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Visual Rhetoric and the Promotion of Scientific Ideas: The Strange Case of the Prion

Carol Reeves
Butler University, creeves@butler.edu

Scientific Visuals, Language, and the Commercialization of a Scientific Idea: The Strange Case of the Prion

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Abstract

In the field that investigates infectious brain diseases such as mad cow disease, the verbal and visual packaging of scientific visuals associated with identifying the agent, prion, its processes, and structure served the community ritual of establishing belief in a highly unorthodox phenomenon. Visual promotion fed into cultural expectations of single agents and simple processes, even though the actual agency and disease process have proven highly complex and perhaps unknowable.

It has at times been greatly frustrating to work in a field that has been so dominated by an almost commercial level of promotion for a single idea.
–Robert G. Rohwer, PhD, Director, Molecular Neurovirology Laboratory, Veterans Affairs Medical Center (personal communication)

Commercialization is not a concept normally associated with science. That is, scientists are not expected to sell their ideas. But during controversies or when anomalies arise that cannot be resolved by current theory, some competition among those offering new explanations is expected. And this competition can lead to what might be called "promotional science communication," wherein advocates for particular hypotheses make rhetorical decisions that may push the boundaries of conventional communication. For example, during the frenzied search for the cause of AIDS, a U.S. laboratory team used factlike language to represent claims that were mostly speculative and that lacked evidence (Reeves, 1998). During the 1970s, climate scientists promoted the concept of global warming in alarmist language in both scientific and popular forums, even though the evidence for human-caused climate change was not thoroughly established (Russill, 2008; Weingart, Engels, & Pansegrau, 2002). The results of promotional scientific communication are mixed. In the first case, promoting the wrong virus kept the real agent and its discoverers in the shadows, slowed scientific progress, and contributed to confusing messages about how to treat AIDS in the early 1980s (Crewdson, 1995). In the second case, the public grew alarmed, Congress held hearings, and new policy developed, but a backlash against hyperbolic rhetoric surrounding climate change encouraged the growth of denier movements funded by the petroleum lobby (Russill, 2008; Weingart, Engels, & Pansegrau, 2002).

In the case examined here, a controversial—even heretical—theory of infectious disease was promoted through linguistic and visual strategies that many scientists now claim, as did Dr. Robert Rohwer quoted above, were more commercial than scientific. Rohwer's comment refers to an interdisciplinary field that investigates transmissible neurodegenerative diseases that affect animals—such as scrapie and bovine spongiform encephalopathy (BSE)—and humans—such as Kuru, Creutzfeldt–Jakob disease (CJD), and fatal familial insomnia. These diseases have all been established as infectious and as deriving from spontaneous and inherited mutations in a gene that codes for the host protein involved in the diseases. Rohwer's comment also refers to the now-mainstream theory that was once unthinkable to microbiologists, the idea of a single molecule made up mostly of protein and having the capacity to self-replicate and infect tissue without the assistance of nucleic acid. This so-called protein-only hypothesis was introduced in 1982 by Stanley B. Prusiner, a neurologist and biochemist at the University of California and recipient of the 1997 Nobel Prize in Physiology or Medicine. Prusiner's aggressive verbal rhetoric—naming an object before its existence was established, changing and promoting new terminology, and employing factlike language—has been shown to have influenced the research community well before laboratory evidence justified that support (Prusiner, 1982; Reeves, 2002, 2003). But the linguistic promotion is only part of the story. Particular visuals, repeated and distributed across several fields both inside and outside the immediate transmissible spongiform encephalopathy (TSE) research community, helped to commercialize—to promote and market—the new idea. By "commercialize," I mean the use of the marketing techniques of repetition and dispersal of commodities, in this case a new hypothesis and a theoretical object, through a broad spectrum of forums.

Scientists rely on visuals—pictures, diagrams, and figures—to generate ideas, present data, support claims, and persuade each other. Visuals are intentionally contrived and packaged, to different degrees, to manage viewers' perceptions of the viability or usability of data, and their persuasive force may be assisted by extensive data packaging, combining graphic and verbal emphasis and the author's scientific ethos (Richards, 2003); yet scientists are not expected to misrepresent the truth, manipulate scientific audiences, or commercially promote ideas. Tufte (2001) insisted that "graphical excellence requires telling the truth about the data" (p. 51), and philosopher Perini (2005) emphasized truth value, arguing that "visual representations must have the capacity to bear truth in order to be genuine components of arguments" (p. 262). Yet the truth may be difficult to establish during periods of controversy, and truth may shift according to context. Scientific visuals appearing during scientific controversies may themselves "become objects of controversy" (Dietrich, 2007, p. 161) and, when appearing in forums where audience members are not specialized consumers of the message, the visuals may play a significant role in shaping views (see Losch, 2006; Ross, 2008; Williams, Kitzinger, & Henderson, 2003). Scientific visuals may also promote ideas within scientific communities, even when the visuals do not actually tell the truth about the data as much as they help to convey exciting research possibilities. Appearing during a time of scientific controversy over the legitimacy and lack of evidence for the theory they depicted, the visuals discussed here do more to advertise, or to enlist belief, in a new theory and shift a theoretical paradigm, than to represent any scientifically validated referent. In the case examined here, visuals helped to promote an unorthodox hypothesis and to extend its "rhetorical life" (Fahnestock, 1986) beyond the boundary of a narrow specialization (where the hypothesis was most controversial) to wider scientific and public forums where the details of the controversy and the paucity of evidence could not be grasped.

In this paper, I will examine the visuals associated with three categories of evidence necessary to establish the etiology of a disease:

- evidence that identifies the agent,
- evidence that explains its pathological mechanism, and
- evidence that determines its molecular structure.

Electron micrographs of a putative agent, line diagrams and cartoons depicting hypothetical mechanisms, and a computer-generated, three-dimensional model all assisted in the social construction of a single agent and theory of disease progression that carried the aura of simplicity and universality. Yet, what these visuals purported to represent—a knowable agent, a simple mechanism, and a structure—were at the time, and still are, experimental penumbra. Even when Prusiner won the Nobel Prize, the prion theory had not been definitely established, a situation noted by the Nobel committee (Taubes, 1997). Even now, after almost 30 years since Prusiner's first utterance of the protein-only hypothesis, a recent reviewer of the subject stated that "three decades of investigation have yielded no direct experimental proof for this stringent hypothesis" (Supattapone, 2010, p. 1091). How prions can mutate into different strains (like viruses) but without nucleic acid is "still unresolved" (Angers et al., 2010). As recently as 2007, researchers have provided evidence of some type of nucleic acid involved (Manuelidis, 2007). The exact molecular structure of the prion has not been identified and its exact mechanism of propagation has not been determined (Eghiaian, 2005; Harris & True, 2006; Penman, 2007; Skinner et al.,

2006). Only recently, in May 2010, has a laboratory reported producing an experimental prion by converting normal protein into the infectious form (Wang, Wang, Yuan, & Ma, 2010). This experiment would, if ratified by the scientific community, prove the protein-only hypothesis. As an objectively obtained agent, the prion is still murky, its mechanism still unknown. The agent or agencies in these diseases are much too complex for an easy and rapid resolution to these issues.

In contrast, the prion's rhetorical presence is quite simple. In the scientific literature published on the subject in the past 25 years, the prion appears as a single, simple agent, even as the experimental evidence points to multiple and complex factors involved in disease transmission. Despite persistent objections from some longtime TSE researchers, the idea of the prion is widely accepted by the public and by scientists in many fields. The rhetorical prion, a mysterious agent that lacks DNA but can destroy neurons, attracted research interest in a wide range of fields even as the "real" prion hovered like a trickster ghost over those laboratories trying to characterize it and determine its mechanisms.

Naturally, theoretical or hypothetical scientific objects are likely clothed in simple language when they are first proposed, before experimentation reveals their complexity. But the rhetorical prion survived each experimental finding that showed reality resistant to simple explanations because it appealed to a common cultural and intellectual goal in science: simplicity. The cultural value of simple, elegant explanations and models may have served as a rhetorical orientation embedded in visual representations that stimulated research interest. Quine (1976), who did not believe there was such a thing as simplicity or uniformity in nature, proposed that simplicity was a basis for selecting one theory over another:

> When two theories are equally defensible on other counts, certainly the simpler of the two is to be preferred on the score of both beauty and convenience. But what is remarkable is that the simpler of the two theories is generally regarded not only as the more desirable but also as the more probable. (p. 255)

The simplicity of any theory, according to Quine, is relative to what he calls its "texture" (p. 255), by which he means the schemas and derivative concepts being applied. A simple, even elegant theory cannot carry "any peculiar presumption of objective truth" (p. 255).

More recently, scholars in the philosophy of science have argued that the language and visual tools we use to represent and to explain phenomena contain patterns that reinforce simplicity and thus might restrain our understanding of complexity. Mitchell (2009), a philosopher of science, argued in a recent book that since the scientific revolution of the 17th century, science has sought to reduce complexity to simple interpretations that fail to capture "the tractable, understandable, evolved, and dynamic complexity that contemporary sciences say aptly characterizes our world" (p. 11). Moreover, the simplicity and elegance that "make representations usable … are also features that limit our claims about the completeness of any single representation" (p. 13). The case of the prion suggests that visuals tapping into a cultural orientation toward simplicity and resolution by, in this case, emphasizing single agents and simple mechanisms can catalyze the productive investigation that uncovers the beautiful complexity of nature and the lie of simplicity. By conveying the lie of simplicity, visuals might have helped make a highly unorthodox idea seem plausible to scientists whose work was occurring outside the main community that had examined TSEs for decades. The persistent disconnect between the simplicity of the rhetorical prion and the actual complexity of

the agent or agencies that cause TSE is not just an example of how language fails but also of how rhetorical decision making can lead to a discourse whose orientations become just as resistant to change as the TSE infectious agent is resistant to the mammalian immune system. The visuals I will discuss might have helped convey the prion, a rhetorically constructed rather than experimentally ratified object, as if it were an experimentally ratified object. Some members of the scientific audience whose expertise lay outside the immediate TSE field may have, as Richards (2003) noted, interpreted highly arranged and constructed visuals as self-evident and unconstructed representations of objects and processes that had been experimentally validated.

To undertake this analysis, I used the Web of Science Citation search engine and collected data on 119 papers produced from 1981 to 1991 by the Prusiner laboratory in the Department of Neurology at the University of California at San Francisco. I also collected data on 87 research reports produced in a laboratory at the New York State Institute for Basic Research in Mental Retardation. I chose this time frame because it represents a period of enormous change within the TSE field. The number of papers reporting research on the subject grew from 96 research reports published between 1975 and 1980 to 436 published between 1981 and 1991. Also during this period, a shift in the discursive and theoretical orientations (Reeves, 2002) in the TSE field catalyzed new questions and new research within the field as well as in related fields. Once subject areas and citations data on the two sets of papers were complete, I conducted focused analyses of the use of visuals by the two laboratory teams. As the head of his laboratory, Prusiner was the lead author or one of two authors on 24 of 119 papers from his laboratory. I focused on these 24 to analyze Prusiner's choices regarding visuals. I also analyzed 11 papers from the other laboratory whose author list contained the name Patricia Merz, who was the first to identify and publish on a disease-relevant particle she discovered through electron microscopy. I analyzed and compared the use of visuals—electron micrographs, models, and cartoons—and the linguistic framing of these visuals and determined the extent to which both laboratories dispersed these visuals into research communities outside the TSE field. Using Web of Science, I tracked the citations to the set of papers from both laboratories, comparing the subject areas and the sources of citing articles with the record of publishing and citations for the TSE field up to 1982. Interviews with TSE researchers, whose comments are included throughout this study, at the National Institutes of Health (NIH) Rocky Mountain TSE laboratory, the NIH National Center for Allergies and Infectious Diseases, New York State Institute for Basic Research in Mental Retardation, and Yale University Department of Neurology provide some backing for my claims. (Prusiner has never agreed to speak with the author).

1970s—THE BIRTH OF A NEW FIELD: SEEING IS BELIEVING

Our story of visuals of the prion begins with an electron micrograph of diseased monkey brains that appeared in a brief *Nature* article in 1972 (Gajdusek & Gibbs). The monkey brains were infected with kuru, a degenerative neurological disease that spread among the Fore people of Papua New Guinea due to the ritual consumption of the brains of dead loved ones. Carlton Gadjusek, an NIH virologist, discovered kuru and demonstrated that it could be passed to rhesus monkeys. In so doing, Gadjusek established kuru as a transmissible disease similar to scrapie, which had been known for many decades as an infectious disease among sheep. Gadjusek's fascinating discovery

was firmly established by the clear resemblance of kuru-infected brain tissue to brain tissue infected with scrapie. In their *Nature* report, Gajdusek and Gibbs displayed a large electron micrograph of the infected monkey-brain tissue as the chief evidence for their claim that kuru was transmissible and that it was a human disease similar to scrapie. The caption to this visual read, "Status spongiosis in the cerebral cortex of a rhesus monkey dying with kuru. In the areas of spongiform alteration there is neuronal loss and gliosis. Haematoxylin and eosin stain" (p. 351). This picture of the signs of disease—well documented and familiar to scrapie researchers—needed no rhetorical adornment to be convincing and to establish that scrapie research had now expanded beyond the veterinary field to general virology and human health. As for our story of the visuals in the field, Gajdusek and Gibbs's micrograph of infected monkey brain, made possible by the scanning electron microscope first marketed in the mid 1960s, affirms a seeing-is-believing philosophy of visual proof and the electron microscope as the means for achieving the sine qua non in virology: to find and to characterize the agent. Gadjusek's image showing brain tissue containing the telltale signs of scrapie infection proved that kuru was an infectious brain disease as well. This finding stimulated considerable research efforts to find the causative agent. Yet finding the agent had always been challenging because the disease left the brain tissue a sticky mess of aggregated protein, highly resistant to purifying agents, so reducing the muck down to a purely infectious particle was impossible.

Although papers like Gajdusek and Gibbs's (1972) that reported research throughout the 1970s contained electron micrographs, those pictures only displayed the obvious destructive signs of disease, not the agent. Purification to the kind of specificity needed to even begin to separate disease-relevant particles from the whole required, in the end, the use of thousands of infected hamster brains, many months of dedicated laboratory space, many trained technicians, and a lot of money. Finally, in the late 1980s, two laboratories had purified tissue enough that investigators could observe particles that were always present when the material was still infectious. Of course, any particle found after purification could be a result of the purification process rather than the agent. Still, a particle remaining after extensive purification could be used as an efficient disease marker or could be the agent itself. The two laboratory teams that had achieved successful purification competed for rhetorical ownership, to be acknowledged as the first to find the agent and to reap the benefits of such standing.

Naturally, electron micrographs of the particles remaining in highly purified specimens were featured prominently in both teams' published papers announcing their discovery. But the teams' approaches to the use of electron micrographs differed in the extent to which the authors tried to establish particular theoretical orientations surrounding those particles and whether the visuals were repeated and dispersed into forums outside the specialized TSE forum. One team followed the seeing-is-believing philosophy, which involved little packaging and only denotative verbal labeling of images, as if the micrograph conveyed reliable information on its own, without text specifying implications or theoretical orientations. The other approach to the use of micrographs made the visuals more "usable," to use Mitchell's (2009) language, as conveyers of a simple, elegant idea that could be grasped by less specialized audiences and applied to more than one disease. Richards's (2003) (see also Gross, 2006, 2009) finding that the more constructed a visual, the more persuasive it may be, applies to this case. The more tendential visuals are those that do

more to exploit the possibilities of meaning transference resulting from the interplay between the verbal anchorage and the visual representation. Such visuals, especially when dispersed to less specialized scientific audiences, may have contributed to the gradual dominance that the one laboratory and its object—the prion—came to have over TSE research. That dominance can be seen in the terministic hegemony of prion terminology (Reeves, 2002) and in the dispersal of grant funding to laboratories researching prions rather than viruses in TSEs (Taubes, 1997). Complex rhetorical decisions that led to layered meanings surrounding the prion helped to promote the prion theory as simple, elegant, and full of explanatory potential. The promotion was successful, as evident in the resilience of the prion or protein-only idea and the simple grammar used to express the prion hypothesis in most of the published TSE reports in the past 29 years. Variations of the statement that "X causes Y" proliferate throughout the literature, even when the only knowable, verified reality in that phrase is Y, the diseases, which have been well characterized. Statements like the one below from a recent report in *Science* (Angers et al., 2010) appear as the first sentence of introductions where community-ratified knowledge, well-characterized objects, and familiar processes tend to appear: "Prions are protein-based transmissible agents causing lethal, incurable neurodegenerative diseases of mammals, including sheep scrapie, bovine spongiform encephalopathy, human Creutzefeldt Jakob disease, and chronic wasting disease …". (p. 1). Statements written in this definitive style presuppose definitive consensus, yet this sentence is more a statement of belief, more promise of eventual support for its truthfulness, than it is a statement representing ratified experimental evidence. The prion itself remains uncharacterized definitively because its tertiary, three-dimensional structure has not yet been determined (Supattapone, 2010). Also, how and even whether one agent or agency causes these diseases is unknown; several lines of evidence point to cofactors, such as endogenous nucleic acids, that create the conditions for the normal protein to turn into the infectious form (Li, Browning, Mahal, Oelschlegel, & Weissmann, 2009). The simplicity of the statement above belies the complexity of the agent and causation. But simplicity in the language survives, in part, as a result of the rhetorical promotion of an idea whose packaged simplicity and elegance were disseminated across scientific forums back in the 1980s and 1990s.

1980s TO 1991—ESTABLISHING OBJECTS AND AGENTS

Merz Team: Establishing an Object

The first pictures of an object remaining in highly purified, scrapie-infected brain appeared in a 1981 paper (Merz, Somerville, Wisniewski, & Iqbal) by a team at the New York State Institute for Basic Research in Mental Retardation. This team, which consulted with Carlton Gadjusek, offered up electron micrographs of particles that they called "scrapie-associated fibrils (SAF)," a descriptive rather than theory-suggestive label. Minimal verbal anchorage accompanying the visuals identified the pictured objects and how they were obtained. In the paper's main text, the authors "report the observation of an abnormal fibril in subfractions of … preparations from the brains of scrapie affected mice and hamsters" (p. 63). Five of the 10 article pages are covered by 19 electron micrograph pictures of SAF at various levels of magnification and obtained from different animal models. The authors' language choices emphasized

- discovery—"SAF were found fortuitously … (p. 64),"

- observation—"SAF have been observed in all 20 detergent treated SPM preparations from … brains of animals infected with … scrapie … but never in brains of uninfected mice (p. 64)," and
- consistent physical features—"SAF were clearly discernible with little differences in their appearance (p. 64)."

The entire focus of the article's verbal text was to report observations and to describe in great detail what the investigators saw rather than to lead readers toward a specific theory about the object. The photographs allowed readers to see for themselves that, for the first time in decades of frustrating attempts, the field of TSE research had pictures of unique objects with clear boundaries and presumably knowable qualities that were always found in purified infected samples. For example, in one full-page display, the authors (Merz et al., 1981, p. 68) showed (see Figure 1) that they can get the same objects through several different methods.

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By calling these objects "typical SAF" throughout the article and showing that similar structures appear in different contexts and are produced via different methods, as in Figure 1, the authors established an object that seemed recognizable and knowable to anyone working in the field, including insiders who would have immediately recognized the possibility that these particles could be the agent itself and who would also have likely assumed the particles were viral.

Patricia Merz, who discovered the particles, indicated her belief in the principle of seeing is believing:

> We just felt [that] they [the fibrils] were significant, and we wanted readers to feel the same way. We included so many pictures because we wanted to leave no doubt that we had found something important. The pictures just were very effective. We got a lot of responses to our work after that. (personal communication, April 23, 2003)

After publication of the previously mentioned paper (Merz et al., 1981), Merz was invited to speak across the country; she hosted visiting scientists in her laboratory and enjoyed the credential of having been the first to find an important, disease-related particle. This paper was cited 345 times in peer-reviewed research articles, with only 4 citations from papers disagreeing with the authors.

From here, Merz's team published 86 more papers during the period defined for this study (1981 to 1991). When compared with the subject areas of TSE research (see Figure 2), the Merz papers (see Figure 3) focus similarly, according to the Web of Science.

FIGURE 2 Pie chart displays the breakdown of TSE publications by subject area, 1975–1981.

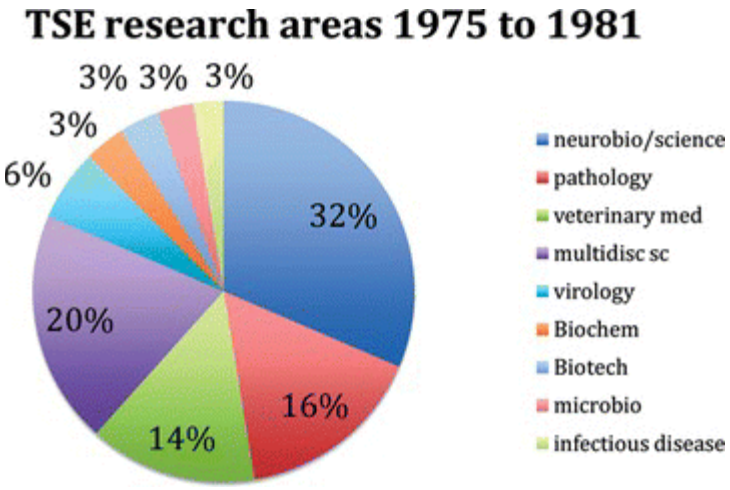
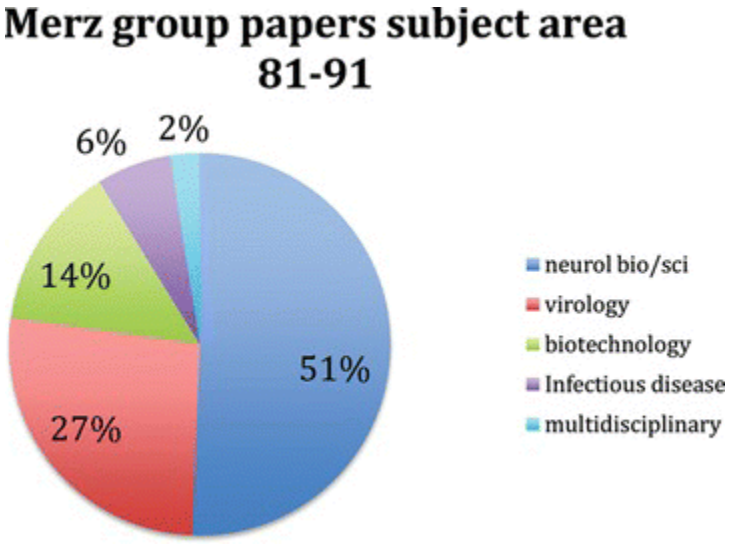


FIGURE 3 Pie chart displays breakdown of the Merz group's TSE publications by subject area, 1981–1991. Breakdown is similar to previous TSE research as a whole.



Fifty percent of the Merz team papers fell into neuroscience and clinical neurology, with expansions in virology and biotechnology but less presence in multidisciplinary science and medicine (see Figure 3).

A closer look at the Merz team's 11 papers reveals that the team is careful to avoid multiplying the meanings of SAF. The authors sought to establish SAF as a "unique class of structures" (Kascsak et al., 1985, p. 1715) by showing the structures at different magnifications, in brain extracts infected with different strains of scrapie from different animal species, but the authors avoided attempting to steer the reader toward a theory of agency. That is, SAF were objects, not agents. They had been "found" or "observed" or "isolated" or "magnified." Bound to their utilitarian value as disease markers, SAF are not linked to any explanatory theory, and only one paper contains a

statement suggesting SAF "may be the etiological agent" (Merz et al., 1984, p. 437). Although the authors often describe SAF as having "a resemblance to amyloid" (Merz et al., 1981, p. 63), which would imply a link to Alzheimer's disease, they resist emphasizing a link between SAF and amyloid diseases or proposing a novel disease agency or process. Instead, according to the authors, SAF "appear to be a consistent pathological finding in scrapie" (p. 69) or "associated with unconventional slow virus diseases" (Kascsak et al., 1987, p. 3688). Again, the language of appearance and association, along with the visuals that confirm appearance and association, serves the aims of a communication that does not say more than the laboratory experience and the data can support. This object *appears* and *seems like*, but no one can say that it *is*. The ontological status of SAF is, thus, only suggested.

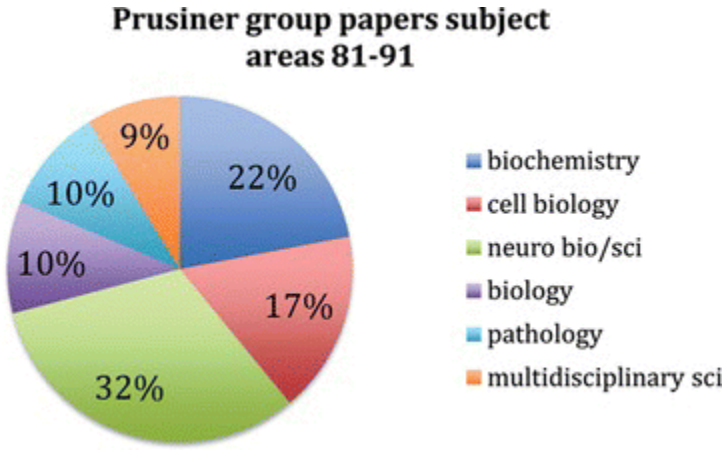
If citation patterns are any indication, the team clearly had an impact on its own field. Of cited articles, 56% were published in journals representing the fields that had long been associated with TSE research. The rest fell into biochemistry (9%), general medicine (8%), and multidisciplinary science (7%), and small percentages of the citations came from immunology, biotechnology, cell biology, and microbiology. The team had successfully established SAF as a scientifically significant object. According to both Merz and her colleague, Richard Carp, the impact of the initial visuals of SAF "was profound." As Carp explained, "Many felt that this was the physical manifestation of the infectious agent or at least could harbor the agent within its structure. That was very exciting." Carp went on to say that the research team "also recognized the possibility that SAF might represent a byproduct of the infectious process and be unrelated to the agent" but that the pictures of the objects were still very "stimulating to the field" (personal communication, October 14, 2007). Paul Brown, a senior researcher in the field whose laboratory at NIH houses the largest collection of human-brain specimens infected with TSEs, explained that "it was just such an intractable problem, breaking down that aggregated tissue. So we never had any really concentrated specimens to look for an agent. But when SAF was described, well, here, at last, we have something. Real good news" (personal communication, March 6, 2003).

The Prusiner Team: Establishing an Agent

Despite the impact on their own TSE community, by the late 1980s the Merz team and SAF fell into the shadows of Prusiner and the prion. The Prusiner team published more papers (119 compared with 87 from the Merz team), and perhaps one could argue that the Prusiner team was more productive and conducted better experiments, but making that sort of assessment is beyond the reach of this project. Several teams, including the Merz team, made significant contributions to the study of TSEs during the 1980s, yet the prion terminology and the concept of infectious protein supplanted the viral terminology and its associated concepts in the literature (Reeves, 2002). Because the experimental evidence necessary to fully characterize an infectious agent, to determine its pathological mechanism, and to identify its final molecular structure is still being worked out, the promotional strategies used by Prusiner may have helped induce belief in the possibility of fruitful discovery for any scientist who invested in the idea. Prusiner's visuals of the same particles presented by the Merz team extended their usefulness beyond the utilitarian marker of disease and beyond an object's appearing and seeming. Prusiner's visuals consolidated the ontological status of the prion as an agent that does not *appear to be* but *is*.

Between 1981 and 1991, the Prusiner team published 110 papers. Looking at the subject areas in which these papers were published, we find a broader swath of subject areas (see Figure 4) than with previous TSE research or with the Merz team's publications, with more papers published in biochemistry and cell biology than those by the Merz team.

FIGURE 4 Pie chart displays breakdown of the Prusiner group's TSE publications by subject area, 1981–1991. The Prusiner group's publications covered a broader swath of subject areas than the those of the Merz group or of previous TSE research.



Prusiner was the lead author or one of two authors for 24 papers focusing on the presentation, characterization, and categorization of prion rods and their relation to prions. Of these, 16 papers were reviews that Prusiner authored or coauthored. In all these papers, the definition of prion rods is expanded beyond their objective existence to their status as agents. Strategic use of terminology helped create the idea of a single, simple, bounded agent. Rather than employ the term “SAF,” which is appropriately descriptive but rather cumbersome thematically, the Prusiner team called the shapes “prion rods.” In each of these 24 papers, prion rods were defined as aggregates of prions, implying that the objects pictured were accumulations of the agent, thus raising their status above the level of “relevant object.”

The verbal and visual rhetoric in the Prusiner papers was more strategically complex to contribute to a simpler and stronger sense of presence and agency than we find in the Merz papers. The simpler and stronger sense of presence and agency would more easily be broadcast and dispersed across different research forums. As we will see below, the Prusiner papers covered a wider spectrum of subject areas and addressed a wider audience than did the Merz team papers. An example of the strategies appearing in a forum outside the mainstream TSE field can be seen in a 1983 paper (Prusiner et al.) published in *Cell*, in which no papers on scrapie or other TSEs had been published before, according to the Web of Science database. In this paper, eleven pictures are used as primary evidence that prions exist even though no actual experimental evidence is supplied. Purified infectious tissue displayed in micrographs was labeled “extensively purified fractions of prions,” whereas the objects showing up in the tissue were labeled “prion rods” (p. 351) that “clearly resemble those of purified amyloids” (p. 355). Linking prion rods to amyloid,

which is the aggregated protein found in such disorders as Alzheimer's disease, then allows the authors to link prions to central nervous system disorders:

> That scrapie prions aggregate to form amyloid-like rods may be significant because amyloid deposits have been reported in a limited number of degenerative disorders of the central nervous system. (p. 355)

In contrast to the Merz team's observational language such as “were observed” or “a resemblance to amyloid” (Merz et al., 1981, p. 63), the Prusiner team's “that scrapie prions aggregate to form” and their use of the verbs “show” and “are,” imply not only the prion's agency but its experimental definitiveness. Visual display rather than experimental confirmation forms the basis of these implied but exciting possibilities.

While the Merz team was publishing research reports in more specialized journals, Prusiner was authoring literature reviews in specialized, general, and popular science forums. His use of the review to broadcast and advertise the prion and the protein-only theory strays outside the norms surrounding this genre. Harmon and Gross (2010) noted that the survey of “a field alive with activity” is an “act of judgment essential to intellectual advancement” and that good reviews ought to, among other things, “summarize and critically evaluate what is known” in a field (p. 105). But Prusiner used the review to plant a speculative object and a theoretical agent as if they had become what is “known” in the field. A 1986 review (McKinley & Prusiner) whose title, “Biology and Structure of Scrapie Prions,” seemed to convey a ratified consensus, was published in the *International Review of Neurobiology*, in which no research on any TSE had been published before. McKinley and Prusiner filled the 8 pages of the review with 28 pictures of prion rods, their “ultrastructure” (p. 31), and their various forms and states. Language associated with Alzheimer's disease was used to describe prions: Prion rods “are aggregates of the infectious prions” (p. 1), and studies “have been useful in demonstrating the amyloid nature of prion aggregates” (p. 283). Several visuals were labeled with terms associated with Alzheimer's disease; “scrapie prion plaque,” “aggregates,” and “amyloid” help to establish a simple conceptual link between prions and the devastating and intractable disease readers of this review treated and studied. Of the seven articles citing this paper, five were authored by laboratory teams whose previous publications were outside the TSE field. In these papers, the agency of prions and the status of prion rods as aggregates of the agent are assumed to be uncontroversial. Prusiner took a similar approach in a 1987 review for the *New England Journal of Medicine* (Prusiner, 1987), in which medical reports on neurodegenerative diseases such as kuru and CJD had been rare before that time, with only eight reports published between 1960 and 1987 and with all of them referring to a possible viral cause. Prusiner's review addressed the general medical audience accustomed to the medical case narrative. The first paragraph contains the story of the discovery of CJD and the diagnostic features of the disease. The review contains six pictures of “ultrastructure of the multiple forms of Hamster scrapie and Human Creutzfeldt-Jacob disease prions,” which were actually pictures of prion rods, not prions. To label the structures pictured “prions” in a journal whose readers are primarily clinicians who diagnose and treat diseases would have certainly attracted their attention, especially those who treated neurodegenerative disease. It is also important to note that this linguistic confusion—between prion rods and prions—did not appear in Prusiner's papers published in nonmedical scientific journals.

Prusiner's 1984 review in the *Scientific American* commercialized the prion to an even broader forum than the *New England Journal of Medicine.* As shown in Figure 5, readers were treated to this colorized micrograph of "a collection of prion rods" (p. 52).

Under the photo, a narrative paragraph explained that the rods were said to "closely resemble amyloid plaques, which are features of several human and animal diseases that may be caused by prion infection" (Prusiner, 1984, p. 52). The tissue sample was found in the hippocampus, "an area where amyloid plaques have been seen in rodents with scrapie and in human beings with Alzheimer's disease" (p. 52). Under two additional electron micrographs of "prions in the brain" (p. 51), the explanatory paragraph claimed that microscopic examination of "stained structures … reveals the presence of prions" (p. 51), which implies that prions have an experimentally reified presence. Presence and agency are further emphasized in a chart called "Prion Disease" (p. 53) that listed six transmissible spongiform encephalopathies, including scrapie and kuru. The accompanying explanation includes the statement that "Scrapie is a prion disease by definition, and there is substantial experimental evidence that prions also bring on Creutzfeldt-Jakob disease" (p. 53). That these visuals and their verbal anchorage do more to promote or commercialize than to scientifically substantiate the prion idea to a broad, interdisciplinary forum is evident in the fact that Prusiner did not provide the experimental sine qua non for determining the causal agent of an infectious disease: the creation of a laboratory version of the agent—that is, a test tube or in vitro transmission. This experiment had not been done by then and has not been done to this day unless the most recent reported attempt (Wang, Wang, Yuan, & Ma, 2010) is accepted as the solution to this persistent roadblock to establishing prions as agents that can cause infection and replicate without DNA. Also, Prusiner did more to commercialize than to report what is known, as is expected in reviews, because at this time, longtime investigators in the TSE field, including the Merz team, were still employing the term "slow virus disease" and "scrapie agent" to classify the diseases and name the infective agent. They certainly did not agree that Prusiner had any solid evidence of an etiological explanation of scrapie or any other TSE (see Carp, Merz, Kascsak, Merz, & Wisniewski, 1985; Kimberlin, 1982, 1986).

Prusiner's collaborators reported their own discomfort with Prusiner's bravado in maintaining that the rods produced under experimental conditions were identical to those occurring in the brain. In a journalistic account (Taubes, 1986), former Prusiner collaborator Dave Kingsbury claimed that "the conditions under which one forms these structures have a lot to do with what they look like. It's always very dangerous to try to extrapolate in vitro manipulations to in vivo observations" (p. 27). Paul Bendheim, who helped establish that a host protein called PrP was necessary for scrapie infection and who worked in the Prusiner laboratory, told me that Prusiner named the rods "prion rods" and linked them to Alzheimer's:

> Prion rods. That's a good example of Stan's need to own everything. And to link everything to possibilities. He didn't want to be wrong, or to miss connections, so when he would write about the possibilities, he would come up with a list of 30 or 40 possibilities. Then you get pictures of the thing—who knows whether it is really important—and it's attached to all these other things. (personal communication, June 23, 2004)

The Prusiner visual rhetoric produced a chain of connections and transferences of meaning among the visual and verbal signs. Rather than complicate, these connections and transferences actually

simplified the prion's marketable impact and its mobility as an attractive idea. As an aggregate of agent, prion rods could represent the agent, the prion, and because the aggregate resembled amyloid plaque, the agent is linked through its visual reference to amyloid diseases such as Alzheimer's, like a classic syllogism: If A (prion rods) is B (prions), and if A is also C (amyloid plaque), then B is C. Yet, the major premise, that prion rods are accumulations of prions, had not been established because prions had not been established, and the term "prion" did not signify any definitive reality—one could have just as easily said "protein" or "virino" or "scrapie agent" instead of prion. Yet, the neat bundle of relations whose key terms seemed to represent an experimentally verified agent seemed to meet the demands for universality and unification that scientific culture expects a new theory to fulfill. As Latour (1990) wrote,

> If you wish to go out of *your* way and come back heavily equipped so as to force others to go out of *their* ways, the main problem to solve is that of *mobilization*. You have to go and come back with the "things" if your moves are not to be wasted … . The "things" you gathered and displaced have to be presentable all at once to those you want to convince and who did not go there. (p. 26)

The "things" here are multiple ideas linked to diverse groups of potential allies—scrapie→prion→prion rod→amyloid→Alzheimer's→[protein biologists], [Alzheimer's researchers], [TSE researchers], [physicians], [the public], etc. These "things" were semiotically and verbally linked to the micrograph of the prion rod. Whereas the Merz team won recognition for SAF, the more theoretically exotic prion made headlines in the popular press (Altman, 1982, 1983; Blakeslee, 1985), attracted criticism from field insiders (Carp, Merz, Kascsak, Merz, & Wisniewski, 1985; Kimberlin, 1982, 1986) and excited scientists in other fields who were intrigued by the new idea.

But is there evidence for my claim that Prusiner's visual and verbal strategies led to greater interest among researchers in forums outside the TSE forum than did the Merz team? Citation records (excluding self-citations) for the period between 1981 and 2001 for both groups of papers from both laboratories provide some support. Both team's papers were almost equally cited by papers published in neuroscience and neurology journals, with fairly equal representation in virology and pathology. However, the Prusiner team papers received more citations from articles related to biochemistry (15%) than did the Merz team papers (8%).

If we isolate those papers for which Prusiner was the lead author or one of two authors, we see more evidence that Prusiner's rhetorical strategies could have had a greater influence on scientists outside the TSE field. Here we see that biochemistry, not among the top subject areas for TSE research between 1975 and 1981, became the area with the largest percentage of citing articles (25%) with neurosciences being the second largest (14%). What is interesting about the sources for the citing articles is that they come from a much broader array of journals from a wider array of subject areas (97 different areas) not typically linked to TSEs, compared with the subject areas for citing articles to the Merz group papers (79 subject areas lying outside the TSE field). Prusiner review articles, moreover, drew even more attention from areas outside the TSE field. Of 393 citations, 205 (52%) came from journals in areas previously active in TSE research. But 188 (48%) citations were from articles published in journals whose subject areas were not traditionally linked to TSE research. The final piece of evidence supporting my claim that Prusiner's visual and verbal strategies worked to attract research investment from forums outside the TSE field is that Prusiner's

16 literature reviews published between 1981 and 1991 were cited in 11 articles appearing in *Medical Hypotheses*, which publishes theoretical essays. Of these 11, only 1 (Adams, 1990) called the prion idea into question. Other authors of essays in *Medical Hypotheses* enlist the prion idea to ground their explanations of such matters as the cause of AIDS (Kelly, 1984) and non-A/non-B hepatitis (Kingdon, 1987). And they cite one or more of Prusiner's literature reviews as supporting sources. Adams (1990), who cited papers from both the Prusiner and the Merz groups and who is critical of the prion idea, is the only author to cite a Merz paper in an article from *Medical Hypotheses* published between 1981 and 2001. These citation patterns help support the contention that the bundle of theoretical and comparative associations surrounding the prion and prion rods, encouraged via visual and verbal production, opened up a wider network of actors who, either by reporting, critiquing, or applying the idea, assured its dissemination.

The prion rod seems all the more a rhetorically rather than scientifically established object once its status as a disease-associated object or the agent itself was questioned by Prusiner himself. Prusiner told a journalist, "The prion rods are an artifact of the detergent extraction, but they faithfully reproduce what you see in the tissue, which is the amyloid filament" (Taubes, 1997). In 1991 the Prusiner laboratory (McKinley et al., 1991) reported evidence that prion rods can only be produced as a result of detergent treatment of purified samples of infectious tissue, meaning that they are not the disease agent and not related to pathology. Although Prusiner continues to stand by this conclusion, other scientists continue to view the prion rod as a disease-related object. Despite the current unclear or debatable status of the prion rod—the rhetorical construction from the 1980s as a visual representation of the agent—the prion helped stimulate research leading to mapping the gene that codes for the normal form of the protein (Liao et al., 1986) and identifying genetic mutations that produce familial forms of TSEs (see Poulter, et al., 1992). Significant progress in several research communities was likely stimulated by the possibilities embedded in the visual images of both Prion Rods and SAF. But the rhetorical life of the prion images extended far beyond the immediate TSE community.

Although dismissed as byproducts by the scientist who employed them as signs of his new theory, the prion rods circulated through, and continue to exist in, popular forums as visual signs of scientific achievement. Images of prion rods were—and still are—distributed to popular forums in which they signified scientific progress. A colorized, computer-generated picture of prion pathogens that resemble the prion rod appears with a January 2010 news report about "specialized proteins that cause mad cow disease [that] are lifeless but still evolve" (Nelson, 2010). On Merck's "Institute for Science Education" site, a colorful image (see Figure 6) of "fibrils associated with prion disease" appears in an article about the Prusiner Nobel Prize (Merck Institute for Science Education, 1997). The official Web site of the Nobel Foundation, nobelprize.org, places this full-color image of "filamentous aggregates" that "gradually damage neuronal tissue" (Nobel Media AB, 2011) within the narrative about Prusiner's Nobel Prize.

A visual whose referent Prusiner himself invalidated was dispersed to the Nobel Prize Web page where the visual is used to illustrate Prusiner's accomplishment.

1990s—ESTABLISHING THE AGENT: PROCESS AND STRUCTURE

To be viable, a theory of disease requires not only an agent—ideally one that is visible through electron micrographs—but also must explain how disease progresses. The protein-only theory of disease had to explain how a normal protein particle could change into an abnormal, disease-causing particle that could induce other normal protein particles to follow suit. Unorthodox and even heretical, the theory was far more complex than the well-known viral theory of disease. In a critical review of the Prusiner team's work, Kimberlin (1986), a longtime TSE researcher from the United Kingdom, charged that Prusiner had gone too far "outside the current framework of molecular biology to accommodate the scrapie agent" (p. 108). Kimberlin insisted on "a much simpler working hypothesis" that involved a very small scrapie-specific nucleic acid that causes disease by binding to host protein. The idea of an infectious agent working without nucleic acid was not the simplest explanation, based on current knowledge at that time. A far simpler explanation was that a nucleic acid molecule, too small or hidden by a protein coat, had simply not yet been detected. Thus, Prusiner's complex hypothesis needed to be strategically situated as both more viable and simpler than the existing explanation.

To suggest a process of prion propagation, the Prusiner team presented drawings of prion pathogenesis—both protein-only and the nucleic acid models—in several scientific forums. For example, the drawings in Figure 7 from a *Science* paper (Prusiner, 1991) were similar to those in other journals. Here two "possible mechanisms of prion replication" (p. 1529) were provided with textual explanation.

Here, the highly complex and controversial "one component prion model" (Prusiner, 1991, p. 1520), B, is placed in visual balance with the less controversial model that involves nucleic acid. Visually, the less controversial model is more complicated and convoluted, even though, basically, this was the model of all infectious diseases at the time. But the squares, wavy lines, circles, and combinations of signs create visual confusion and complexity. Model B, the protein-only model, looks much simpler, with only squares and circles and a more streamlined, linear process.

Textual anchoring also balances the impression of equality among these explanations: The hypothesis deemed simplest by TSE insiders—that nucleic acid is involved—is coated with an aura of complexity and becomes "a two-component model" with a "putative, as yet unidentified, nucleic acid or other second component" (Prusiner, 1991, p. 1520). The prion-only explanation is clothed in simplicity: a "one-component model" (p. 1520) in which prions (PrPsc) bind to normal host protein (PrPc) and form new molecules (heterodimer) that help to replicate the infectious prions through a succession of cycles.

The conventional model of DNA-derived agency was entirely eliminated in a review essay for the *Scientific American* (Prusiner, 1995). By that time, the mad cow crisis in the United Kingdom had reached the popular media. Also, by 1995, there was no experimentally grounded evidence to explain how prions form or even whether they contain a nucleic acid. Yet Prusiner presented a simplistic cartoon (Figure 8) of "scrapie PrP propagation" (p. 54).

Readers could easily have interpreted this simple cartoon (Figure 8) as a model of well-known agents and an accepted hypothesis. The textual anchorage conveyed the idea of a single, simple agent and a straightforward, linear process; the word "apparently" and the phrase "a favored

hypothesis" suggested inevitability and community consensus around the prion idea. All mystery and complexity appeared to be resolved as they are with any simple model of a well-established process. But this cartoon is more like an advertisement than a model because it did not so much represent as establish; that is, it did not tame and homogenize a known entity but tamed and homogenized a highly unorthodox theory by advertising the prion as a single agent that follows a straightforward pathogenic process.

One likely result of dispersing his idea through visual models similar to the one above into popular science forums is that Prusiner gained more allies from outside his specialized field than from inside. Paul Brown, an established virologist at NIH, told a journalist that although he and other TSE investigators scoffed at Prusiner, scientists from other fields took Prusiner seriously: "People outside the field read Prusiner," said Brown. "They don't read the twenty years of literature. And they say everyone inside the field screaming at Stan is biased because he's this successful young turk" (Taubes, 1997). Retired UK TSE scientist Alan Dickinson agreed that although insiders were crying foul, outsiders and noviates "entering the field since the late 80 s, [*sic*] had very limited understanding and no perspective of the subject. The flood of new entrants was one outcome of the BSE epidemic" (personal communication, May 8, 2003). But Prusiner's promotional efforts also were to blame:

> If there had been no Prusiner, events would have taken a much more rational course. As you know, from 1987 "PrP is the agent" and the 'obviousness' made everyone think the work could be done at the lab bench by novices lacking any awareness of complicating details. (A. Dickinson, personal communication, May 8, 2003)

The prion's dominance was a result of its mobility, achieved, in part, through rhetorical construction that appealed to both scientific cultural values—simplicity and universality—as well as the general public's hunger for a good story: Tenacious scientists discover rogue protein.

Yet, while Prusiner was distributing his simple story, the story back in the laboratory was far from simple. In 1995, when the *Scientific American* displayed the visual above (Figure 8), crucial problems with the prion theory persisted. By the early 1990s, scientists had found that mice genetically altered to lack the normal protein involved in developing prions did not develop disease when inoculated with prion-infected tissue. Thus, a factor besides just protein conformation had to be involved. Recognizing and conceding to this complexity, Prusiner eventually developed the theory of "protein X" in 1997. In one paper (Kaneko et al., 1997), the Prusiner team provided a revised model of propagation that included the addition of protein X, which remains a hypothetical component of the disease process. Another problem that persisted since the 1990s is that even though the host protein, called PrP, had been established as the major component of the prion particle, efforts to break down the aggregated tissue sufficiently to identify the prion itself—the actual infectious component distilled from other biological material—consistently failed. In addition, although infected brain tissue added to samples of normal PrP could change PrP into the abnormal shape, the resulting material, when injected into animal hosts, did not cause disease.

Despite these problems, the visuals used to portray prion propagation continued to convey a simplicity that was not matched by experimental evidence. The visual below, appearing in a paper by two of Prusiner's colleagues (Weissman & Hood, 2001), purported to explain different strains of scrapie, a fact that had always pointed to a viral agent. The visual (see Figure 9) depicted the

movement from normal protein to the aberrant form to different strains of disease in cattle and sheep.

Like its predecessor, this model (Figure 9) depicted a straightforward process but did not account for all the complexities discovered through experimental work. By 2004, this same laboratory presented another illustration (Figure 10) to compare yeast and mammalian prion replication (Chien, Weissman, & DePace, 2004).

Although the illustration (Figure 10) appeared straightforward, the authors' explanation in the text was replete with uncertainties: After the spontaneous formation of an infectious particle, the mechanism of which is unknown, the "newly formed prion must replicate itself … [and] the new infectious particles must somehow be released from the aggregate … . Though how division is accomplished by mammalian prions is unclear …." (Chien, Weissman, & DePace, 2004, p. 631). In a 2007 review, chemist Sheldon Penman argued that for this model to be plausible, the prion as a protein must be "endowed with unprecedented properties" (p. 1071), such as the ability to survive digestion, to cross the blood-brain barrier, and to exist in a long latency period after which it breaks into degenerative disease and evolves into different aberrant forms that cause different disease strains—all properties of viruses. For Penman, "Elementary physiology suggests this is a great deal to expect from a simple polypeptide" (p. 1071). But the visual illustrations of prion pathogenesis, introduced by Prusiner and revised by subsequent authors, masked the improbable nature of the prion theory. Although research papers on TSEs from several subfields have become increasingly complex, the visuals used to clarify and to illustrate pathological processes continue to portray single agents and a simple, linear process. The idea of simplicity, perhaps helpful in attracting interest to a new, highly unorthodox theory, has lingered in the visual culture long after it became clear that nothing is simple about these diseases (see Wilson [2005] for a thorough review of the mystery).

1990s—ESTABLISHING THE AGENT: STRUCTURE

Determining the tertiary or functional three-dimensional structure of the prion molecule is, as with all disease agents, important to the development of effective preventative and curative therapies. The function of a protein depends not only on its amino acid content but also on its three-dimensional structure. Although each protein is produced as a long chain of amino acids, the protein quickly assumes a specific conformation due to the formation of chemical bonds between its constituent amino acids. The resulting shape of each protein is characteristic of the protein and confers on it the ability to interact with other proteins and molecules. Yet due to the difficulty in breaking down infected material in its aggregated condition, a minimal infectious unit does not exist, and thus the third component of an entity's "thingness," its three-dimensional structure, could not be solved. Still, the Prusiner team staked a claim in the race to identify this structure by proposing a highly speculative model of the molecule (Huang, Prusiner, & Cohen, 1996). They proposed a "plausible model" (Figure 11) of the disease-causing particle, the prion or Prpsc, based on computational techniques and their proposed three-dimensional structure for the normal PrP.

Without a molecule of the infectious agent itself—because of the insolubility of the infectious material—they had to be creative by selecting a "biologically relevant fragment" (Huang, Prusiner,

& Cohen, 1996, p. 13) of PrPSc. Yet a fragment of amino acid from purified infected tissue is not the same as the thing itself. Though highly speculative and with minimal scientific usefulness, this model was distributed through several scientific forums including biochemistry (Baldwin, James, Cohen, & Prusiner, 1998) and general science (Cohen et al., 1994). Prusiner went on to include this model in review articles published in *Cell* (Prusiner, 1998b; Prusiner & Cohen, 1998) and the *Proceedings of the National Academy of Science* (Prusiner, 1998a). He also included a visual of this model in his Nobel lecture. Paul Brown, a senior investigator at NIH, said, "I think it's so ironic that he included that model in his talk because it was really more of an icon of the prion. And it's also a little ironic that the Nobel was awarded to Stan for having shown that the protein replicates because that's still not been shown" (personal communication, March 6, 2003).

Several investigators criticized the model and developed alternatives (Nelson et al., 2005). Winner of the 2002 Nobel Prize in Chemistry, Kurt Wüthrich, along with his colleagues, published the solution for the structure of the normal prion protein, PrP (Zahn et al., 2000). In this paper, the investigators showed that the predictions about PrP and prion structure made by the Prusiner team were incorrect. According to Reed Wickner, who discovered an analogue to mammalian prions in yeast, Wuthrich stood during a professional conference presentation as Prusiner displayed his favored model of the prion molecule and said, "Take that down. It is incorrect" (personal communication, March 15, 2006).

Nevertheless, the speculative model of the prion molecule's three-dimensional structure has been and continues to be displayed as a speculative model on educational sites, such as Beloit College's bioinformatics site (BioQUEST Curriculum Consortium, n.d.) and a site for biochemistry class at St. John's University (Jakubowski, 2010). In some places, the model appears without the hedging or attribution as a sign of the prion as a known object. For example, a British science museum (Science Museum, n.d.) labels the visual "structure of prion," while the National Cattlemen's Association (n.d.), Stanford University's HOPES (Huntington's Outreach Project for Education, 2004), and a general health site (Hall, 2001) present the visual as a representation of the diseased prion. The model survives as indication that the prion is a reality and its structure has been definitively characterized and, in many instances, is a representation of reality rather than an expected structure or a computational theory or speculation. The model has become an advertisement bearing preferred readings of Prion science as having done what medical sciences intend: discover disease agents and tame complexity.

CONCLUSION

When attempting to explain why the prion concept has gained such prominence though it lacks experimental support, scientists tend to identify extratextual factors—personality, celebrity status, or salesmanship. For example, in his review of the science of prions, Penman (2007) asked, "How can a concept whose substantiation is so thin have such a grip on the scientific community?" (p. 1072). His answer was "the imposition of a theory or belief, not necessarily correct, by force of personality and prestige" (p. 1072). Byron Caughey, the TSE researcher at NIH, acknowledged Prusiner's ability to sell his idea:

> All those years where Prusiner was running around, and still is, doing these horrendous things, and just running roughshod over his field, all these scientists who had a different idea about it and a more careful idea about it, wanted

to stick close to the evidence, there was nobody who had the charisma and the intestinal fortitude to stand up and insist that, to really fight the battle, and you say, OK, well, why is that. Well, partly it's because a lot of us want to do the science and don't want to play those political, public relations games and we probably, incrementally, as we went through the process didn't realize how important that game can be, and in hindsight, you say, well, duh, it's extremely important and you gotta be better salesmen. (personal communication, April 23, 2003)

Prusiner's former colleague, Paul Bendheim, acknowledged that Prusiner had an important impact on the field:

Stan was driven to be famous and would let nothing get in his way. The outcome is very clear. He achieved that. I'll never forget this. One evening, Stan and I were talking and he said, “You know what I'm doing is bigger than Pasteur.” He had this need, some basic insecurity. The flip side is that Stan drove this field like nobody else in history. (personal communication, June 23, 2004)

Behind personality and fame and salesmanship was a rhetoric—visual and verbal—that helped to construct objects and their processes as if they were simple, applicable, plausible, and possible. The rhetorical construction of that object, the prion, as a single, simple agent with a knowable process and structure prevailed even as laboratory investigation demonstrated multiple causative factors, a highly complex process, and a structure that is taking decades to work out. Indeed, this highly unorthodox phenomenon has turned out to be more complex than any language, verbal or visual, can convey. Promotional scientific rhetoric, like advertising, stirs the audience to believe in magic. In this case, the magic was an agent that, in defying everything known about agency, promised another kind of magic—the chance to study something entirely new. But also like advertising, promotional scientific rhetoric often promises what it cannot deliver, at least not any time soon.

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