July 2019

Honey Bees: Species protection with genetic engineering

Honey bee colonies – superorganisms under stress

Industrial agriculture has put enormous strain on honey bee colonies. Amongst other things, honey bees are exposed to diverse toxins largely due to the spraying of crops. Other factors include a frequent lack of suitable flowering plants. Additionally, all of these factors can contribute to increasing parasitic infestation. In short: honey bee habitats have been changed so severely that the survival of honey bees is under threat. Investigations into honey bee colonies in Africa do indeed suggest that harmful environmental influences have an enormous effect on resistance to Varroa mites (Muli et al., 2014).

Honey bees are absolutely essential as pollinators, therefore, there are two possible strategies for solving this problem: either create (or rather recreate) an environment in which the honey bees can thrive or engineer an altogether new type of bee. The discussion on whether it makes sense to protect species protection in the future with genetic engineering has become much more intense with the availability of new genetic engineering techniques, such as CRISPR/Cas.

The DNA of honey bees was first decoded in 2006 (The Honey Bee Genome Sequencing Consortium, 2006). At the same time, detailed documentation of the interactions between the environment and the honey bee genome was compiled. As previous observations show, their food is decisive for whether the larvae turn into queen bees or worker bees; depending on specific proteins in their food, genes are turned on or off. This means that the queen bees can, even with the same DNA as the worker bees, not only lay 2000 eggs per day but also live ten times longer than normal honey bees. Food and environmental influences have further far-reaching effects on the worker bees: the less food there is available the faster they become adults. Moreover, it is the worker bees that decide, according to requirements, which larvae are fed with which food. In effect, the honey bee colony, gene regulation and the environment are all locked into one endless loop. It is the worker bees who orchestrate the whole biological program of the beehive, which can adapt flexibly to frequently changing outside influences without faltering. Altering the genome of the honey bees or changing their gene regulation will always mean that the whole honey bee colony is affected, not only the individual honey bees. But that is exactly what genetic engineers want to do by manipulating the genome of the honey bees with CRISPR. There are further additional risks for honey bees from the application of genetic engineering.

Threat to honey bees from the cultivation of genetically engineered plants?

Honey bee colonies forage over areas extending several kilometres, and thereby pollinate a broad range of plants. In this way they can, for example, spread pollen from genetically engineered plants. In Europe, this would mostly be a risk in relation to the cultivation of genetically engineered rapeseed if cultivation were to be allowed, or from seed losses alongside transport routes that may allow plants to spread into the environment. Rapeseed cultivation in Europe would have a huge potential for spreading (see for example Bauer-Panskus et al, 2013).

Honey bees also collect pollen from maize plants. Genetically engineered maize plants produce a so-called Bt insecticide. The Bt toxins produced by the plants are normally supposed to be harmless for honey bees. However, interactions between the Bt toxins and other stress factors, such as environmental toxins, pathogens or pesticides, can lead to a considerable intensification in the poisonous effect of the toxins (Then, 2010). This means that the Bt toxins could affect honey bees. Even experts who agree that Bt toxins produced by genetically engineered maize are not in general harmful to bees believe that the interactions between the toxins and other stress factors should be investigated (Duan et al., 2008).

Other possible co-factors could be, amongst others, environmental toxins and microrganisms in the intestines: Broderick et al. (2006 and 2009) found that specific intestinal bacteria play an important role in the toxicity of Bt toxins. Insects whose intestinal flora had been destroyed with antibiotics did not show such a distinct reaction to the toxin. Kramarz et al. (2007 and 2009) investigated snails and found that there were interactions between environmental toxins, such as cadmium, and Bt toxins which could lead to these toxins affecting organisms not normally thought to be affected. This could include honey bees: a study published in 2005 showed that the presence of intestinal parasites (nosema) can lead to honey bee colonies becoming more vulnerable to Bt toxins[1]. However, although these investigations were widely reported in the media[2], they were neither concluded nor published. Despite assertions to the contrary, these risks have never been fully clarified, partly because no further public funds were granted for this project. Despite other claims, until today these risks have still not been completely clarified. In 2016, studies with water fleas highlighted the crucial need for extensive research in this area (Bohn et al., 2016). *Daphnia* are a popular choice for scientists for use in the laboratory and are not thought to be sensitive in particular to Bt toxins. However, it has been shown that in interaction with other factors even they had a significantly increased mortality rate.
In another study, Bt toxins were found to adversely affect the learning ability of honey bees (Ramirez-Romero, et al., 2008). This could have enormous consequences for honey bee populations if this impaired their orientation whilst foraging.

Further, the pollen of herbicide-resistant genetically engineered plants (e.g. glyphosate) may contain residues and by-products of the herbicide with which the plants are sprayed. This could mean a additional stressors for honey bees. It appears that so far, there has been only insufficient investigation into this risk. Recent research shows that risks to bees are likely to be underestimated. For example, Herbert et al. (2014) show that pure glyphosate has negative effects on the learning ability of bees and thus possibly long-term negative consequences for honeybee colonies. Balbuena et al. (2015) found that honeybees receiving glyphosate containing feed needed more time to return to the hive. In addition, disturbances in learning of direct homing flights were measurable. According to this study, glyphosate therefore affects the cognitive abilities of bees needed to process spatial information for a successful return to the hive. Thus, negative consequences for honeybee navigation and the performance of the entire bee colony are likely.

[1] www.gen-ethisches-netzwerk.de/kleiner-parasit-grosse-wirkung
[2] www.spiegel.de/spiegel/print/d-50910321.html

Honey bees themselves are being genetically engineered
Researchers at the University of Duesseldorf showed that it is possible to genetically manipulate whole honey bee colonies. They genetically manipulated queen bees and found that the queen bees passed the artificial DNA on to the following generation with a high rate of success. According to the researchers, this would enable basic research and also pave the way for breeding genetically engineered honey bee colonies (Schulte et al., 2014).

New methods of genetic engineering, such as CRISPR-Cas, are also being used to experiment with the DNA of honey bees. Researchers in Japan want to use this DNA-scissor to block various honey bee genes in order to find out more about how they function (Kohno et al., 2016). Similar research is being carried out on wasp species; researchers are using CRISPR-Cas technology to genetically manipulate the eye colour of the wasp (Li et al., 2017).

A paper published in 2019 reports on how the development of honey bee queens can be investigated and influenced with the help of the ‘gene scissor’ CRISPR/Cas. Making honey bee colonies resistant to pesticides is mentioned as a possible application. In addition, a paper published in 2019 in South Korea, describes an attempt to make honey bees resistant to an insecticide. The insecticide was spinosad, which is toxic to honey bees. Whether the intervention was successful or not cannot be concluded from the publication (Lee, 2019).

Such approaches are often praised as a contribution to the protection of biodiversity. However, the problem of species extinction cannot be solved with genetic engineering. If we want to save honey bees, we need to protect their natural populations. Given the extremely complex biology of honey bees and their multitudinous interactions with the environment, any intervention in their genome would be irresponsible.

Influencing gene activity
Apart from the above, new biologically active substances known as miRNAs can now be synthesised and used to alter gene regulation and activity. If researchers find suitable genes in their experiments with genetically engineered bees, they can produce specific miRNAs which could, for example, block those specific genes. The miRNAs can be administered to the honey bees e.g. in their food.

The biologically active substances are further intended for use against Varroa mites that frequently infest honey bees. Beeologics is a company that has specialised in these applications and was bought up by Monsanto in 2011.[3] Monsanto has in the meantime increased its activities in this sector and filed patents on miRNA (WO201506681 and WO2016179180); this miRNA can be administered to the honey bees via feed and thereby be taken up by the parasites that have infested the honey bee colony. Once in the parasites, the biologically active substances will cause a change in gene regulation – in particular, in varroa mites – and they will die.

Monsanto clearly believes that it can extend its new arsenal of „bio-weaponry“. According to the patent, other parasite species can be dealt with in the same way e.g. ichneumon wasps, crustaceans, flies, fleas and lice.

Honey bees, wasps, bumblebees, as well as crabs, mites and fleas belong to the large arthropod group, all of which have many jointed legs or limbs. As described in the patent, each particular species of arthropod can be either eradicated or protected. Each species lives in close contact with

[3] www.croplife.com/crop-inputs/the-buzz-on-beeologics/

other species and in complex ecosystems. Again, according to the patent, the biologically active substances can affect those species which are not meant to be targeted.

Clearly, side effects on ecosystems, honey bees, or even the honey itself cannot be ruled out. The biologically active miRNAs are extremely varied and part of wholly diverse processes. Moreover, the structure can be altered by interacting with other elements of cell regulation so that the effects can also be different.

Plans to genetically engineer honey bees or other wild insects, or to manipulate them with biologically active substances using miRNA as a kind of insecticide, clearly pose an extreme risk to biodiversity.

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