the equivalents of cells — true morphological units — are masses of protoplasm, devoid alike of cell-wall and nucleus" and described[27,28] development in 1880 as "progress from almost formless to more or less highly organized matter, in virtue of the properties inherent in that matter". However, he also recognized that recent cytological investigation, and especially the unfolding understanding of the role of chromosomes in nuclear division, necessitated a refinement in the previous opposed alternatives of 'preformation' versus 'epigenesis'.

Late nineteenth- and early twentieth-century biologists indeed attempted to forge just such a synthesis — to integrate preformationist principles into epigenetic explanations of development — particularly after the advent of genetics[29,30]. So, although Huxley's concept of histological structure might not have advanced cytology, it did serve the important function of focusing biologists' attention on the physiology as well as the morphology of the cell, and it spawned an epigenetic tradition in British biology that continued to resonate well into the twentieth century[31]. Conrad Hal Waddington's concept of the 'epigenetic landscape', for example, can be linked to this tradition, as can the current interest among developmental biologists in exploring the interaction between genes and the environment[32–34].

Marsha L. Richmond is Associate Professor of Science and Technology, Interdisciplinary Studies Program, Wayne State University, Detroit, Michigan 48202 USA.
e-mail: marsha.richmond@wayne.edu

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1. Duchesneau, F. *Genèse de la Théorie Cellulaire* (Bellarmin, Paris, Montreal, 1987).
2. Harris, H. *The Birth of the Cell* (Yale Univ. Press, New Haven, 1999).
3. Haeckel, E. *Generelle Morphologie der Organismen* (G. Reimer, Berlin, 1866).
4. Rinard, R. The problem of the organic individual: Ernst Haeckel and the development of the bigenetic law. *J. Hist. Biol.* **14**, 249–275 (1981).
5. Nyhart, L. K. *Biology Takes Form: Animal Morphology and the German Universities, 1800–1900* (Univ. Chicago Press, Chicago, 1995).
6. Coleman, W. Cell, nucleus, and inheritance: an historical study. *Proc. Amer. Phil. Soc.* **109**, 124–158 (1965).
7. Roe, S. A. *Matter, Life, and Generation: Eighteenth-Century Embryology and the Haller–Wolff Debate* (Cambridge Univ. Press, Cambridge, 1981).
8. Jacyna, L. S. Immanence or transcendence: theories of life and organization in Britain, 1790–1835. *Isis* **74**, 311–329 (1984).
9. di Gregorio, M. *T. H. Huxley's Place in Natural Science* (Yale Univ. Press, New Haven, 1984).
10. Desmond, A. *Huxley: From Devil's Disciple to Evolution's High Priest.* (Addison-Wesley, Reading, MA, 1997).
11. Desmond, A. Redefining the X axis: 'professionals,' 'amateurs' and the making of mid-Victorian biology — a progress report. *J. Hist. Biol.* **34**, 3–50 (2001).
12. Lyons, S. L. *Thomas Henry Huxley: The Evolution of a Scientist* (Prometheus, Amhurst, NY, 1999).
13. Winsor, M. P. *Starfish, Jellyfish, and the Order of Life: Issues in Nineteenth-Century Science* (Yale Univ. Press, New Haven, 1976).
14. Huxley, T. H. The Cell-Theory. *Brit. Foreign Medico-Chirurgical Rev.* **12**, 285–314 (1853).
15. Huxley, T. H. *The Scientific Memoirs of Thomas Henry Huxley* (eds Foster, M. & Lankester, E. R.) 4 vols (Macmillan, London, 1898–1901).
16. Review of T. H. Huxley, "The Cell-Theory". *Edinburgh New Phil. J.* **53**, 172–177 (1853).
17. Review of T. H. Huxley, "The Cell-Theory". *Quart. J. Microsc. Sci.* **1**, 307–311 (1853).
18. Review of T. H. Huxley, "The Cell-Theory". *Medical Times & Gazette* 396 18 October (1856).
19. Lyons, R. D. Annals of micrology. *Brit. Foreign Medico-Chirurgical Rev.* **13**, 418 (1854).
20. Carpenter, W. B. President's address. *Quart. J. Microsc. Sci*. **4**, 17–33 (1856).
21. Huxley, L. (ed.) *Life and Letters of Thomas Henry Huxley* 2nd edn **1**, 203 (Macmillan, London, 1913).
22. Baker, J. R. *The Cell Theory. A Restatement, History, and Critique* (Garland, New York, London, 1988).
23. Hughes, A. F. W. *A History of Cytology* (Abelard–Schuman, New York, 1959).
24. Churchill, F. B. in *A Conceptual History of Modern Embryology* (ed. Gilbert, S.) 16 (Plenum, New York, London, 1991).
25. Kölliker, A. *Manual of Human Histology* (Translated by Huxley, T. H. & Busk, G.) 2 vols (Sydenham Society, London, 1853–1854).
26. Huxley, T. H. Biology. *Encyclopaedia Britannica*, 9th edn. **3**, 682 (Scribner's, New York, 1878).
27. Huxley, T. H. The coming age of the origin of species. *Nature* **22**, 1–4 (1880).
28. Huxley, T. H. *The Physical Basis of Life* (Chatfield, New Haven, 1870).
29. Baxter, A. L. Edmund B. Wilson as a preformationist: some reasons for his acceptance of the chromosome theory. *J. Hist. Biol.* **9**, 29–57 (1976).
30. Richmond, M. L. British cell theory on the eve of genetics. *Endeavour* **25**, 55–60 (2001).
31. Richmond, M. L. T. H. Huxley's criticism of German cell theory: an epigenetic and physiological interpretation of cell structure. *J. Hist. Biol.* **33**, 247–289 (2000).
32. Robertson, A. Conrad Hal Waddington, 8 November 1905–26 September 1975. *Biogr. Mem. Fell. Roy. Soc.* **23**, 575–622 (1977).
33. Chadwick, D. J. & Cardew, G. (eds) *Epigenetics* (Chichester, New York, J. Wiley, 1998).
34. International Interdisciplinary Symposium, Contextualizing the genome: the role of epigenetics in genetics, development & evolution, 25–28 November 2001, Ghent University, Het Pand, Belgium.
35. Jahn, I., Löther, R. & Senglaub, K., *Geschichte der Biologie: Theorien, Methoden, Institutionen, Kurzbiographien* (Fischer, Jena, 1982).

Online links

DATABASES
The following terms in this article are linked online to:
Encyclopedia of Life Sciences: http://www.els.net
Charles Darwin | Thomas Henry Huxley | Matthias Schleiden | Theodor Schwann

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OPINION

The Rockefeller Foundation and the rise of molecular biology

Pnina G. Abir-Am

The Rockefeller Foundation began to support a systematic transfer of physico-chemical technology to experimental biology in the early 1930s. A close look at three key projects in the United Kingdom shows the impact and limits of private philanthropy on scientific innovation.

The role of philanthropic foundations in society is of interest to historians, economists and sociologists who seek to understand the prominence of such institutions at historical junctions, such as the sudden endings of the First and Second World Wars, and, more recently, the Cold War. At such times of transition, foundations — situated at the interface of the public and private sectors, or of the state, the corporate/industrial sphere and civic society — seem to have anticipated important policy initiatives on both social and scientific innovation. Foundations have the advantage of greater flexibility than the state or other bureaucracies[1,2], and such innovative policies were later pursued on a larger (both national and international) scale by governments or by large corporations and non-governmental organizations.

Scholarship on the role of foundations in science has greatly increased in the past two decades, not only because of a rising interest in the organizations that mediate between the state and civic society, but also owing to the rise of science to cultural prominence[3]. Against this background, the interaction between one of the foremost philanthropic foundations, the Rockefeller Foundation (RF), and major scientific change — such as the rise of cellular and molecular biology between the 1930s and the 1960s — sheds light on issues of interest to both scientists and historians.

How did the RF come to be one of the most stable sources of funding during the transition from classical (organismic) biology to cellular and molecular biology in the period between the mid-1930s and the mid-1960s?

What was the impact of its specific funding strategies on scientific progress? And can the RF's long-term funding patterns — which required that it be kept closely informed of scientific developments in the laboratories of its grantees — shed any light on the philosophical and ethical issues associated with turning points in science? These points include pivotal problems such as the relationship between theory and experiment; between biology, chemistry and physics; between individual and institutional cooperation; and between equal opportunity and harassment according to criteria of gender or ethnicity.

The three case-studies of long-term RF-sponsored projects discussed below: in cellular physiology at the Molteno Institute in Cambridge; protein structure at the Cavendish Laboratory, also in Cambridge; and biophysics at King's College in London, illustrate all these problems, as well as the more specific themes of the rise of molecular biology, and the impact and limits of philanthropy in scientific innovation.

The Rockefeller Foundation

The RF's support of science has previously been tackled from various angles by many authors[4–19]. Historians, in particular, have often emphasized its impact on the development of institutes, but also on specific disciplines or scientists. Here, I integrate such previous emphases, and pay special attention to an analytical distinction that is often ignored or belittled — namely, the distinction between the intentions of the RF, as stated in policy-framing documents, and its actual implementation of such policies. Although many good intentions were shown in the policy-framing documents, their implementation was subject to many practical constraints. Such constraints tended to accumulate and led to 'unintended consequences'[4,5,13,18,19]. This gap between framing and implementation explains why this article diverges from rosier accounts of the RF's influence[10–12].

The officers of the RF agonized over many choices — between large- and small-scale investments; between entrepreneurial or famous scientists versus unknown ones; between prestigious and peripheral institutions; expensive versus modest cost instruments; or the exercise of direct versus indirect or delegated power by the trustees of the Foundation[19]. Last, but not least, there was the issue of accountability, not only within the RF, but also in the scientific community, sponsored academic/research institutions, and, ultimately, the civic society that granted the RF and other foundations a tax-exempt status.

Figure 1 | **John D. Rockefeller, Sr (1839–1937) and John D. Rockefeller, Jr (1874–1960).** © Reprinted with permission from the Rockefeller Archive Center.

Education and medical research. The Rockefeller philanthropies were founded by John D. Rockefeller, Sr (1839–1937) and John D. Rockefeller, Jr (1874–1960) between 1902 and 1923 (FIG. 1; BOX 1). Rockefeller, Sr considered education to be key to the eradication of poverty and crime, as well as a source of knowledge advancement. His emphasis on education is best seen in four enduring institutions he established: the Spelman College for the education of black women in Atlanta (founded in 1881); the University of Chicago, a pioneer in graduate education (founded in 1891); the Rockefeller University, a leading medical research institute established in 1901; and the Peking Union Medical College (founded in 1917). Medical research emerged as another favourite target of Rockefeller philanthropy. In this, Rockefeller, Sr was guided by the charismatic baptist minister Frederick T. Gates. The International Health Board was established in 1913, succeeding the Rockefeller Sanitary Commission for the Eradication of Hookworm Disease, which focused on the southern United States.

Funding policy in the 1920s. During the 1920s, a policy of "making the peaks higher", which was initiated by Wycliffe Rose, head of the International Education Board (yet another institution that was established in 1923 by Rockefeller, Jr), led the Rockefeller philanthropies to fund a few highly meritorious recipients who received large sums — often for both buildings and research — and had no obligations other than doing their own research and providing advice. During this period, the RF funded all disciplines, although they often selected middle-sized institutions and scientists with established reputations, mainly in the physical sciences (which were in the midst of exciting developments in the theory of relativity and quantum mechanics). However, after a consolidation of the Rockefeller boards between 1928 and 1932, the RF announced a new policy for its Division of Natural Sciences[4–19].

The RF's then-new director of the Natural Sciences Division was Warren Weaver (1894–1978), a mathematical physicist who had begun his career teaching engineering students at Caltech before moving to the University of Wisconsin. Weaver saw technology as the embodiment of scientific progress, and placed an emphasis on the transfer of technology from the physico-chemical sciences to experimental biology. Weaver was inspired by the scientific philosophy of leading scientists, notably the Nobel laureate biochemist from Cambridge, Frederick G. Hopkins (1860–1947). Hopkins portrayed biology as the science of life, which held the promise of helping with the increasingly violent 'social unrest' that was caused at that time by the Great Depression. He also argued that biology should displace physics — the science of death — which represented the peak of scientific activity by the early 1930s[4,20,21].

Initially, Allan Gregg, a physician (who, in 1930, became Director of the Medical Sciences Division), hoped to cover biological research as well[22]. However, Weaver's position as a 'pet' of Max Mason — the President of the RF from 1929 to 1936 and Weaver's former mentor at the University of Wisconsin — eventually meant that his Natural Sciences Division could shift its pattern of investments from physics to biology, and negotiate borderline cases with Gregg's division. Weaver's approach to funding — to give many small grants for short terms, as opposed to the previous policy of a few large, long-term grants — was detested by Gregg, who likened it to distributing "chicken feed"[23]. However, Weaver's approach prevailed, and was to have both fortunate and unfortunate consequences for scientific progress[4–19].

On the one hand, the emphasis placed by the RF on technology transfer accelerated the 'molecularization' of biology, as it funded expensive new equipment (as well as supplies and research assistance) at a time when scientific trends were subject to rapid change towards international and cross-disciplinary research[7–21]. The racist policies in central Europe following the Nazi rise to power meant that many scientists had to change and often lower their institutional or disciplinary affiliations. So, the refugee scientists, as well as those willing to help them outside central

Europe, became more responsive to the opportunities that were created by the new policy of the RF[14].

On the other hand, the RF's new emphasis on 'safe investments' in the aftermath of the Great Depression, as well as the complex relationship between the officers and the trustees, often meant that scientists could benefit from the RF's policy of encouraging interdisciplinary research only if they had entrepreneurial patrons with a prominent position — usually as directors of institutes or departments. The RF's officers favoured such established figures as formal grantees, as they were more likely to impress the RF trustees who had the ultimate say in the officers' project selections in the field. Furthermore, given some previous embarrassing charges of interference — which had led to major universities such as Cambridge and Harvard returning RF cheques[4,18,19] — the officers insisted on being approached not only by the scientist grantees, but also by the highest authorities in their institutions, usually the vice-chancellors.

These constraints eroded the initial potential of the RF's policy to encourage interdisciplinary innovators, whether they were newcomers or established scientists. Although this argument has previously been illustrated by looking at projects from the United Kingdom (in Leeds and Cambridge) and the United States[4,18,19] (at Caltech), I strengthen it here by looking at three key projects — in Cambridge and London — that came to define the scientific frontiers during the transition from classical biology to cellular and molecular biology in general, and from the study of proteins to nucleic acids in particular.

The Molteno Institute (1932–1952)

The early success of the RF in identifying suitable grantees is exemplified in its rapport of two decades with David Keilin, a pioneer of research on respiratory pigments and the cellular respiratory chain, and Director of the Molteno Institute for Biology and Parasitology at Cambridge University. In the mid-1920s, on discovering the cytochrome *c* system, Keilin switched his research almost entirely to cell biology, although he continued to supervise research in parasitology as well. Initially selected for support by the Medical Division of the RF in 1932, Keilin became one of the first RF grantees to enjoy long-term support[29].

Keilin's research fitted well into the RF's new programme of technology transfer from physical sciences to experimental biology, as he used spectroscopy to observe the spectra of oxygen carriers and catalysts of oxidation in the cell, and also compared the kinetics of various metalloprotein-coloured respiratory pigments from plants, parasitic insects and red blood cells. Keilin's research on the spectra of respiratory pigments began as a logical extension of his parasitology research — a core field in classical or organismic biology, which dealt with the intersecting life cycles of parasites and their hosts — into cellular biology, and pre-dates the RF's new policy by almost a decade.

Keilin's comparative research on reversible oxidation by metalloprotein carriers provided an intellectual framework for the work on the structure of the blood pigments haemoglobin and myoglobin. His institute provided biological expertise in the growth of these crystals, as well as an interdisciplinary affiliation for Max Perutz (since 1938) and John Kendrew (since 1946), who would share the Nobel Prize for Physiology or Medicine in 1962 for their solutions of the three-dimensional structures of haemoglobin and myoglobin, respectively[24–28]. Keilin, who grasped the crucial role of protein structure for clarifying the mystery of respiration at the molecular and cellular level, further incorporated both Perutz and Kendrew in his institute's teaching, and stabilized the precarious position of their interdisciplinary research in a university that had little interest in chemists who were working on biological substances with physical techniques.

Of equal importance for creating a space — both intellectual and institutional — for cellular and molecular biology, was Keilin's role as a science advisor. Keilin had studied or worked in several European capitals (notably with Maurice Caullery in Paris) before arriving in Cambridge in 1915, and was well informed of changes in science policy — whether by foundations or by government agencies. He was familiar with the funding strategies of the RF which, since the mid-1930s, had focused on equipment and research assistance involving physico-chemical techniques on biological material. So Keilin suggested in 1938 that Max Perutz (BOX 2), then a graduate student at Cambridge working on the X-ray diffraction of haemoglobin, be appointed assistant to Sir Lawrence Bragg, the Director of the Cavendish Laboratory (FIG. 2; BOX 2), so that they could jointly qualify for RF grants.

The Molteno Institute also hosted a virus research unit, later adopted by the Agricultural Research Council (ARC), which carried out pioneering work on both viruses and nucleic acids. Ironically, when James D. Watson recounted his personal experience in Cambridge's Medical Research Council (MRC) and ARC units during the two years before the structure of DNA was published in 1953, the only reference to Keilin was that the Molteno Institute was better heated because of its Director's asthma[31]. But Keilin provides better reasons to be remembered, among them his foresight to involve both the RF (in 1938) and the MRC (in 1947) in protein-structure research.

Although the RF supported Keilin's research for two decades, its lack of a long-term strategy after the Second World War, when it contemplated pulling out of science altogether (an event that fortunately took two decades to complete), meant that it failed to stabilize cellular biology after Keilin's retirement in 1952. Such a goal could have easily been achieved had the RF capitalized on its two decades of support. Conceivably, Keilin's (and also Hopkins') outlook of graciously accepting — but not soliciting — RF grants[4,18], and, even more so, Cambridge's refusal to endorse the RF's keen interest in them, made a great difference to their modest fortune with the RF. Ironically, this occurred despite the fact that cell biologists and biochemists such as Keilin and

Box 1 | The Rockefellers and their main educational endowments

John D. Rockefeller, Sr (1839–1937) was the founder of Standard Oil Trust (1882) which, by the time it was broken up by the United States Supreme Court in 1909, had made him the world's richest man. He gave away half of his fortune — about $500 million — primarily to education, medicine and philanthropic endowments. He founded the General Education Board (GEB) in 1902, the Rockefeller Foundation (RF) in 1913, the International Health Board (IHB) in 1913 and the Laura Spelman Rockefeller Memorial (LSRM) in 1918.

In the first half of the twentieth century, the Rockefeller organizations were an important source of philanthropic support of science. Although none of these institutions were created primarily to support science, the GEB endowed scientific departments at American universities, the IHB founded public health institutes, the LSRM supported social science research and the RF gave grants to scientists on a global scale.

John D. Rockefeller, Jr (1874–1960) also gave a comparable sum in charitable contributions. He founded the International Education Board (IEB) in 1923, which gave fellowships in the natural sciences.

Box 2 | **Funding the structure of haemoglobin**

The RF began supporting work on the structure of haemoglobin late in 1938, when Sir Lawrence Bragg (FIG. 2), then newly appointed Director of the Cavendish Laboratory of Physics, approached them at David Keilin's suggestion, for a grant to allow him to employ Max Perutz as his assistant in X-ray diffraction studies of haemoglobin. At that time, Perutz was a research student who had become a refugee overnight when his native Austria was annexed by Nazi Germany. The RF's interest in his project, probably saved not only his future in science but also his life and that of his immediate family, whom he was able to bring to the United Kingdom shortly before the outbreak of the Second World War[18].

The RF sponsored research on haemoglobin structure for over two decades, being the only stable source of support in the crucial period between 1939 and 1947. In 1947, Keilin rescued the pivotal studies on both haemoglobin and myoglobin by proposing that this work — which until then was split between the Molteno Institute (which housed the biological facilities for growing crystalline enzymes) and the Cavendish Laboratory (which housed the physical technology of X-ray diffraction used to find their structure) — be brought to the attention of the (British) Medical Research Council (MRC) as a potentially new research unit.

In 1947, the MRC established Perutz and Kendrew as a unit for the molecular structure of biological systems, shortened to molecular biology in the mid-1950s. After 15 years in a 'hut', a new Laboratory of Molecular Biology was inaugurated in Cambridge by the MRC in 1962. When this lab marked its fortieth anniversary in 1987, it counted among its members a world record of seven Nobel prize-winners. It is difficult to see how these developments would have happened without Keilin's crucial advice, both in 1938 and 1947. Although this situation kept Perutz in a dependent status for 16 years, after Bragg's departure from Cambridge in 1954, both the RF and the MRC began giving grants to Perutz in his own name, especially after he became Director of the MRC Unit at Cambridge in 1954.

Hopkins epitomized the interdisciplinary and innovative research that the RF's new policy was supposed to support.

By contrast, the big beneficiaries of large-scale and long-term RF grants tended to be physical scientists (see below), who shifted their research to biology in response to the RF's (or other) new funding opportunities. They had no concrete research agenda beyond the willingness to use physical techniques on biological material, yet such physicists did not hesitate to make frequent, bold and large-scale demands on both the RF and their home institutions. Although Keilin had advised the RF officers in 1934 that spectroscopy, or any other physical technique, would not lead to important results unless coupled with properly controlled chemical and biological investigations; and even though such advice was repeated by many other non-grantee scientists in the late 1950s, it was not heeded by Weaver or his successors.

The Cavendish Laboratory (1938–1963)

The RF's support for protein-structure research in the Cavendish Laboratory of Physics began in 1939, and was to continue for a quarter of a century — long after research in this area had been stabilized by the MRC in 1947. This gave the laboratory an edge in terms of acquiring equipment — notably, expensive X-ray cameras and electron microscopes that had to be bought in the United States, where RF grants were a source of much-needed foreign currency. The MRC — the lab's governmental sponsor — paid the salaries of the staff but gladly agreed that the RF (which had preceded it in the Cavendish Laboratory by almost a decade) continue with research assistance, fellowships, and grants for equipment. Until his departure from Cambridge in 1953, Sir W. Lawrence Bragg was the RF nominal grantee in molecular biology. As Bragg readily admitted in his numerous promise-ridden letters to the RF, its grants were crucial in carrying Perutz's work on protein X-ray crystallography from the late 1930s to the late 1940s[25–28].

The RF's long-term support of both Keilin's and Bragg's research projects on the structure and function of blood and other pigments created the institutional foundations for the rise of molecular biology in Cambridge after the Second World War. Although Perutz was the only link between cell biology and physics for almost a decade (1938–1947), he was eventually joined (in the late 1940s) by many of the would-be founders of molecular biology. In 1962, four of the five Nobel laureates in molecular biology had carried out their award-winning work at Cambridge, in a laboratory that housed equipment and materials bought with RF grants in the period between 1939 and 1966. The fifth awardee, Maurice Wilkins, who shared the DNA prize that year with Watson and Francis Crick, did his work in the Department of Biophysics at King's College, London, also with considerable RF support.

King's College, London (1946–1964)

Founded in 1946, also as an MRC research unit, Biophysics at King's enjoyed the most remarkable entrepreneurship of the unit's founder, Sir John T. Randall[32]. While still at St Andrews University, Scotland, Randall had approached the RF with a project in cell biology that used various optical techniques. Randall's service during the Second World War as a co-inventor of the cavity magnetron — a core part of the radar system that had a key role in stopping the aerial *Blitzkrieg* on London in 1940 — made him a perfect candidate for the emerging policy of using personnel and other assets of war research for peace purposes, especially in biophysics[33]. His proposal for a new Biophysics Unit reflected the predicament of interdisciplinary research: whereas the Royal Society considered it to be "too biological", the MRC assessed it as "too physical".

Unlike Keilin's and Bragg's projects at Cambridge University, which began as RF-sponsored projects that were grounded in local research traditions in the 1930s, Randall's unit was built 'from scratch' immediately after the Second World War. It stabilized in the mid-1950s at around 25 members, and the RF remained a steady source of grants for equipment for two decades.

Randall approached the RF at the suggestion of Archibald V. Hill, a Nobel Laureate and science statesman from University College London, whose own work on neurophysiology had brought him into contact with the RF's Medical and Natural Science Divisions. Hill, a neurophysiologist, hoped that Randall would not limit himself to cytogenetics. But although Hill told Weaver that Randall's vision was restricted to cytogenetic problems, Weaver was not deterred, and dismissed Hill as "not a biophysicist" (apparently Weaver believed that biophysicists were only those who turned to biology after a career in physics)[34]. For Weaver, Randall epitomized the ideal grantee, despite Weaver's observations that Randall's lab had "immature" people and "junky and messy" equipment. Moreover, Weaver had to apologize for having failed to inform the MRC Secretary, Sir Edward Mellanby (1884–1955)[36], of the RF's parallel interest in Randall's unit.

On Mellanby's retirement in 1949, he was succeeded by Sir Harold Himsworth (1905–1993)[37], who enabled the MRC units in Cambridge and at King's College to expand while shoring up the MRC's relationships with the RF. Randall's biophysical empire continued to grow during the 1950s, with the RF continuing to fund his never-ceasing requests for equipment. In 1950, the RF gave Randall $37,000 for four years, and kept on renewing at the same or higher level until the mid-1960s. Some of these RF funds were used to buy equipment that was ordered by Rosalind Franklin (1920–1958) from French manufacturers for her seminal work on the structure of DNA.

The structure of DNA

Mellanby's 'insularity' with respect to other foundations' interest in MRC staff (he did not, for example, welcome the RF's aid for British laboratories), as well as his overt anti-semitic and anti-foreigner prejudice, were to have a lasting effect on the work on DNA structure that came to preoccupy some members of both Randall's and Bragg's laboratories in the early 1950s.

To monitor Randall's entrepreneurial behaviour — of which he did not approve (stating that he was "always afraid of Randall because he seems too ready with requests, makes them too often, and has too many Jews and foreigners in his laboratories")[34] — Mellanby set up a visiting committee that was composed of members of other MRC units. During a visit of this committee in 1952, Randall instructed his staff to document their most recent results, to convey most fully their progress and productivity. Among them was Rosalind Franklin, who joined Randall's unit in January 1950 to provide expertise in X-ray diffraction. So, the 1952 'MRC Report' included her most recent results, among them the key parameters of DNA structure — notably, the evidence for the number of chains, the pitch of the helix and the symmetry type of the cell unit, which was crucial for deducing the anti-directionality of the two strands.

On seeing these data, Max Perutz, who was a member of the visiting committee, gave the confidential report to his then Ph.D. student, Francis Crick, who was about to be expelled from the laboratory by Bragg for lack of progress and unprofessional behaviour. The rest is history. The crucial role of the MRC Report in 'deducing' the structure of DNA was revealed only 15 years later in Watson's autobiographical *The Double Helix*[31]. In response, Perutz stated that, at the time, he had been inexperienced in the handling of confidential reports. However, this leak deprived Franklin of recognition for her unique results. It also deprived Randall of recognition for his pioneering emphasis on a comprehensive research programme on DNA structure, which included the hiring of Franklin, at a time when most would-be molecular biologists were preoccupied with pre-Second World War emphases on proteins and viruses. Ironically, the structure of DNA was unveiled in 1953 by Bragg, who only a year earlier had forbidden DNA work in his lab. The RF — a key funding source for both Randall's and Bragg's labs — noted that the model from Cambridge had something to do with experimental data from Randall's lab in London, its officer further scribbling Rosalind Franklin's name, in handwriting, in the left margin.

In 1962, Randall's second-in-command, Maurice Wilkins, shared the Nobel Prize after repeating Franklin's work on DNA while using equipment that was ordered by her in 1950 and paid for by the RF. The RF never asked what happened to the three cameras it bought at Franklin's specifications from manufacturers in Paris, let alone what happened to her (she had been forced to abandon her DNA work after leaving Randall's lab in April 1953, and relocating to Birkbeck College, London, where she worked on the structure of the tobacco mosaic virus until her premature death in 1958; REF. 38). Although the RF funded Franklin's trip to the United States in 1956 to lecture on virus structure at a Gordon Conference, it never approached her as a potential grantee.

At the same time, the RF continued to renew long-term grants for Randall's lab, despite the many advisors who pointed out its lack of chemical and biochemical expertise at the dawn of molecular biology. They ranked it as mixed — even mediocre — despite its large influx of both RF and MRC funds. As one of the advisors put it, the biophysicists in Randall's lab were eager to measure no matter what, as long as instruments kept arriving. This is precisely the danger that Keilin warned the RF against as early as 1934. There is good reason to believe that both the protein and DNA structure fiascos in which Bragg and Randall had been involved in 1950 and 1953, respectively, were derived in part from the unlimited power they commanded and the failure of their sponsors — the RF in particular — to demand not only financial but also interdisciplinary and moral accountability.

By 1960, however, the RF had lost its great momentum of the early 1930s. Although other foundations, most notably the Ford Foundation, blended their chosen mission rather well with the Cold War era, the RF seemed to have no clear mission. Rather than responding to the profound changes in the role of science in society that were triggered by the Second World War and the nuclear age, the RF remained a benevolent bystander, and

Figure 2 | **Sir Lawrence Bragg (1890–1971).** Professor of Physics at Cambridge, 1938–1953. © Science Photo Library.

limited its support to favourite grantees who almost always dated to the pre-war days. Starting in 1943, but especially after 1953, the RF switched the gist of its funding effort to promoting the 'green revolution' in the Third World. But that is another story.

Conclusions

The full story of the impact of funding by both private foundations and governmental agencies on the rise of molecular biology remains to be told[13,15,39,40]. However, these three case studies show key features of the RF's investments in experimental biology — namely a good selection of promising projects, coupled with a relative failure to stabilize innovative research (as in Keilin's case) or support innovative scientists (as in Franklin's case) who did not enjoy the patronage of entrepreneurial physicists such as a Randall or a Bragg. As such, they present useful lessons that science funding today can draw from the RF's experience between 1930 and 1960.

One obvious lesson pertains to allocating research grants directly to principal investigators on the basis of proposal merit, without making innovative but unestablished investigators dependent on the patronage of entrepreneurial lab directors or the Byzantine politics of universities. Grant officers in foundations and governmental agencies should be converted from administrators to science statesmen who can negotiate long-term deals with host institutions on behalf of meritorious grantees. By the same token, the accountability of such officers, as well as of grantees, has to be refined — essentially by periodical evaluations of performance.

Better coordination of research by funding agencies — which are more likely to know the entire research landscape and can organize interdisciplinary collaborations — is also a lesson to be learned from the RF's historical experience[7,19]. The RF's initiatives in stimulating international cooperation remain among its best accomplishments. Nonetheless, they lacked a long-term strategy, responding only sporadically to initiatives from some grantees. Long-term strategic planning of international, interdisciplinary workshops by funding agencies should be instituted as one of their missions.

Another area where the RF's experience can provide valuable lessons is in the use of advisory panels for both allocating and evaluating research grants. In the case studies discussed above, as well as others previously documented[4,18,19], the RF managed to collect a great deal of suitable 'intelligence' on its network of grantees, which ranged from "mere gossip" to an accurate assessment of academic politics. Yet, the RF had great difficulty in discerning good from bad advice, or knowing whether its advisors had conflicts of interest. The use of advisory systems must therefore be enhanced by introducing mandatory disclosure of conflicts of interest, as well as systematic mechanisms for pursuing both positive and negative advice. That is, advisors should be used not only as a ratifying device, but also for enhancing accountability in both research and human resources.

As for-profit funding becomes increasingly pervasive, the challenge of judicious public funding of science remains greater than ever. Historical lessons such as the RF's successes and failures are among the best available sources for seeking to creatively adapt science policy to the changing world of biopower in the twenty-first century.

Pnina G. Abir-Am is at 249 Orchard Street, Belmont, Massachusetts 02478, USA.
e-mail: pgabir@fas.harvard.edu

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1. Anheier, H. K. & Toepler, S. (eds) *Private Funds, Public Purpose, Philanthropic Foundations in International Perspective* (Kluwer, New York, 1999).
2. Condliffe Lageman, E. (ed.) *Philanthropic Foundations, New Scholarship, New Possibilities* (Indiana Univ. Press, Bloomington and Indianapolis, 1999).
3. Science and its Cultures (ed.) *International Social Science Journal* 168 (Blackwell UNESCO, Oxford, 2001).
4. Abir-Am, P. G. The discourse on physical power and biological knowledge in the 1930s: a reappraisal of the Rockefeller Foundation's 'policy' in molecular biology. *Soc. Studies Sci.* **12**, 341–382 (1982).
5. Abir-Am, P. G. Beyond deterministic sociology and apologetic history: reassessing the impact of research policy upon new scientific disciplines. *Soc. Studies Sci.* **14**, 252–263 (1984).
6. Abir-Am, P. G. The Biotheoretical Gathering, transdisciplinary authority and the incipient legitimation of molecular biology in the 1930s: new perspective on the historical sociology of science. *Hist. Sci.* **25**, 1–70 (1987).
7. Abir-Am, P. G. in *Denationalizing Science* (eds Crawford, E. *et al.*) 153–186 (Kluwer Dordrecht, 1993).
8. Abir-Am, P. G. in *Science in the 20th Century* (eds Krige, J. & Pestre, D.) 495–520 (Harwood, London, 1997).
9. Zallen, D. The Rockefeller Foundation and spectroscopy research: the programs at Chicago and Utrecht. *J. Hist. Biol*. **25**, 67–89 (1992).
10. Kohler, R. E. *Partners in Science, Natural Scientists and Foundations* (Univ. Chicago Press, Chicago, 1991).
11. Kay, L. E. *Molecular Visions, Caltech, The Rockefeller Foundation and the New Biology* (Oxford Univ. Press, Oxford, 1993).
12. Picard, J.–F. *La Fondation Rockefeller et la Recherche Medicale* (PUF, Paris, 1999).
13. Abir–Am, P. G. 'New' trends in the history of molecular biology. *Hist. Stud. Phys. Biol. Sci.* **26,** 167–196 (1995).
14. Gemelli, G. (ed.) *The Unacceptables, American Foundations and Refugee Scholars between the Two World Wars* (Presses Interuniversitaires Europeenes, Brussels, 2000).
15. Gemelli, G. (ed.) *American Foundations and Large Scale Research* (CLUEB, Bologna, 2001).
16. Weindling, P. Philanthropy and World Health: The Rockefeller Foundation and the League of Nations Health Organization, *Minerva* **XXXV**, 269–281 (1997).
17. Stapleton, D. H. Internationalism and nationalism: The Rockefeller Foundation, public health, and malaria in Italy, 1923–1951. *Parasitologia* **42**, 127–134 (2000).
18. Abir-Am, P. G. The assessment of interdisciplinary research in the 1930s: the Rockefeller Foundation and physico-chemical morphology. *Minerva* **XXVI**, 153–176 (1988).
19. Abir-Am, P. G. in *American Foundations and Large Scale Research: Construction and Transfer of Knowledge* (ed. Gemelli, G.) 71–90 (CLUEB, Bologna, 2001).
20. Kamminga, H. & Weatherall, M. The making of a biochemist. I: Frederick Gowland Hopkins' construction of dynamic biochemistry. *Med. His.* **40**, 269–292 (1996).
21. Weatherall, M. & Kamminga, H. The making of a biochemist. II: The construction of Frederick Gowland Hopkins' reputation. *Med. His.* **40**, 415–436 (1996).
22. Schneider, W. H. Allan Gregg and the Rockefeller Foundation's Medical Sciences Division. *Minerva* (in the press).
23. Weaver, W. Medicine: The new science and the old art. *J. Med. Edu.* **35**, 313–318 (1960).
24. Morange, M. *A History of Molecular Biology* (Harvard Univ. Press, Cambridge, 1998).
25. Chadarevian, S. & Kamminga, H. (eds) *Molecularizing Biology and Medicine* (Harwood, London, 1998).
26. Abir-Am, P. G. A historical ethnography of a scientific anniversary in molecular biology: the first protein X-ray photo, 1934. *Social Epistemology* **7**, 323–354; 361–362; 372–373; 380–387 (1992).
27. Perutz, M. F. *Is Science Necessary?* (Barrie and Jenkins, London, 1989).
28. Perutz, M. F. *Protein Structure* (Freeman, San Francisco, 1992).
29. Keilin, D. *The Molteno Institute of Biology and Parasitology* (Cambridge Univ. Press, Cambridge, 1951).
30. Keilin, D. *A History of Cell Respiration and the Cytochrome* (Cambridge Univ. Press, Cambridge, 1965).
31. Watson, J. D. *The Double Helix* (Atheneum, New York, 1968).
32. Wilkins, M. H. F. John Turton Randall, 1905–1984. *Biogr. Mem. Fel. Roy. Soc.* **33**, 493–535 (1987).
33. Rasmussen, N. The mid-century biophysics bubble. *Hist. Sci.* **35**, 245–296 (1997).
34. Weaver's diary, May 26, 1948, Series 401D, Biophysics, King's College, Rockefeller Archive Center (RAC), Sleepy Hollow, NY.
35. Austoker, J. & Bryder, L. (eds) *Historical Perspectives on the Role of the MRC* (Oxford Univ. Press, Oxford, 1989).
36. Dale, H. H. Edward Mellanby, 1884–1955. *Biogr. Mem. Fel. Roy. Soc.* **1**, 193–222 (1955).
37. Black, D. & Gray, J. Harold P. Himsworth, 1905–1993. *Biogr. Mem. Fel. Roy. Soc.* **39**, 201–218 (1995).
38. Sayre, A. *Rosalind Franklin and DNA* (Norton, New York, 1975).
39. Appel, T. A. *Shaping Biology, The National Science Foundation and American Biological Research, 1945–1975* (Johns Hopkins Univ. Press, Baltimore, MD, 2000).
40. Abir–Am, P. G. *Research Schools of Molecular Biology in the UK, US, and France: Science Policy and the Origins of the Biotech Revolution* (in the press).
41. Tate, P. Obituary Notice, David Keilin, 1987–1963. *Parasitology* **55**, 1–28 (1965).
42. Perutz, M. Keilin and the Molteno. *The Cambridge Review,* October, 152–156 (1987).

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