Invasion of the ‘frankenbees’: the danger of building a better bee

Bernhard Warner Last modified on Fri 19 Oct 2018 15.49 BST

The spring of 2008 was brutal for Europe’s honeybees. In late April and early May, during the corn-planting season, dismayed beekeepers in Germany’s upper Rhine valley looked on as whole colonies perished. Millions of bees died. France, the Netherlands and Italy reported big losses, but in Germany the incident took on the urgency of a national crisis. “It was a disaster,” recalled Walter Haefeker, German president of the European Professional Beekeepers Association. “The government had to set up containers along the autobahn where beekeepers could dump their hives.”

An investigation in July of that year concluded that the bees in Germany died of mass poisoning by the pesticide clothianidin, which can be 10,000 times more potent than DDT. In the months leading up to the bee crisis, clothianidin, developed by Bayer Crop Science from a class of insecticides called neonicotinoids, had been used up and down the Rhine following an outbreak of corn rootworm. The pesticide is designed to attack the nervous system of crop-munching pests, but studies have shown it can be harmful to insects such as the European honeybee. It muddles the bees’ super-acute sense of direction and upsets their feeding habits, while it can also alter the queen’s reproductive anatomy and sterilise males. As contaminated beehives piled up, Bayer paid €2m (£1.76m) into a compensation fund for beekeepers in the affected area, but offered no admission of guilt.

The die-off forced a reckoning among European farmers. Hundreds of studies examined the safety of neonicotinoids, known as neonics, and their links to colony collapse disorder (CCD), in which worker bees abandon the hive, leaving the queen and her recent offspring unprotected, to starve. In 2013, the evidence led to a landmark European commission ruling,

imposing a moratorium on clothianidin and two other major neonics – the world's most popular pesticides. This April, Europe went a step further. The commission extended the ban on the trio of neonics to virtually everywhere outside greenhouses, citing evidence that by harming pollinating insects, neonics interfere with the pollination of crops to the value of €15bn a year. Environmentalists cheered the victory. Regulators beyond Europe plan to follow.

For Haefeker at the beekeepers association, who had spent years campaigning against the use of neonics, victory was sweet, but short-lived: faced with multiple threats from modern farming methods, beekeepers know the insecticide ban alone is not enough to save the honeybee.

Honeybees originated in Eurasia roughly 35m years ago, and as long as they have had steady access to flowering plants, they have thrived. But in the modern world, bees face all kinds of dangers. Colony collapse is not a single malady, but rather an amalgamation of different challenges. Alongside the dangers of pesticides, diseases such as Israeli acute paralysis virus, gut parasites and invasive parasites such as the varroa mite can overwhelm the bees' immune systems. Industrial agriculture imposes its own threats: a mania for monocultures has led to shrinking foraging habitats, while, according to the US Environmental Protection Agency, bees employed in commercial pollination, in which hives are stacked high on trucks and driven around the country to pollinate almond trees and other crops, get highly stressed, which damages their resilience and eating habits.

Since the EU began phasing out neonics, in 2014, the honeybees' recovery has not been as dramatic as hoped. Neonics are probably not the biggest factor in the demise of bees, but they are the easiest to outlaw. To farmers, this seems outrageously unfair. Citing an industry-funded study, they say the ban will cost the EU agriculture sector €880bn annually in diminished crop yields.

Another, more controversial, response to the slump in bee populations is in the works. This is the plan to create a more resilient strain of honeybee –

a genetically modified superbee. The technology for creating GM honeybees is in its infancy, and still confined to the laboratory. But, if successful, it could lead to a hardier species, one that is resistant to natural and manmade hazards: viruses, varroa mites, pesticides and so on. If we can't change modern farming practices, the thinking goes, maybe we should change the bees.

The prospect horrifies many bee people – from commercial beekeepers such as Haefeker to passionate amateurs – who see a lab-made superbee as a direct threat to the smaller, struggling bee species. Traditional beekeepers have a name for them that expresses their fear and suspicion: Frankenbees.

Like many beekeepers, Haefeker is an activist and conservationist. A kind of bearded Lorax, Dr Seuss's valiant spokesman for threatened trees, Haefeker speaks for the bees. For much of the past two decades, he has sounded the alarm on declining bee health, bringing his message to lawmakers in Brussels, Berlin and Munich, before judges at the European court of justice in Luxembourg, to investor roundtables in London, to beekeeper conferences in Istanbul, Austria and Rome, and to corporate gatherings of the agrichemical industry around Europe.

When we met in Bavaria a week after the EU extended its neonics ban, I expected Haefeker to be in celebratory mood. But over lunch at a favourite roadway tavern an hour outside Munich, he explained that he considers the development of GM bees – however long it takes to get them in production – an even greater threat to the humble honeybee. "I don't expect it to be commercialised next week, but then I don't want to leave anything up to chance," Haefeker said. "The public has been pretty late on a whole bunch of bad ideas. We don't want to be late on this one."

Some beekeepers worry that, if the agriculture industry succeeds in building and patenting a blockbuster, mite-free, pesticide-proof superbee, it would dominate and destroy the vibrant local market in conventional bee strains. There are health fears, too: the sting of GM bees may introduce new allergy risks. And beekeepers are afraid they would not be able to

protect the gene pool of traditional strains such as the beloved *Apis mellifera*, the scientific name for the European honeybee, against a dominant, pesticide resistant, lab-designed version.

Jay Evans heads the bee research lab at the US Department of Agriculture, where they are looking at various threats to bee health. Designing a truly pesticide-resistant honeybee, a "bulletproof bee", as Evans calls them, would "throw a lot of nature under the bus".

It is always hive-like – 30C and humid – in the narrow, windowless laboratory where genetically engineered honeybees are created on the campus of Heinrich Heine University in Düsseldorf, Germany. One June day, three students in T-shirts were on the morning shift. Two of them silently inspected plastic honeycomb discs. Each disc contained 140 tiny plug holes, in each of which a single honeybee embryo was growing. These discs were then passed to a third student at a separate workstation, where, with remarkable dexterity, she injected each egg with an sgRNA gene-manipulation solution, a main ingredient in a revolutionary new gene-editing technique called Crispr-Cas9.

Crispr technology has transformed microbiology in recent years by allowing scientists to copy a desirable part of the DNA strand and insert it directly into the chromosome of the target specimen. Now, with great precision, scientists can remove harmful mutations or unwanted traits, or insert a desired trait. In the US, you can buy a Crispr apple that doesn't brown. Medical researchers, meanwhile, see Crispr as a promising route to making mosquitos resistant to the malaria parasite.

The director of the Düsseldorf lab is Martin Beye, a giant in the field of evolutionary genetics. In 2003, Beye and his colleagues were the first to pinpoint the gene variants, or alleles, that determine the sex of honeybees. Three years later (coincidentally, just as scientists determined the likely causes of colony collapse disorder), Beye and an international team of biologists decoded the *Apis mellifera* honeybee genome, a breakthrough that transformed the field of bee biology. Scientists now have an

understanding of bee health down to the chromosomal level, enabling them, for example, to analyse precisely how pathogens and parasites affect their bee hosts. Genomics can take much of the guesswork out of breeding, too, revealing the precise gene markers that make stocks more resilient to stressors and disease. Once the genome was cracked, it was only a matter of time before the scientific community would build a designer bee. In 2014, Beye's lab claimed that crown.

The gene-injection method Beye's team pioneered, and laid out in their 2014 research paper, is painstaking and fraught with risk. To demonstrate, a student motioned for me to peer into her microscope. The faint outline of a tiny needle and its intended target, the egg, came into focus. Magnified, the egg looked like a smooth grey balloon, the kind performers at children's parties tie into poodles and giraffes. Poke the egg at the wrong angle, or with too much pressure, or with an imprecise dosage, and it will pop. And the injection has to be stealthy enough to leave no marks. If the worker bees, the hive's fastidious caretakers, sense in any way the pupae are not perfect, they cast them from the nest, leaving them for dead. Only the pristine survive.

Honey bees in flight. Photograph: Andre Skonieczny/Getty/Imagebroker

To increase the odds of success, Beye's team keep their injected embryos away from the workers at first, incubating in an artificial hive. Only after 72 hours do they slip the fittest of their modified larvae specimens into a queen-rearing colony. What happens next is similar to the conventional

queen-breeding method. The researchers graft the larvae into cell cups lined with royal jelly, the nutrient rich compound that young larvae gorge on to become queens. Even so, the workers, on average, rejected three out of four mutant larvae. But the survival rate was enough to guarantee the birth, in 2014, of the world's first genetically modified honeybee queens.

I was also shown the transgenic queens. Up close, they looked vigorous, but unremarkable. The researchers affixed a magenta-coloured ID tag to the queen's back, between the base of her wings. She mingled with ordinary worker bees in a small wooden nucleus hive. The sides were made of a hard plastic for viewing. Beye's research team told me their transgenic bees behave no differently than any other *Apis mellifera* honeybees. The queen and the workers covered every inch of their cramped confines, popping in and out of a small well containing water. After a week or so, the queen would be moved outside to a flight cage.

Beye's researchers believe manipulating the genome of the European honeybee will lead to new insights into what makes this species unique – which genes make them such meticulous groomers, or which genes programme the worker bees' super-assiduous attention to looking after their young. They want to know why bees are so good to each other. Is this instinct to work tirelessly for the good of the hive something learned, or genetic?

Beekeepers, dismayed at the prospect of GM bees becoming a reality, made a huge fuss about Beye's work. Many suspected his lab was bankrolled by the agriculture industry, or "Big Ag".

"The beekeeper associations … " Beye said, shaking his head in lingering disbelief. In person, he is affable and professorial. "They thought we were working with Bayer. I mean, they're very close by: Bayer's headquarters is maybe 20km from here." He insisted inferences of a Bayer connection were totally false.

Beye and Marianne Otte, his research partner, explained that the purpose of their work was to understand the genetic basis for bee behaviour and

health. It was never to build a pesticide-resistant bee. Building a GM bee, Beye said, is “a stupid idea”. The world doesn’t need chemical-resistant bees, he says. It needs farming practices that don’t harm bees. “They should be working on that. Not on manipulating the bee.”

But the truth is that Beye’s highly detailed paper serves as a kind of blueprint for how to build a bee. Thanks to research like his, and the emergence of tools such as Crispr, it has never been cheaper or so straightforward for a chemical company to pursue a superbee resistant to, say, the chemicals it makes. Takeo Kubo, a professor of molecular biology at the University of Tokyo, was the second scientist in the world to make a genetically modified bee in his lab. He told me that he, too, is focused on basic research, and has no ties to the agriculture industry. But, unlike Beye, he welcomes the prospect of GM bee swarms buzzing around the countryside. Lab-made, pesticide-resistant bees could be a real saviour for beekeepers and farmers, he says. And, he adds, the science is no more than three years away. “I’m now 57 years old,” he told me via email, “and completely optimistic to see such transgenic bees in the marketplace in my lifetime!”

It is not yet legal to release genetically engineered bees into the wild, but the private sector is already watching closely. One US startup contacted Beye’s lab offering to help commercialise their breakthrough research. Beye said no.

Beekeepers tend to see the world through the eyes of their bees. After a few hours in their presence, you too begin to re-evaluate your surroundings. The monochrome sameness of our farmlands – that vast, neat checkerboard of green and brown that feeds us mammals so well – can be a desert for foraging pollinators. The shocking yellow brilliance of rapeseed in blossom each spring can be a reservoir of pesticides. Beekeepers have learned to mitigate the risks and adapt, mainly by moving their hives around an ever-dwindling patch of safe zones. But the genetically modified bee, which can breed with other species and looks just like bees hand-raised from carefully chosen strains, is an altogether more dangerous

challenge.

Jay Evans at the US agriculture department, an entomologist and beekeeper, admires Beye's work, but thinks his breakthrough GM bee should remain confined to the lab. "The road to making a superbee looks really long to me, and probably not necessary," he said. "I don't see the justification."

Haefeker, a former tech entrepreneur, came to beekeeping late in life, around his 40th birthday. After spending two decades in Silicon Valley, he, his wife and two sons returned home to Germany in 2001, settling in a picturesque village on Lake Starnberg, halfway between Munich and the Bavarian Alps. What started as a backyard hobby quickly became an obsession, then a growing business. Haefeker studied everything about beekeeping, from hive maintenance to nutrition. Later, he developed an iPhone app for breeders called iQueen and started a podcast called *Bienenpolitik*, or Beekeeping and Politics. One of the few tech-savvy beekeepers in bucolic Upper Bavaria, in 2003 Haefeker was recruited to join the local professional beekeepers association where second- and third-generation beekeepers routinely grumbled about modern farming practices gobbling up open space. His first assignment was to investigate an issue that nobody at the organisation knew much about: GM crops. "I had no opinion of GMOs (genetically modified organisms)," he recalls. "But as the new kid on the block it was my job to figure out: is this going to have an impact on us?"

Haefeker's investigations into GMOs turned into a decade-long crusade. What began as a local case involving a Bavarian beekeeper with GMO-contaminated honey grew into an epic battle, pitting Europe's beekeepers against two giants: Monsanto, the biotech giant that markets MON810, the pest-resistant genetically modified maize, and the World Trade Organization, which, at the time, was pressuring the EU to give GM crops a chance. The beekeepers eventually won a huge victory in 2011 in the European court of justice, keeping European honey, for now, virtually GMO-free. The fight continues, but the beekeepers' message was clear:

don’t underestimate us.

A beekeeper in California with his hives. Photograph: Brett Murphy

The agrichemical companies’ business model is to dominate both ends of the market. They sell the farmer the chemical that kills the pests, and then they sell them their patented seeds, genetically engineered to withstand those very chemicals. (Monsanto’s top-selling line of Roundup Ready herbicide-resistant seeds are marketed as the best defence against Roundup, Monsanto’s top-selling herbicide.) The multinationals have locked farmers into contracts that prevent them from manipulating the seeds to develop their own cross-breed.

Beekeepers fear genetic engineering of honeybees will introduce patents and privatisation to one of the last bastions of agriculture that is collectively managed and owned by no one. “Think about it,” Haefeker told me, “the one area Big Ag doesn’t yet control is pollination.” And pollination is huge. The UN’s Food and Agriculture Organization (FAO) estimates that pollinators help farmers grow crops worth up to $577bn (£437bn) annually.

Damage to the bee population, by harming a vital pollinator, is already threatening crops worldwide. Outside FAO’s headquarters in Rome, a neon billboard flashes in English, Italian and Arabic a series of urgent save-the-planet messages. Save the bees tops the list. If bees disappear, food crops and animal feeds, not to mention the raw materials for biofuels (from

canola and palm oil), textiles (cotton) and medicines, will simply vanish from much of the planet. It has got so bad in some parts of China that humans already pollinate some crops by hand. In what feels like a riff on a Black Mirror episode, Harvard researchers are working on the RoboBee, a flying robotic pollinator that is half the size of a paperclip and weighs less than one-tenth of a gram. In March, Walmart filed a series of patents for its own tiny robotic pollinators.

Beekeepers and conservationists believe bees should be left to evolve on their own, helped only by protection of open spaces and best-practice natural breeding methods. Conventional bee breeding has embraced technology in recent years via the introduction of apps, tracking software and temperature-controlled "finishing" incubators. But the method is otherwise little changed from ancient times. During the year, beekeepers will perform what they call "splitting the hive", or separating a portion of the colony, frame by frame, and putting the frames in new hives with new inhabitants. This can invigorate the gene pool by introducing hardy newcomers.

"Before the introduction of neonicotinoids," Haefeker said, "about 15 years ago, you'd open up the hive and it was bursting with healthy bees. That level of reproductive energy is really crucial."

During 2008, Germany's infamous season of heavy colony losses, the dead piled up on the ground under Haefeker's hives and along the hive's inner floor. "It's got better in recent years, since the bans went into place. But we're not yet back to where we were in the days before neonics," he said. "That will take years." He tests the spring pollen for traces of neonics and other chemicals. The level of contamination is much improved, he says. On his property in Bavaria, he offered me a pinch of raw pollen. The sharp, sweet taste lingered on my tongue. I peered down to get a good look at the workers entering one of the hives. They streamed in one by one, their thighs weighed down with yellow balls of dandelion pollen. "It's good, isn't it?" Haefeker chuckled proudly.

By late July, cracks had appeared in the new neonics law. More than a

dozen EU member states sought loopholes to stay the ban, and Bayer pledged to appeal against its legal basis, warning that the ban would limit our ability to grow the quantities of "safe, affordable" food we need.

Despite the setback, Haefeker remains defiant. "Their business model is obsolete," he told me on the phone in July. The "big six" companies of Big Ag are in the process of merging into three, forming Bayer-Monsanto, Dow-DuPont and Syngenta-ChemChina. This historic, quarter-of-a-trillion-dollar spending spree is a sign of market uncertainty, Haefeker asserts, not strength. The future, he says, is big data. Sensor- and computer-assisted crop care – digital crop protection, as it is known, in which tiny robots and drones will tend to rows and rows of crops round the clock, picking off pests and releasing super-precise flows of irrigation – will feed the planet's billions, not chemicals. "I've been telling them this for years."

However ground down by Haefeker's tireless advocacy for bees they may be, Bayer officials told me they largely concur with his view that the industry is beginning to grow less reliant on chemicals, and investing more in big data and tiny robots. They even let Haefeker in the building from time to time to discuss that digital future.

Humans have been consuming honey since our hunter-gatherer days. Not long after we began farming, we started keeping bees (sugar came several millennia later). About 10,000 years ago artists depicted apiculture on the walls of Spanish caves, and, centuries after that, demand for bees wax and honey drove commerce across the empires of ancient Greece and Rome. In the 20th century, apiology, the study of bees, took off. In the 1920s, Austrian zoologist Karl von Frisch was the first to explain the meaning of the honeybees' waggle dance, which communicates to other bees the direction and distance of a food source; a half-century later he won the Nobel Prize. Honeybees are eusocial creatures, making them one of the most studied insects on the planet. Researchers study the species to understand how the human brain works and to improve the design of supercomputers. Bees, it turns out, can even do abstract maths.There are

22 million beekeepers across 146 countries, estimates Apimondia, a 123-year-old organisation that protects and promotes the livelihood of beekeepers, and lately they have been seeing a dramatic rise in membership. “During a downturn in the economy of a country, the number of new members increases,” Philip McCabe, an Irish beekeeper and president of Apimondia, told me. The media attention around colony collapse and bee health continues to bring in new members as well.

In October, 2017, Haefeker delivered a presentation at Apimondia’s International Apicultural Congress in Istanbul, unveiling Apimondia’s answer to Frankenbees. Like Haefeker himself, the fix he proposes is geeky and left-leaning: an open-source license for honeybees. A software engineer, he takes inspiration from the free software movement of the 1980s and 90s, which gave birth to the “open source” concept. Now, he sees such a licence promoting open collaboration as the perfect model to protect the beekeepers from a nightmare scenario – powerful corporations building a genetically engineered bee that they then commercialise and lock down with patents and trademarks.

A bee covered in pollen from a sunflower. Photograph: EPA

In his opening remarks, Haefeker launched into what he called “the big question”. “Did anybody ask our permission before they took our bees, the bees we have been working on, selecting and breeding within Apimondia, before the scientists decided to take these bees and modify them?” The answer was, of course, no. Until that moment, nobody, not even

beekeepers, claimed an ownership stake on the bees' genetic code. Anyone can start a hive, which might explain why you can find beekeepers tending to hives in Yemeni war zones, on the roof of Paris' Bastille opera house and in Tanzanian refugee camps. The free exchange of breeding materials – from the queens and her eggs to the drones' sperm – has long been encouraged to keep colonies genetically diverse. Through this free exchange, we preserve a common resource, benefitting everyone and everything. The beekeepers get healthier colonies out of the arrangement. We get flowers, food and honey.

To get around any attempt by the agriculture industry to distribute and license superbees, Apimondia is seeking to enshrine this freedom as a right in the form of an open-source contract, establishing bee breeding as a public good that nobody can own outright.

"This is the most efficient way to legally protect our bees from patenting and privatisation by commercial interests," Haefeker insists. Later, he told me, "we don't want to get screwed, the way farmers did by corporations and their GM patented seeds."

Apimondia has minuscule lobbying resources, but it has lined up powerful allies, including the FAO, environmental NGOs and scientific advisers. Together, they press for international treaties to protect vital pollinators. Now Apimondia, too, is sounding the alarm on GM honeybees. Radical bee-breeding experiments don't always end well, McCabe reminded me. Beekeepers won't soon forget the story of the Africanised bee, a cross-breed between the African bee and European strains introduced in South America in the 1950s. It escaped quarantine, mated with indigenous species and then multiplied and multiplied, venturing thousands of miles north into the US, breeding with local species and quickly coming to dominate their gene pool. It landed the unfortunate, even nativist, nickname "African killer bee" for the aggressive manner in which it defends its nest. "That's what we're concerned with," McCabe says, "any inter-breeding that messes with the genetics of indigenous bee populations."

Jay Evans keeps bees on the grounds of his job at the USDA, at the government research facility in Maryland, 30 minutes north of Washington DC. I contacted him by phone and asked how things were going.

“Terribly,” he said with a wry laugh. “The losses have doubled in the last 10 years.” He blames a host of factors, with disease and parasites such as the varroa mite chief among them. Beekeepers, he added, are closely watching what happens next in Europe. “I go to beekeepers’ meetings all the time. They’re suffering. They’re trying to keep their operations afloat. They’re desperate for a new solution, or technology, or regulation. Anything,” he says. But there’s consensus on what they don’t want. “When I talk to a group, I talk a lot about genetics. And occasionally they’ll say: ‘Are you making a transgenic bee, one of those Frankenbees?’”

Haefeker and his business partner, Arno Bruder, run their beekeeping enterprise on a field bordering two organic farms in Upper Bavaria. Their colonies have recovered somewhat since the neonics ban went into effect, he said, but they take steps to protect their hives. A lot of beekeepers pack their hives on to trailers and position them near nature reserves or in fields like the one in which we stood. “Over time you learn where you have the worst exposure to whatever it is that harms the bees,” Haefeker said.

He pulled out a frame to reveal a queen. Like an awkward commuter on the tube, she brushed up against every inhabitant near her as she made her way from one end of the frame to the other. The jostling has a purpose; it reassures the cavorting masses. “It’s the queen’s pheromones,” he explained. It makes them relaxed and productive. “The pheromones affect us beekeepers, too.” He says he plans to harness this anti-stress essence and build a kind of a bee-powered wellness centre on the two-hectare property. I pictured Munich’s pampered classes soaking up queen-bee pheromones in a lodge in the hills around Lake Starnberg. A moment later, Haefeker put the frame back, closed the lid, and surveyed his hives with satisfaction. He and Bruder then discussed what’s next.

Keeping bees safe from pesticides is labour-intensive and requires

specialist local knowledge. Bruder agreed to wake before dawn the following morning and pack up some of the hives, load them on to a trailer and drive the bees to higher ground. They had decided on a region in the foothills of the Alps, about an hour away, near the Wieskirche, an 18th-century church on the Unesco world heritage list. There would be fresh dandelion flowers up there. The bees would be further away from intensive agriculture, said Haefeker. “We’ve scouted out the locations.”

Meanwhile, it is possible that humankind has even more extreme designs on bees. Earlier this month, Haefeker sent me a message pointing to something called Insect Allies, a $45m research project sponsored by Darpa, the US Department of Defense’s military research department. It proposes using insects to carry immune-boosting mutations designed to protect crops from drought, flooding, pathogens and bioweapons. In essence, the visiting insects would modify the plant’s genetic makeup. A group of academics from universities in Germany and France declared the programme’s existence alarming, saying it turns the insects themselves into bioweapons.

Darpa does not say what kind of insects it plans to use, but Haefeker did not like the sound of it. “We need to keep an eye on this craziness,” his text read, “in case they want to use bees to transport their genetically modified viruses into crops.”

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• This main image in this article was changed on 16 October 2018 to replace a photograph of a hoverfly.

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