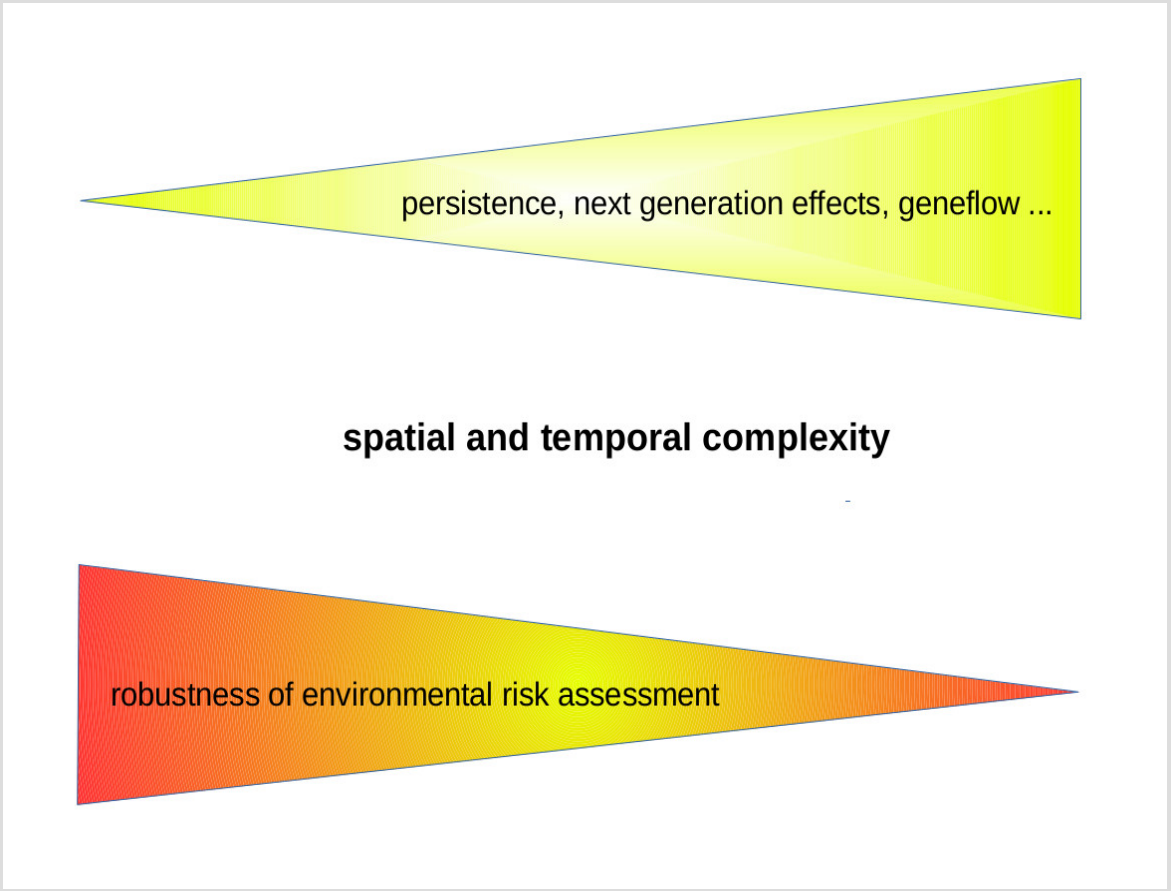
Tipping points in risk analysis of SPAGE and the case of genetically engineered olive flies

TEST BIOTECH
Testbiotech e. V.
Institut für unabhängige Folgenabschätzung in der Biotechnologie



Juni 2018
Dr. Christoph Then

www.testbiotech.org

www.genetip.de

GeneTip

The role of Testbiotech within GeneTip

The role of Testbiotech is to summarise the input from the stakeholders and the Work Packages 1 and 2. Within Work Package 3, Testbiotech will present recommendations for regulatory purposes.

This presentation represents the views of Testbiotech, but not necessarily the opinion of the GeneTip consortium. The presentation provides initial results which will need further discussion.

The example: GE olive flies developed by Oxitec

The GE (genetically engineered) olive flies developed by Oxitec are based on so-called RIDL-technology („release of insects carrying a dominant lethal genetic system"). The effects are sex-specific: Male transgenic flies will mate with the native female flies and thereby introduce their artificial genes into the native population. While the male offspring will survive and persist for a longer period of time, the female offspring will die at the larval stage. As a result, the population of olive flies will supposedly decrease. The GE olive flies do not inherit a gene drive.

Overview

- We develop a hypothesis on new challenges in risk analysis related to SPAGE
- We explore our hypothesis against existing experience with GE plants and EFSA guidance on GM insects (EFSA 2013)
- We test our findings in risk analysis of the GE olive flies
- We present preliminary conclusions

What is new in the concept of SPAGE & GE olive flies?

The concept of SPAGE (Self Propagation of Artificial Genetic Elemens) essentially implies the persistence of genetically engineered individuals in native populations, or even replacements of wildtypes by genetically engineered genotypes.

What is new in the concept of SPAGE & GE olive flies?

As yet, risk assessment is mostly applicable to populations derived from breeding (plant varieties) that have reduced genetic diversity due to selection (breeding); these are not meant to reproduce spontaneously, but be propagated by farmers or breeders.

Wild populations very often inherit a broad spectrum of heterogeneous genetic backgrounds. SPAGE will introgress this broad range of genetic backgrounds without additional controls in place.

What is new in the concept of SPAGE & GE olive flies?

As yet, GE organisms (plants) are meant to be cultivated in agricultural land and most of them are only present for one growing period.

Insect populations with SPAGE might persist for several years and move to a wider range of environments compared to crop plants.

Does SPAGE cause new challenges in risk assessment?

Our hypothesis is YES. With the introduction of SPAGE, we expect a substantial increase in spatial and temporal complexity and a decrease in the robustness of risk analysis.

Exploration of our hypothesis against existing experience with GE organisms

Are there supporting indications or evidence that

- a higher range of genetic diversity within the target populations increases uncertainty regarding genetic stability in the offspring generations?
- the process of spontaneous self-reproduction of GE organisms increases uncertainty regarding genetic stability in the offspring generations?
- a wider range of environmental stressors can increase the likelihood of unintended effects in GE organisms?
- interaction with a more complex environment increases the likelihood of hazardous interaction with non-target organisms?

Exploration of our hypothesis against existing experience with GE organisms

- Unintended changes in the characteristics of the GE organism can be triggered by changing environmental conditions.
- Unintended effects can emerge from interaction with the genetic backgrounds.
- Next generations of GE organisms can show effects that were not observed or intended in the original event.
- Changing environments can impact the expression of the transgenes.

Thus, we consider existing experience to be in line with our hypothesis.

detailed references upon request

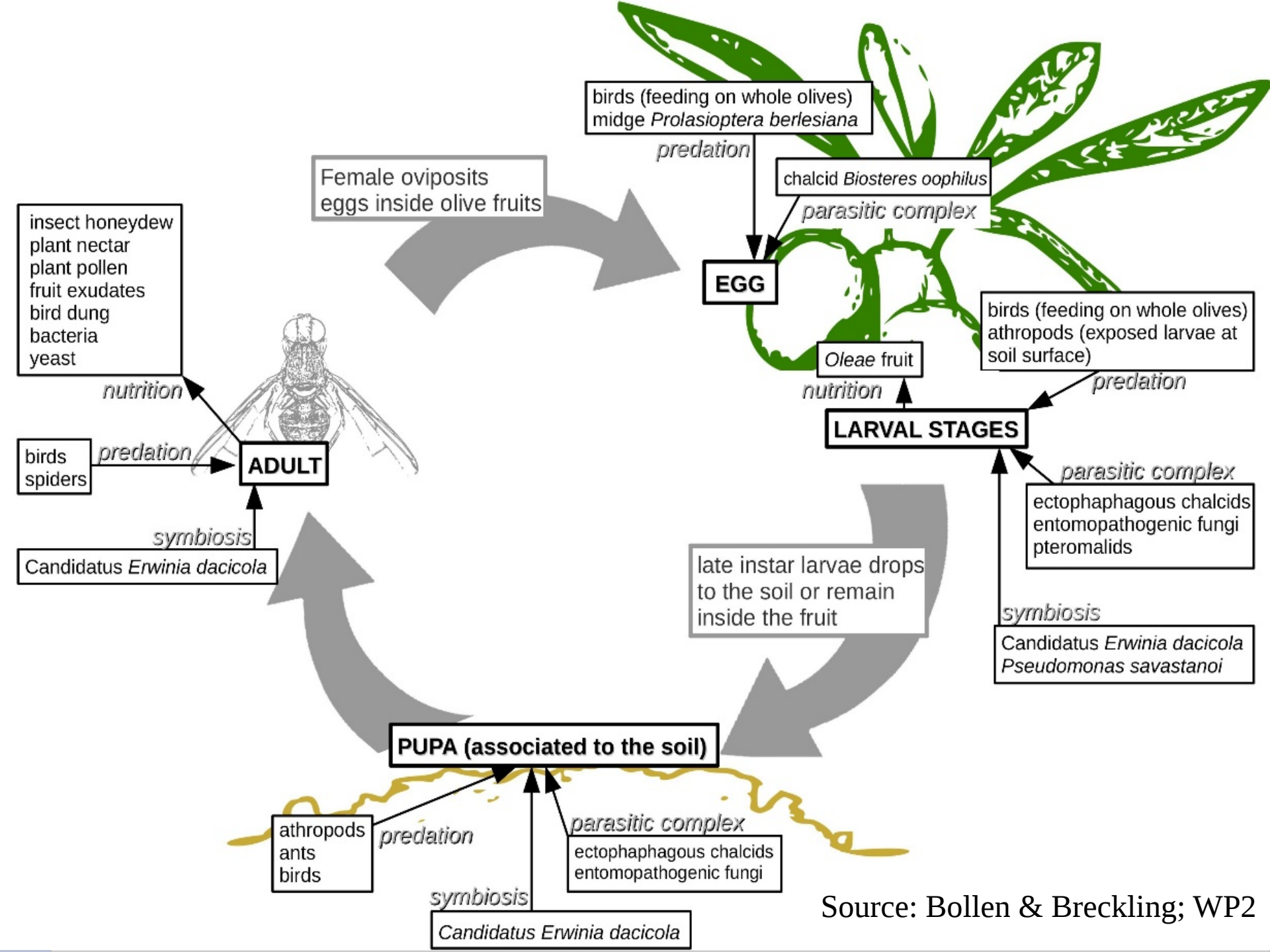
Exploration of our hypothesis against EFSA guidance for environmental risk assessment of GE insects

EFSA (2013) assumes that risk assessment of GE insects can indeed lead to higher levels of uncertainty. Relevant issues in regard to target organisms include genetic background, whole life cycle and spatial temporal complexity. Relevant issues in regard to non-target organisms (and the environment) include the ecological functions of specific species and their complex biotic or abiotic interactions.

Furthermore, EFSA has identified uncertainties and limitations in current methodology of risk assessment.

We consider EFSA guidance to be in line with our hypothesis.

detailed references upon request



Source: Bollen & Breckling; WP2

Case study: risk analysis of GE olive flies (I)

> how can genetic stability be preserved in following generations?

once released, the spread of the SPAGE in natural populations will lead to emergence of next generations without human intervention. Next generation effects might occur without being noticed.

> what is known about genetic diversity in natural populations?

high degree of genetic diversity in natural populations exists, but can not be tested in the lab.

Case study: risk analysis of GE olive flies (II)

> What is known about the impact of population dynamics and life cycle aspects?

Bottlenecks in the population dynamics due to wintery season might result in inbreeding and changes in genetic variability. Bottlenecks can have significant impact on tipping points within the populations.

Case study: risk analysis of GE olive flies (III)

> what is known about reaction to environmental stressors?

The olive flies are exposed to a wide range of seasonal weather conditions which influence their life cycles. However, no data are available on gene (epigenome) x environment interactions of SPAGE.

> what is known about interaction with the microbiome?

There are specific and symbiotic microbes associated with the olive flies, but no data are available on about gene x microbiome interactions of SPAGE.

Case study: risk analysis of GE olive flies (IV)

> How can the receiving environment be characterised and confined?

Under specific conditions, such as high population densities, maximum dispersal distances for olive flies reported in literature range from 4000 to 5000 m. Furthermore, molecular analyses indicate a high level of gene flow among the Mediterranean populations.

Case study: risk analysis of GE olive flies (V)

> What is known about interrelations with other species?

There are complex interactions with other species such as birds, spider, ants, chalcid wasps and symbiotic bacteria. The interrelationships include grazing, predation and symbiosis. The interrelations vary greatly throughout the fly's life history and different developmental stages (egg, larva, pupa, adult).

How to deal with uncertainties and limits of knowledge?

We suggest the limits of knowledge be made more explicit in order to make the risk analysis sufficiently robust and to strengthen the precautionary principle.

For the sake of clarity and transparency we suggest developing cut-off criteria for GE organisms.

These criteria might have some similarity to those which are already established in the regulation of Chemicals (REACH). However, there will be also some differences.

What are the commonalities and differences to cut-off criteria in current EU Regulation 1107/2009 (REACH)?

According to REACH, no registration may be granted if a substance falls into one of three criteria: persistent organic pollutant; persistent bio accumulative, toxic; or very persistent, very bio accumulative.

Thus long-term effects are important, similarly to the situation in the risk analysis of GE organisms which can persist and propagate in the environment.

What are the commonalities and differences to cut-off criteria in current EU Regulation 1107/2009 (REACH)?

However, unlike chemicals, biological effects very often cannot be so well defined at the level of molecular data (such as the DNA). Therefore, for the risk analysis of GE organisms it is important to make the limits of knowledge more explicit.

Proposed cut-off criterion for GE risk analysis

In conclusion, we consider spatial and temporal controllability is a criterion that can be defined to a necessary degree and could therefore be used as cut-off criterion in GE risk assessment.

However, there might be other or even better criteria. In any case, further discussion is needed.

Further reasons why the risk manager might apply spatio-temporal controllability as cut-off criterion

Spontaneous transboundary movements: if genetically engineered organisms can spontaneously cross borders, their release can be considered to be a violation of the rights under Cartagena Protocol / CBD.

No possibility for co-existence: if coexistence with relevant standards for food production, such as organic agriculture, is not possible, the release of SPAGE would infringe consumers' choice and the livelihood of organic producers.

Summary

With regard of existing uncertainties and limits of knowledge that can be identified being involved with SPAGE, Testbiotech substantiated the necessity for a further discourse on cut-off criteria within EU GMO risk analysis.