depictions of medical practitioners, Porter suggests, grew increasingly flattering, just as newer platforms for graphic humour — such as *Punch* (founded in 1841) and *Vanity Fair* (1868) — tended to eschew the coarseness and vulgarity of Georgian and Regency caricature.

Broader cultural shifts plainly fostered these new aesthetic conventions, but the role of changes in medicine itself is less clear. And in Porter's treatment of the nineteenth century, as throughout the book, one would have welcomed something about private representation as a counterpoint to public images and media constructs. If public representations of Victorian healers and healing shed much of their earthiness and theatricality, then what are we to make of certain more covert genres of medical self-portraiture, such as grizzly photographs depicting medical students at work in the dissecting room, or of late-Victorian advice books that unabashedly instructed doctors on how to succeed in business by putting on a good show? If the reader is left wanting more, however, it is because Porter's book is one of the best studies we have of public representations of medicine, a highly visual culture in which spectacle and ritual performance, although transformed, have hardly vanished. ■

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The director's tale

The Recombinant DNA Controversy: A Memoir. Science, Politics and the Public Interest 1974–1981
by Donald S. Fredrickson
American Society of Microbiology Press: 2001. 408 pp. $39.95, £32.50 (pbk)

Susan Wright

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View from the inside: Fredrickson (right), seen here with NIH committee member Charles McCarthy.

Some 25 years ago, unease within the molecular-biology community over the implications of the emerging techniques of genetic engineering triggered a major public controversy over possible hazards and misuse of the new field. In the United States, the National Institutes of Health (NIH), the world's leading biomedical research institution, was designated as the government agency responsible for developing voluntary controls. The controversy quickly encompassed the nature of the controls themselves, which had been developed largely by scientists whose career (and in some cases business) interests were closely linked to the new field.

The still-dominant view of these events is that the American public, along with a few dissident scientists, overreacted to early concerns about the hazards of genetic engineering. Eventually, the hazards were shown to be exaggerated, allowing the NIH controls to be dismantled. This conventional wisdom casts the story as a confrontation in which rational belief in science ultimately prevailed over irrational fear of the unknown.

Donald Fredrickson, the NIH director who presided over the rise and fall of the NIH controls, elaborates on this story with his legendary panache. He covers the struggles of the NIH not only with the attentive public but also behind the scenes, with the executive and legislative branches of the US government. This previously invisible face of the recombinant DNA controversy is now, apparently, revealed in Fredrickson's papers and personal letters and diaries being deposited in the US National Library of Medicine. This collection promises to substantially augment the public record provided by the NIH and the important Recombinant DNA History Collection at the Massachusetts Institute of Technology archives.

The memoir leaves little doubt about Fredrickson's own view of the genetic-engineering question as he describes the adroit manoeuvres of the NIH to protect "the gossamer quality of [its] pseudo-regulations" from conversion by the US Congress into mandatory controls that encompassed the private sector and all government agencies. Battle metaphors permeate this account of the struggle between those deemed to be 'for' or 'against' the voluntary policy espoused by the NIH. As he wrote in an unpublished article on the eve of the first major weakening of the NIH controls: "I think we have won a significant victory over a dangerously excessive reaction first set in motion by scientists." The fact that policymaking in certain other countries — notably the United Kingdom — took the turn towards uniform regulation without a bitter struggle is not noted here. This is very much an American story, told by the person at the epicentre of the American controversy.

But this narrative, with its strong focus on genetic engineering as a research tool, is strained. That the technique would move out of the research laboratory and into medicine, industry, agriculture and, most problematically, the military, was anticipated almost as soon as news of the first successful experiments began to circulate. As British molecular biologist Sydney Brenner wrote in 1974 to the British committee convened to examine genetic engineering, there were likely to be problems of controlling "institutions which can, and probably do, practise secrecy in their activities, such as defence research laboratories and, more importantly, the major drug companies".

This wider potential was marked by Stanford University's application for a patent on the early genetic-engineering techniques — an action that sent a shock wave through the NIH as the government sponsor of this work. "'The patent' was widely perceived as a modestly seismic event, a nervous shift at the conjunction of the academic/not-for-profit and commercial tectonic plates sustaining the crust of the biomedical research enterprise," writes Fredrickson. From its inception, genetic engineering promised to yield socially disruptive technologies along with advances in scientific knowledge and socially useful products.

Fredrickson is aware of these larger dimensions of genetic engineering, yet they are never allowed to intrude on his narrative. During his tenure, he was in contact with leaders of the pharmaceutical industry who made it clear that they would adhere to "the intent and spirit" of the NIH controls but not necessarily to their specific requirements — a position underscored by the flouting of the NIH controls by the rising star of the biotechnology field, Genentech, in 1978–79, when it ignored NIH procedures for approval of large-scale cultures of genetically modified organisms. That industry rebellion, underscoring the need for regulation of the new industry and posing a real dilemma for the NIH, which wanted at all costs to avoid legislation, remains invisible in this account.

Similarly, the prospect of military use of genetic engineering is mentioned but quickly dismissed on the grounds that the problem is addressed by the 1972 Biological Weapons Convention. That treaty has troubling loopholes, through which the genetic alteration of highly pathogenic agents of biological warfare has since slipped in the name of defence. These loopholes were not addressed when they were raised by members of Fredrickson's advisory committee in 1982; nor are these problematic developments confronted in this account.

Even viewing the genetic-engineering problem through the lens of research, Fredrickson skirts a question on which his narrative depends: did the risk-assessment experiments of the 1970s clear the field of significant hazard? An important answer is contained in a transcript of the first scientific meeting convened at the NIH in 1976 to discuss risk assessment. The transcript shows a key risk-assessment experiment being designed by the participants not to test a worst-case scenario, but rather to reassure the public that genetic engineering was harmless. As a participant noted, without any sign of moral indignation from his colleagues, "[This is] molecular politics, not molecular biology". As an astute *Nature* reporter later observed of the treatment of the hazard question: "One must accentuate the positive. The evidence, however, does not seem substantial."

Fredrickson acknowledges that the policies he pursued as NIH director, while yielding important scientific advances and medical benefits, also opened a Pandora's box of social and ethical problems. The new evidence on the recombinant DNA controversy promised by the release of his papers, and by the release of other sources as they become available, may reveal perspectives on the controversy more troubling than the soothing one presented in this memoir. ■

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Mitigating mutations

The Cooperative Gene: How Mendel's Demon Explains the Evolution of Complex Beings/ Mendel's Demon: Gene Justice and the Complexity of Life
by Mark Ridley
Simon & Schuster/Weidenfeld: 2001/2000. 320 pp. $26, £20

Andrew Berry

The Cooperative Gene is a masterpiece of scientific exposition. Mark Ridley has deftly packaged a hugely complex subject — the interplay of deleterious mutation with the evolution of genetic systems — into one long argument. He has distilled an area of biology that is rife with abstruse mathematics and the arcana of molecular genetics into a series of carefully explicated thought experiments and metaphors.

Despite the reassuring presence of a glossary, Ridley even manages to avoid jargon, and in principle the book is accessible to the general reader. However, it is not aimed at the Stephen Jay Gould-reading (or indeed Matt Ridley-reading) public. It lacks the anecdotal colour that is *de rigueur* these days if a book is to sail up the bestseller lists; there are neither pen portraits of crusty old professors peering down their microscopes nor strange tales of Y-linked ear hairiness in Indian men. Ridley's long argument is too dense and unrelenting to appeal to readers without a real interest in the subject; *The Cooperative Gene* is, in fact, a monograph masquerading as popular science.

Ridley's thesis is that the history of life has been shaped by evolution's attempts to overcome the effects of mutation. The occasional mutation is beneficial — indeed, they are the basis of adaptive evolution — but the vast bulk of all mutation is, without doubt, deleterious: "A random mistake in the DNA is about as likely to improve the creature it codes for as a random change in Hamlet is to improve the play." Ridley's premise is that deleterious mutation must be kept within bounds if evolution is to occur: if the average rate of deleterious mutation exceeds one per genome per generation, then all the descendants of a parental generation with a mutation-free genome may be carrying deleterious mutations. Natural selection is then stymied because none of the competing genomes in the population is free from the taint of deleterious mutation and so it is not possible to select in favour of an intact, non-mutated genome.

Ridley sees a tension between the evolution of complexity — which necessarily involves encoding more information and therefore requires more genes — and the depredations of mutation. Assuming a constant mutation rate per nucleotide, the large genome of a complex being is more likely to exceed the critical threshold of one deleterious mutation per genome per generation. Ridley concludes that: "Live complexity hits its ceiling when the DNA message is so long that a mistake happens every time it is copied. When life is near this upper limit, complexity cannot evolve upwards even if there is an ecological opportunity there." The history of life has been punctuated by the evolution of "enabling mechanisms" that improve the fidelity with which hereditary information is replicated. The advent of DNA, which is less prone to degradation than RNA, as the vehicle for that information represents one such mechanism; the evolution of error-checking and DNA-repair systems is another; and sex yet another. With each innovation, the complexity ceiling rose.

Also militating against the evolution of complexity are genetic elements that subvert biological processes for their own 'selfish' ends, thus thwarting the cooperation between genes that is required for complexity. The simplest case of 'mendelian law-breaking' is meiotic drive, in which the probability of an allele being transmitted to the next generation is greater than the canonical mendelian expectation of 50%. For Ridley, the central player in the collision between the forces that promote complexity and those trying to tear it apart is meiosis. He emphasizes that the genetic randomization — through independent assortment and recombination — inherent in the mendelian process is critical in limiting the power and spread of genetic subversion.

Ridley's summary of the logic underlying this claim is masterful: "Mendelian justice is similar to the theory of human justice given by John Rawls in his book *A Theory of Justice*. Rawls argues that human beings will choose justice if they are operating behind a 'veil of ignorance'. Imagine you are going to devise or apply laws, or allocate resources, among a number of people. Maybe you have to divide a pie among five people including yourself. If you know which piece is to be received by which individual you may allocate most or all of the pie to yourself; but if you do not (you are veiled in ignorance) you may divide the pie into equal pieces. The gene shuffling mechanisms we have been thinking about enforce Mendelian justice by drawing a veil of ignorance over the genes."

Ridley refers to meiosis, the primary agent of mendelian justice, as "Mendel's Demon", but the implicit parallel to science's other distinguished demon is more misleading than illuminating. In physicist James Maxwell's famous thought experiment, 'Maxwell's Demon' does the impossible: it oversees an imaginary process that breaks the laws of thermodynamics. In contrast, the process overseen by Mendel's is real: meiosis is no thought