact, the importance of cellular microbiology has its roots in the renewed and growing interest in bacterial infections, once thought defeated but currently still increasing and diversifying in spite of antibiotics and some efficient vaccines. The understanding of what is happening during the infection process is thus of primary importance, a fact which explains why several journals specializing in infection and host defences have recently been launched. However, most microbiologists ignore cellular biology (and vice versa), and most immunologists ignore both these subjects and focus mainly on the properties of T and B cells. There is a great need for a textbook that provides the necessary basic knowledge in the three aforementioned disciplines for students and scientists.

Cellular Microbiology: Bacteria–Host Interactions in Health and Disease is such a book, aimed at bridging the gap between microbiology, cellular biology and immunology. I have read it with pleasure and great interest, and I consider that its initial goals have been reached. Whatever their research field, readers will learn a lot from the chapters concerning disciplines they are less familiar with. The way the book is organized might at first look surprising because well known, basic information is provided. Could numerous pages have been saved for more detailed descriptions by removing this basic information? The answer is clearly no: the manner in which the information is presented in the book generates a form of 'landscape', in which the reader can 'see' bacteria and host cells interacting. It was a genuine pleasure to be reminded of the complexity and diversity of the mechanisms involved in the infection process and this can also assist researchers greatly in placing the molecular mechanisms they are working on in a general physiopathological context. On the down side, the iconography is rather poor and often outdated, and the absence of coloured figures does not help. It also would have been useful to see some original figures (e.g. tissue sections, 3-D structures) rather than just sketches. In spite of these few reservations, *Cellular Microbiology* is a timely and extremely welcome textbook.

Gabriel Gachelin
Department d'Immunologie,
Institut Pasteur,
25 rue de Dr Roux,
75724 Paris Cedex 15,
France