

BATTLEFIELD

Papers suggesting that biotech crops might harm the environment attract a hail of abuse from other scientists. Emily Waltz asks if the critics fight fair.

mma Rosi-Marshall's trouble started on 9 October 2007, the day her paper was published in *Proceedings* of the National Academy of Sciences (PNAS). Rosi-Marshall, a stream ecologist at Loyola University Chicago in Illinois, had spent much of the previous two years studying 12 streams in northern Indiana, where rows of maize (corn), most of it genetically engineered to express insecticidal toxins from the bacterium Bacillus thuringiensis (Bt), stretch to the horizon in every direction.

Working with colleagues including her former adviser Jennifer Tank at the University of Notre Dame, Indiana, Rosi-Marshall had found that the streams also contain Bt maize, in the form of leaves, stalks, cobs and pollen. In laboratory studies, the researchers saw that caddis-fly larvae herbivorous stream insects in the order trichoptera fed only on Bt maize debris grew half as fast as those that ate debris from conventional maize. And caddis flies fed high concentrations of Bt maize pollen died at more than twice the rate of caddis flies fed non-Bt pollen. The transgenic maize "may have negative effects on the biota of streams in agricultural areas" the group wrote in its paper, stating in the abstract that "widespread planting of Bt crops has unexpected ecosystem-scale consequences"1.

The backlash started almost immediately. Within two weeks, researchers with vehement objections to the experimental design and conclusions had written to the authors, PNAS and the US National Science Foundation (NSF), Rosi-Marshall's funder. By the end of the month, complaints about the paper had rippled through the research community. By the time Rosi-Marshall attended a National Academy of Sciences (NAS) meeting on genetically modified organisms (GMOs) and wildlife on 5 November 2007,

'The response we got — it went through the jugular." — Emma Rosi-Marshall

"She looked hammered", says Brian Federici, an insect pathologist at the University of California, Riverside, one of her work. "I felt really sorry for her. I don't think she realized what she was getting into."

No one gets into research on genetically modified (GM) crops looking for a quiet life. Those who develop such crops face the wrath of anti-biotech activists who vandalize field trials and send hate mail. But those who, like Rosi-Marshall and her colleagues, suggest that biotech crops might have harmful environmental effects are learning to expect attacks of a different kind. These strikes are launched from within the scientific community and can sometimes be emotional and personal; heated rhetoric that dismisses papers and can even, as in Rosi-Marshall's case, accuse scientists of misconduct. "The response we got — it went through your jugular," says Rosi-Marshall.

Problem papers

Behind the attacks are scientists who are determined to prevent papers they deem to have scientific flaws from influencing policy-makers. When a paper comes out in which they see problems, they react quickly, criticize the work in public forums, write rebuttal letters, and send them to policy-makers, funding agencies and journal editors. When it comes to topical science that can have an impact on public opinion, "bad science deserves more criticism that your typical peer-reviewed paper", Federici says.

But some scientists say that this activity may be going beyond what is acceptable in scientific discussions, trampling important research questions and stifling debate. "It makes public discussion very difficult," says David Schubert, a cell biologist at the Salk Institute in La Jolla, California,

who found himself at the sharp end of an attack after publishing a commentary on GM food² (see 'Seeds of discontent'). "People who look into safety issues and pollination and contamination issues get seriously harassed."

To see the effect that biotech crop research can have on policy — and why some researchers feel that they need to weigh in against such studies as quickly and forcefully as possible — it is instructive to look back to a study³ published in *Nature* in 1999. In it, John Losey, an entomologist at Cornell University in Ithaca, New York, and his colleagues reported that nearly half of the monarch butterfly caterpillars eating leaves dusted with *Bt* maize pollen died after four days, compared with none exposed to untransformed pollen. The media and the anti-GMO community erupted. "Gene Spliced Corn Imperils Butterflies" headlined the 20 May 1999 *San Francisco Chronicle*. Greenpeace activists demonstrated in front of the US Capitol dressed as monarch butterflies, collapsing from 'killer' GM maize.

In response, the US Environmental Protection Agency (EPA) told seed companies to submit data about the toxicity of Bt maize pollen in monarch butterflies or lose the right to sell the maize. Scientists dived into the research, using industry and government funding. The effort produced six PNASpapers in 2001 that concluded that the most common types of Bt maize pollen are not toxic to monarch larvae in concentrations the insects would encounter in the fields⁴. (Losey had used higher concentrations in his lab studies.) "The Losey paper resulted in a lot of good work and brought to a close that particular question," says Alison Power, who studies ecology and evolutionary biology at Cornell University. Yet some scientists were dismayed that a single paper with preliminary data gave so much ammunition to anti-GMO activists and caused an expensive diversion of resources to calm the scare. They did not want it to happen again.

The caddis-fly study was Tank and Rosi-Marshall's debut

in GM research. The idea stemmed from a 2002 talk that Tank gave at Michigan State University in East Lansing about nitrogen dynamics in streams. A researcher in the audience asked whether organic debris from fields of transgenic maize drains into streams, and whether it has any effect on stream life. "We've never thought about that," Tank told the questioner. And once the paper was complete, Tank, Rosi-Marshall and their collaborators had little idea of the storm it was about to kick up. "I thought the response would be 'So what? We're going to lose a few trichopterans," says co-author Todd Royer, an assistant professor at Indiana University in Bloomington.

On a Friday after the paper was published, Federici and plant biotechnologist Alan McHughen, also at the University of California, Riverside, met at a campus bar for a beer after work. "[McHughen] was really annoyed," says Federici. "I don't think there's been another case where I've seen him so really ticked off." Federici says he too was annoyed — Rosi-Marshall's study was "bad science", he says, and they feared that activists

would use it to forward an anti-GMO agenda. McHughen and Federici wanted to neutralize any effects that Rosi-Marshall's paper might have on policy.

The two discussed the key points of a rebuttal letter. McHughen wrote the critique and "circulated it around to people who might be sympathetic", says Federici. The letter listed six grievances with the "sloppy experimental design", and said the publication of the paper had "seriously jeopardized the credibility of *PNAS*". "How many busy scientists and how much scarce money will we need to divert to calm this new scare?" the researchers wrote. McHughen got ten other scientists' signatures, including Federici's. On 22 October, they sent the letter to the journal and to the NSF. Days later, Klaus Ammann, a retired botanist and professor emeritus at the University of Bern in Switzerland who had signed the McHughen letter, posted it on an online discussion forum.

Critical mass

Wayne Parrott, a crop geneticist at the University of Georgia in Athens, also began working on a rebuttal to Rosi-Marshall's paper as soon as he saw it. He said recently that in his opinion: "The work is so bad that an undergrad would have done a better job. I'm convinced the authors knew it had flaws." He e-mailed the authors, the NSF and *PNAS* two bulleted lists of flaws that he said invalidated the paper. He wrote: "It is risky to extrapolate from lab results to field results, particularly when key factors were not monitored, measured or controlled appropriately." In January 2008, *PNAS* published a slimmed-down version of this letter⁶ and the one from McHughen⁷.

Tank and Rosi-Marshall were dismayed by Parrott's e-mail. A few days after receiving it, Tank called James Raich, her contact at the NSF, to talk it over. "I told her to

ignore it," says Raich, an ecosystem ecologist at Iowa State University in Ames who worked for the NSF for two years reviewing grant proposals. He told her that letters like these were unusual. But the critiques kept on coming. On 30 November, Monsanto, a maker of *Bt* maize based in St Louis, Missouri, sent the EPA a six-page critical response⁸ to the paper, and posted it online. Eric Sachs, director of global scientific affairs at Monsanto, says that regulators ask seed companies to notify them of papers that relate to crop safety, so Monsanto often includes with its notification evaluations of these papers.

Four other signatories of the McHughen letter went on to publish scathing opinion articles over the next few months. In a March 2008 article criticizing four papers on biotech crops, Ammann joined forces with Henry Miller, a research fellow at the Hoover Institution in Stanford, California, to ask "Is biotechnology a victim of antiscience bias in scientific journals?". They called Rosi-Marshall's conclusions "dubious", and said their use of

Under fire: a 2007 paper on transgenic maize's impact on stream insects was





Jennifer Tank (left) and Emma Rosi-Marshall study stream ecology.

evidence "arguably amounts to investigator misconduct". And in a July 2008 commentary in *Current Science*¹⁰, Shanthu Shantharam, a visiting research scholar at Princeton University in New Jersey said Rosi-Marshall's "offending" paper "carried a wrong message to farmers and environmentalists", and that anti-biotech crop activists would use the paper to "hamper the progress of science".

Rosi-Marshall took the hits hard. "I experienced it in person and in writing," she says. "These are not the kind of tactics we're used to in science." She was a few years out from her PhD, she did not have tenure at Loyola and her first paper in a prominent journal was getting trashed, along with her reputation. "She's young and was getting picked on," says Michelle Marvier, a biologist at Santa Clara University in California who attended the NAS November 2007 meeting.

It was at least some comfort to Rosi-Marshall and Tank that e-mails and phone calls of encouragement came pouring in from other scientists. Some of their supporters had observed similar attacks on other biotech crop papers. "The most reassuring thing we learned was that it had happened before and by the exact same people," says Tank.

What was it about Rosi-Marshall's paper that prompted such a strong reaction? The wording of the abstract — "widespread planting of *Bt* crops has unexpected ecosystemscale consequences" — was a particular point of contention. Her critics say that the data do not support such a definitive conclusion. "They absolutely went too far," says Randy Schekman, editor-in-chief of *PNAS*. Of the half-a-dozen letters received by the journal, most of them protested at this wording, he says. "Why this would have escaped the attention of the referees beats me."

The authors agree that the wording was unfortunate and in retrospect say that the sentence should have articulated the potential for ecosystem-scale consequences within streams, rather than suggesting that such consequences were observed. "This was an oversight," says Rosi-Marshall. "But we did not expect that this sentence would, in light of all of the other statements in our paper, elicit the response it

"It is critical to assert the right of scientists to question each other's work."

— Wayne

did. We thought the paper would be taken as a whole."

The study's methods also came under fire. It is unclear, for example, whether it was the Bt toxin itself affecting the caddis flies, or some other difference between Bt and non-Bt plants. To test this possibility, critics say the caddis flies should have been fed isogenic lines: strains of maize that are genetically identical except for Bt genes. The authors say they chose not to use such lines because their nutritional quality would have differed — Bt maize has higher concentrations of lignin than non-Bt maize, and so is less nutritious. So the authors matched the Bt samples with non-Bt samples that had similar levels of lignin and other nutrients. "To do otherwise would have resulted in a confounded experiment. Pairing the treatment on the basis of isolines might be standard for agronomic studies, but was inappropriate for an ecological feeding study," the authors told Nature in an e-mail. Rosi-Marshall and her colleagues made this point and other responses to their critics in a correspondence11 published online in PNAS the week after McHughen's and Parrott's critiques.

It is also unclear how much *Bt* toxin the caddis flies ate. The authors let the insects eat as much as they wanted, as they would in the wild. Critics argue that the authors should have fed the insects known amounts of the toxin in a method called a dose-response study that is routine in toxicity assessments. "The Rosi-Marshall *et al.* paper would have benefited from additional toxicological data," says Doug Gurian-Sherman, a senior scientist at the Union of Concerned Scientists in Cambridge, Massachusetts, and a former reviewer for the EPA. But the method the authors used "is a widely accepted method, and is generally adequate for a preliminary study of possible toxicity", he says.

Omitted study

The paper was also accused of omitting contrary findings. In June 2007, four months before Rosi-Marshall's *PNAS* paper was published, Jillian Pokelsek, a master's student at Loyola University Chicago working with Rosi-Marshall, presented results from a preliminary field experiment at the annual meeting of the North American Benthological Society in Columbia, South Carolina. The work showed that *Bt* maize pollen did not influence the growth or mortality of filter-feeding caddis flies. The society posted an abstract¹² of the presentation on its website attributing the work to Pokelsek, Rosi-Marshall, Tank, Royer and four other scientists who also authored the *PNAS* paper. It was not mentioning this study that prompted Miller and Ammann's accusation of misconduct⁹.

The authors defend the omission on the grounds that the data in the meeting presentation were not published or peer-reviewed, and were less reliable than those in the *PNAS* paper. "Field experiments are inherently difficult to control and have lower statistical power to detect significant differences compared with controlled laboratory experiments, thus we included the more controlled and statistically rigorous lab experiments in our paper," Tank and Rosi-Marshall told *Nature*. Also, the caddis flies in the student presentation belonged to a different family, with different feeding mechanisms to those in the *PNAS* study. Miller's response: "I don't want to split hairs," he says. "If you don't do appropriate controls or if you draw conclusions that are erroneous, I

Parrott

Seeds of discontent

Several scientists say they have been sharply attacked by others in the research community when they have published papers that reflect negatively on biotech crops. In October 2002, for example, David Schubert at the Salk Institute in La Jolla, California, suggested in a Commentary in Nature Biotechnology that not enough attention was being paid to the potential unintended molecular effects of inserting genes into plant cells². Almost immediately, he received a barrage of mail from around the world, he says: "I've never received such an obscene response for offering an opinion." Schubert says people complained directly to the Salk Institute, and an administrator called him into his office to say he was jeopardizing funding for his institution. "I've written hundreds of articles some of them controversial — and never had this kind of response," he says, adding that he has given up trying to have a public discussion about the technology.

One letter¹⁵ critical of Schubert

published in Nature Biotechnology and signed by 18 people. admonished: "Good scientists go astray when they leave their area of expertise to offer an opinion when they have not studied the literature." Henry Miller at the Hoover Institution in Stanford, California, also a critic of Rosi-Marshall's paper¹, told Nature that "[Schubert] is an accomplished immunologist who has no grasp on agricultural biotech whatsoever." Not true, says Schubert. "The basic technology used to make transgenic plants was invented using bacterial and animal cells, and my lab uses this technology on a daily basis," he says.

In some cases the attacks start before a paper is out. In September 2007, Bruce Tabashnik, an entomologist at the University of Arizona in Tucson, was preparing a paper showing evidence of insect resistance to Bt cotton. He got an e-mail from William Moar, an entomologist at Auburn University, Alabama, warning him that the paper's consequences

would be "devastating". "Your statement ... would be all of the ammunition many special interest groups would need ... Just for a moment think 'monarch butterfly and Bt corn' and the repercussions that surrounded that fiasco," he wrote. Tabashnik's paper was published in Nature Biotechnology¹⁶. Moar, who now works for Monsanto, a maker of Bt maize (corn), based in St Louis, Missouri, criticized the paper at conferences and challenged it in Correspondence¹⁷ to the journal saying that the comparisons and conclusions that Tabashnik made were scientifically unsound and based on lab measures, whereas proof of insect resistance must ultimately come from field studies. Tabashnik says: "The rigorous analysis in our paper was based on systematic, objective analysis of all of the relevant data."

One author on Moar's letter was Anthony Shelton, an entomologist at Cornell University in Geneva, New York. He was in action again this year, challenging a review

article by Gabor Lövei, an ecologist at Aarhus University in Denmark, and two co-authors. Lövei's article reviewed laboratory experiments that examined whether crops engineered to kill pests affected the predators and parasites that normally feed on those pests. They found more effects, some negative, some positive, than other reviews had reported. Lövei and his colleagues argued that their method provided a more accurate summary of the literature because it directly examined the data within published papers, rather than relying on authors' conclusions.

Environmental Entomology accepted Lövei's paper¹⁸ but, in January, three months before it was published, Shelton and three colleagues were given a proof by a colleague of one of the authors. Shelton prepared a rebuttal¹⁹ that was published days after Lövei's paper. The six-page critique called the study "negatively biased", "erroneous" and

think that's misconduct." But Ammann says he has a "bad feeling" about the accusation. "Maybe we should have been more careful with the wording.

Scientists who were not involved in the debate over Rosi-Marshall's paper say the results were preliminary and left some questions unanswered, but that overall the data are valuable. "The science is fine as far as I'm concerned," says Arthur Benke, an aquatic ecologist at the University of Alabama in Tuscaloosa, who called the strong language in some of the criticisms "inappropriate".

What drives the critics? Financial or professional ties to the biotech industry don't seem to be the impetus. Such ties do exist — like many people researching biotech crops, some have received research grants from industry or have other interactions with it — but in interviews they say that these are not the major driving force. Rather, many of them feel strongly that transgenic crops are safe and

beneficial to the environment and society, and that the image and regulation of these crops has been too harsh. Many of the critics have been studying biotech crops since they were developed commercially in the late 1980s, and some were involved with the first regulatory approvals. They have specific ideas about how the risks of these crops should be scientifically assessed. And they worry that papers that fall short of high standards will give anti-GMO activists ammunition to influence policy, just as the

Protesters can brandish science suggesting that genetically modified crops are harmful.



monarch-butterfly study did. "When bad science is used to justify bad public policies, we all lose," says McHughen, who says he is on a "campaign to make academic scientists a little less politically naive and a bit more careful in their scientific work". Miller adds that "agricultural biotech has been so horrendously, unscientifically regulated and so over-regulated and so inhibited over the past 30 years that to have these pseudo-controversies stirred up unnecessarily does a disservice to everyone and everything".

Ammann points to the example of golden rice, a variety engineered in the late 1990s to contain more vitamin A. Regulations have delayed the rice's development, he says, although more than 250,000 children a year go blind from vitamin-A deficiency. "We have to get emotional," says Ammann. "I can't agree with the cool scientists' perspective — only dealing with the facts. We live in the real world." In 2006, Ammann formed a rebuttal team called ASK-FORCE

to challenge reports about biosafety of GM crops. On one online site, Ammann criticizes 20 reports — none of them positive toward biotech crops — that he considers biased or bad science. In July, he was revising a critique 🗧 of a paper that appeared in *The Lancet* ten years ago. "I'm working nearly day and night on these things," says Ammann.

The emotional and sometimes harsh quality of some of the attacks strikes some scientists as strange and unlike the constructive criticism to which they are accustomed.



"inappropriate". For example, it says the authors didn't distinguish whether predators and parasites of insects that feed on biotech crops were affected by the toxins in the plants or by the health of their prey. Lövei and his co-authors say they hope to defend their paper in the October issue of *Environmental Entomology*, and will agree that the distinction would have been useful, but that it would not have changed their conclusions.

Shelton says that he and his group wanted to counteract any effect Lövei's work might have on policy, particularly as that month the European Food Safety Authority was writing up a risk assessment on unintended effects of genetically modified plants. "I could envision a regulator having this Lövei article appear on his desk and saying 'We've got to rethink approval methods'," says Shelton.

Shelton's critique was a "way over-reaction", says an editor at the Entomological Society of America, which publishes *Environmental Entomology*, who asked to remain anonymous. "They seem to have read it with eyes predisposed to

dismiss anything reflecting poorly on GMOs [genetically modified organisms]." Shelton disagrees. "I have been critical of some aspects of genetically engineered plants and microbes in the past when I thought they were warranted, based on scientific data," he says. "I am also an editor in the **Entomological Society of America** and felt that our reaction was not a 'way over-reaction'." He adds that as an editor he routinely rejects papers that could be considered supportive of GMOs because of their quality. "Poor science can occur on both sides of issues."

When asked to point to a good paper that reflects negatively on biotech crops, most critics Nature spoke to said they couldn't name any. "I have seen very little substantive data that are negative towards Bt crops that can't be easily overturned," says Moar. Wayne Parrott at the University of Georgia in Athens, however, says: "There is plenty of biotech-safety research out there that has not come under attack, even when the answers are not what everyone would have liked."

Benke points out that none of the criticisms on the caddisfly paper, for example, called for further study on the insects. "What papers like this do is alert us to possible reasons to look into this more carefully," he says. "No one mentioned this." To try to dismiss the research out of hand ignores how science is supposed to work, adds Power — you make a hypothesis, test it, refine it, test it and refine it again. "You keep doing that until you have an answer that is as close as you're going to get," she says. "I don't understand the resistance to that notion."

Arbiters of the truth

Some scientists say they are galled by the certainty with which some of the critics state their opinion. "Part of what exasperates me is that they have declared themselves to be the experts in this field, and forcefully present themselves as the ultimate arbiters of truth," says an editor for the Entomological Society of America who asked to remain anonymous. "I personally am in favour of GMOs in general, and think that they are very beneficial for the environment. But I do have problems with the tactics of the large block of scientists who denigrate research by other legitimate scientists in a knee-jerk, partisan, emotional way that is not helpful in advancing knowledge and is outside the ideals of scientific inquiry."

The critics respond that they are simply pointing out flaws in research, and that this is an important part of the scientific process. "It is neither fair nor accurate to equate pointing out serious deficiencies with experimental design "When bad science is used to justify bad policies, we all lose."

— AlanMcHughen

and data interpretation as 'denigration'," Parrott says. "For science to maintain its integrity and move forward, it is critical to assert the right of scientists to question each other's work." McHughen says that he doesn't condone *ad hominem* attacks. "They are invariably unproductive," he says, and points out these tactics are often used against scientists who don't oppose GM crops.

Federici says he finds it inappropriate to call the reactions 'knee-jerk' ones. "Losey and colleagues, and Rosi-Marshall and colleagues at the time of their studies were newcomers to the field. Most of the people who found their studies flawed and protested had extensive experience with *Bacillus thuringiensis*." He also points out that the critics varied in how strongly they responded to the Rosi-Marshall paper, saying "I don't consider writing a letter to the editor a harsh response."

Ignacio Chapela, a microbial ecologist at the University of California, Berkeley, says that the attacks may be deterring young scientists from pursuing careers in biotech crop research. "I have a very long experience now with young people coming to me to say that they are not going into this field precisely because they are discouraged by what they see," he says. Chapela faced criticism from pro-GMO scientists after publishing a 2001 paper in *Nature*, in which he reported that native maize varieties in Mexico had been contaminated with transgenic genes¹³. Following the criticism, *Nature* decided that "the evidence available is not sufficient to justify the publication of the original paper".

At its worst, the behaviour could make for a downward

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spiral of GM research as a whole, says Don Huber, a emeritus professor of plant pathology at Purdue University in West Lafayette, Indiana. "When scientists become afraid to even ask the questions... that's a serious impediment to our progress," he says. Miller says: "I don't see how criticism of flawed science that verges on misconduct should discourage anybody." Researchers could be invigorated by entering a field with such lively debate. "For some people it might be exciting because you're doing science that is relevant to society," says Power.

Pervasive spread

Rosi-Marshall's caddis-fly paper did find its way into the anti-GMO rhetoric, although on nowhere near the scale that the monarch butterfly paper did. For example, the London-based Institute of Science in Society, a not-for-profit organization involved in the GM debate, on 30 October 2007 posted its summary of the paper, saying that: "calling a halt to planting *Bt* corn next to streams... would be in keeping with the evidence [the authors] have provided". Greenpeace included the paper in an April 2008 briefing on *Bt* maize, citing it as evidence of environmental risk.

The impact went further than that. On 9 January 2008, three months after Rosi-Marshall's paper was published, France's watchdog on GM foods ruled that one of Monsanto's types of *Bt* maize, known as MON810, may have an impact on wildlife. The evidence it cited included Rosi-Marshall's paper. Two days later, the French government announced a ban on cultivating the maize. "[The paper] got to every agency and non-governmental organization that doesn't like the technology and gave them a flag to wave," says Parrott. Not that he considers the effort wasted: "I have no doubt the impact on policy-makers would have been much worse had it not been countered."

Nearly two years since the paper was published, the critics' comments are still pointed. "It was just an idiotic experiment," Miller said this July. But Rosi-Marshall and her co-authors stand behind their paper. "We believe our study was scientifically sound," they wrote in an e-mail, "although many questions on the topic remain to be answered. The

"Young people are not going into this field because they are discouraged by what they see."

— Ignacio Chapela repeated, and apparently orchestrated, *ad hominem* and unfounded attacks by a group of genetic engineering proponents has done little to advance our understanding of the potential ecological impacts of transgenic corn."

And Rosi-Marshall's career seems to have survived the furore. In May 2009 she secured tenure at Loyola University Chicago, and in August she moved to the Cary Institute of Ecosystem Studies in Millbrook, New York. There she will study human-dominated ecosystems and will continue to investigate the influence of maize varieties on stream ecosystems. Since the caddis-fly paper, she has co-authored another study on transgenic crops showing that *Bt* maize debris decomposes in streams at a faster rate than conventional maize¹⁴. She says more data produced with the NSF grant are on the way and that the attacks won't deter her from her studies.

"It toughened me up a lot," she says. "I'm not going to be intimidated."

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