

▶ supporting instead a “base level” price for developing countries, with others setting higher prices. He backs this in part by appealing to basic welfare economics. But that, as he notes, assumes that financial transfers from rich to poor countries are infeasible, which sits oddly with the fact that rich countries have pledged billions of dollars to the UNFCCC’s Green Climate Fund to help poorer nations to mitigate emissions and adapt to climate impacts.

The book’s greatest weakness is its lack of an overarching framework. The introduction acknowledges the importance of global collective action, but states that the problem is beyond the book’s scope. Grubb concludes that the “next phase of the global effort ... is a question of investment and returns”. But which nations are to make the investments, which to earn the returns? Countries care about the answers. That is why so much effort has gone into climate negotiations.

Such answers will not be central to how countries address most of the issues in Grubb’s first domain. Measures to increase energy efficiency must satisfy mainly domestic criteria, although international trade links will be important for setting technology standards. However, global questions and answers are key to the other domains. They will matter when a country sets a carbon price. They will matter in relation to the investment that countries are willing to give to decarbonization, not least because such investments will pay off only if the carbon price is high.

Despite the criticisms, the book’s thesis is relevant to current climate negotiations, which seem to be focusing on what countries are willing to do individually: a kind of enhanced ‘business as usual’ approach. But for the immense scale of action needed to stabilize concentrations of greenhouse gases — even at a level allowing global temperatures to rise by more than 2°C — collective action is essential. ■

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MEDICINE

Outside the fold

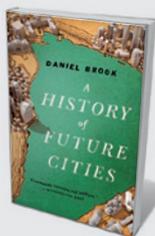
Giovanna Mallucci assesses the autobiography of Stanley Prusiner, the discoverer of prions.

In his autobiographical book, *Madness and Memory*, Stanley Prusiner charts his journey to winning the 1997 Nobel Prize for Physiology or Medicine, 30 years after his first laboratory posting as a fourth-year medical student — in Sweden, coincidentally. As the subtitle states, the story hinges on Prusiner’s discovery of prions, “a new biological principle of disease”. It is a remarkable tale: for the scientific discovery at its centre; for its recording of the extraordinary resistance the idea engendered; and for the sheer unfettered animosity, both personal and

professional, directed at him throughout from scientists and the media.

Prusiner introduces us early on to how, in 1972, his imagination was caught by the then-unknown infectious agent causing scrapie, a degenerative brain disease of sheep. Then, in the first year of his neurology residency, he was caring for a patient with Creutzfeldt-Jakob disease (CJD), a scrapie-like neurodegenerative disorder we now know to be a human prion disease. What follows is a chronicle of his voyage to isolate and characterize the scrapie agent during the 1970s, up

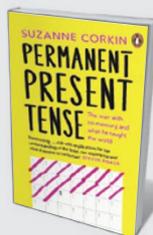
ILLUSTRATION BY MARTIN O'NEILL;
STANLEY PRUSINER PHOTO: RUSS FISCHHELLA



A History of Future Cities

Daniel Brook (*W. W. Norton, 2014*)

As urban innovation soars in skyscraper-studded Dubai, Daniel Brook looks to the original instant cities, where Western architecture invaded Eastern streets. St Petersburg, Shanghai and Mumbai, he argues, traded culture for economic power. (See Mike Davis’s review: *Nature* **494**, 427–428; 2013.)



Permanent Present Tense

Suzanne Corkin (*Penguin, 2014*)

Neuroscientist Suzanne Corkin worked with Henry Molaison, who had irreparable memory loss, for decades. Here she documents discoveries such as the hippocampus’s role in classifying memories. (See Douwe Draaisma’s review: *Nature* **497**, 313–314; 2013.)



Madness and Memory: The Discovery of Prions — A New Biological Principle of Disease
 STANLEY B. PRUSINER
 Yale University Press: 2014.

to his demonstration in 1981 that the agent is a protein, devoid of nucleic acid and capable of replicating itself and transmitting disease.

Details of scientific milestones are interwoven with Prusiner's accounts of personal interactions with colleagues at each stage; descriptions of dramatic epidemics of prion diseases across the globe punctuate the story. These include the phenomenon of kuru, a scrapie-like disease first described by Carleton Gajdusek in the 1950s, found among the Fore people of Papua New Guinea who practised ritualistic cannibalism; and the late 1980s disaster of bovine spongiform encephalopathy (BSE) in UK cattle, which spread to humans as variant CJD. Altogether, the story highlights the extraordinary scientific, medical and political climate of this period. There are struggles for funding, Prusiner's battle for tenure at the University of California, San Francisco, and the fight for scientific recognition at every stage of his career.

The idea of an infectious protein was first mooted in London in the 1960s by the mathematician John Stanley Griffith, and separately by the radiation biologist Tikvah Alper. Both published papers in *Nature* in 1967: 'Self-replication and scrapie' (J. S. Griffith *Nature* 215, 1043–1044; 1967) and 'Does the agent of scrapie replicate without nucleic acid?' (T. Alper *et al. Nature* 214, 764–766; 1967). But it was Prusiner who pursued the idea and Prusiner who proved it, with a determination that earned him both admiration (including the Lasker and Nobel prizes) and blind hostility.

Prusiner's proof of the revolutionary concept that infectivity in these disorders proceeds without nucleic acids, and his coinage of the term prion — for proteinaceous infectious particle (S. B. Prusiner *Science* 216, 136–144; 1982) — engendered disbelief, anger, denial and widespread refusal from a hostile scientific community, including many virologists. This antipathy persisted right up to the awarding of his Nobel prize. A 1997 article in *The New Yorker* asked, "But what if he's wrong?"; one in *Slate* was entitled 'Nobel Gas: Sure, Stanley Prusiner deserves a prize — for his persistence, not for his prions.' That Prusiner withstood these public attacks in his moments of greatest recognition is laudable, and gives some insight into his tenacity.

Scientifically, the story progresses from descriptions of labs full of antediluvian centrifuges with custom-built safety cabins around them (for isolation of the infectious agent from infected hamster brains) to the elegant transgenic mouse experiments of the prion era and the concept of misfolded endogenous

proteins associated with disease. The story is testament to the staggering intellect and courage involved in one of the most exciting discoveries since the DNA double helix.

But for all its drama, this extraordinary scientific story is not always an easy read. Prusiner's description of scientific rivalries inevitably reflects his version of events. His relationship with Gajdusek, whom he had visited in Papua New Guinea, ends bitterly, with arguments over Gajdusek's claims to the prion concept. Prusiner's collaboration with Swiss molecular biologist Charles Weissmann began brilliantly but became strained. Weissmann discovered that prion protein is encoded by a host gene — a finding as important to the prion story as the infectious protein itself. Prusiner's account of that collaboration's end, complete with transcripts of letters he sent to Weissmann, is an uncomfortable read. 'Scientific Interludes' explaining concepts and technicalities in some detail are interspersed through the text. There are other inserts: technical, graphical and bibliographical. Many are fascinating, but they tend to interrupt the flow of the compelling narrative.

The concluding chapter's meditation on the prion concept in widespread neurodegenerative disorders such as Alzheimer's is highly topical, albeit inordinately specialized in its detail. The book ends with an exhortation to the US government to fund research into cures for neurodegenerative disorders, diseases that Prusiner claims have "been ignored". He will be glad that last December's G8 Dementia Summit means that the world is heeding his call and taking this issue seriously at last. ■

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PRUSINER'S PROOF ENGENDERED DISBELIEF, ANGER, DENIAL AND WIDESPREAD REFUSAL.

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Time Reborn: From the Crisis in Physics to the Future of the Universe

Lee Smolin (Mariner, 2014)

Scientists unscrambling the fundamentals of the Universe dub time an illusion. Theoretical physicist Lee Smolin resurrects the concept as a constant around which other universal laws evolve. (See Pedro Ferreira's review: *Nature* 496, 430–431; 2013.)



Jane Austen, Game Theorist

Michael Chwe (Princeton Univ. Press, 2014)

Using Jane Austen's novels and craftiest characters, such as George Wickham in *Pride and Prejudice*, Michael Chwe proves that game theory — mathematics-based strategizing — has been harnessed for social and emotional advancement as well as for military victory.