Ecological Vulnerability Analysis for Gene Drives

A prospective assessment

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Gene drives

Molecular genome editing tools able to bias normal Mendelian inheritance (50:50)

- Ability to be inherited over generational time at increased frequencies despite lowering the organisms' fitness (Champer et al., 2016)

Modification or suppression drives

- Modify, insert and/or delete genes (Burt, 2003)

A desired gene will be transmitted in the whole population within a few generations

Applied to sexually reproducing organisms with short generation time (insects, rodents)

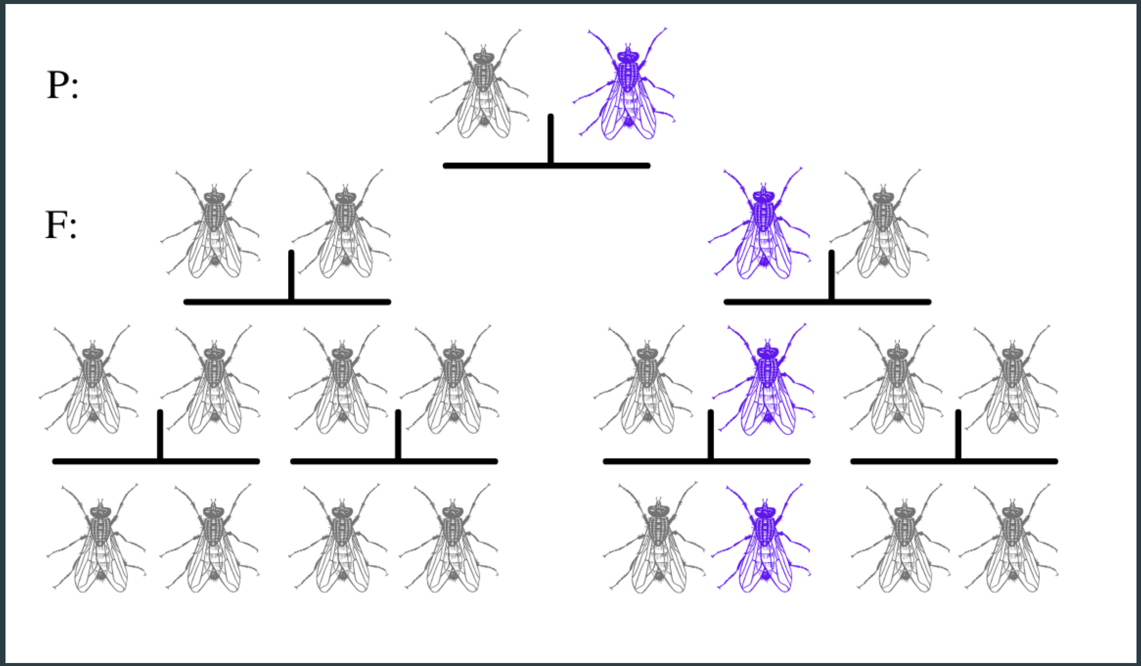


Illustration of a Mendelian inheritance, the offspring (F) have a 50% chance to inherit a copy of the gene from the parents (P)

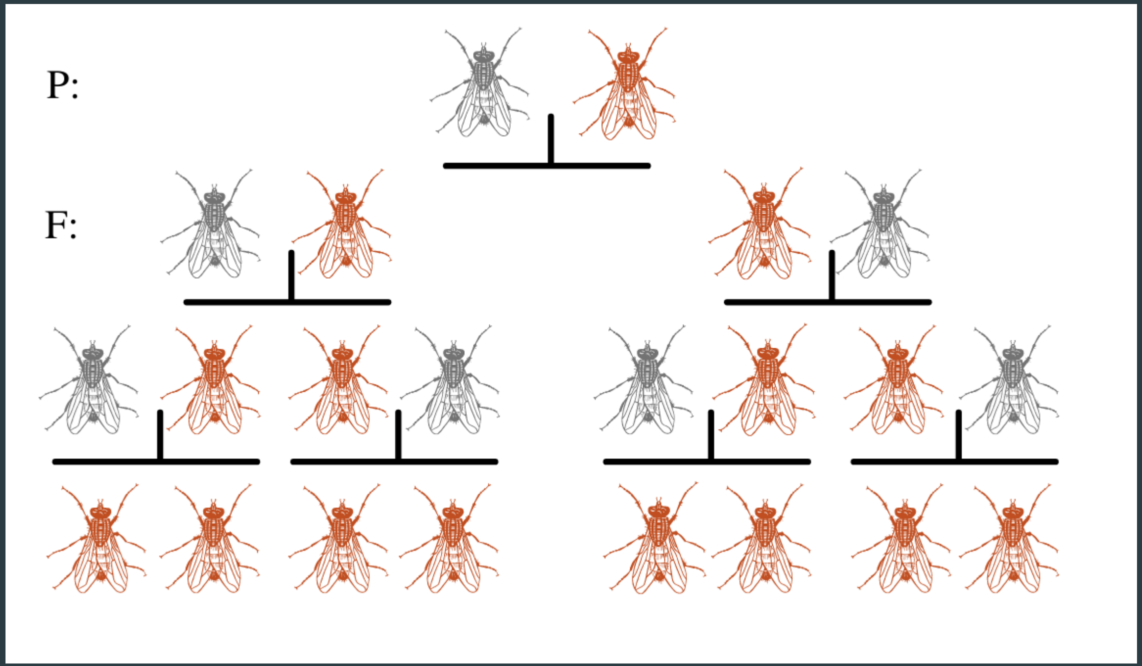


Illustration of super-Mendelian inheritance where the offspring (F) have a 100% chance to inherit a copy of the gene from the parents (P)

Use of gene drives

Public health

- Control/eradicate diseases by altering the organisms that carry or cause the disease

Conservation

- Control/eradicate invasive species

Agriculture

- Control/eradicate organisms that damage crops

Research

- Alter organisms to research the effects of gene drives

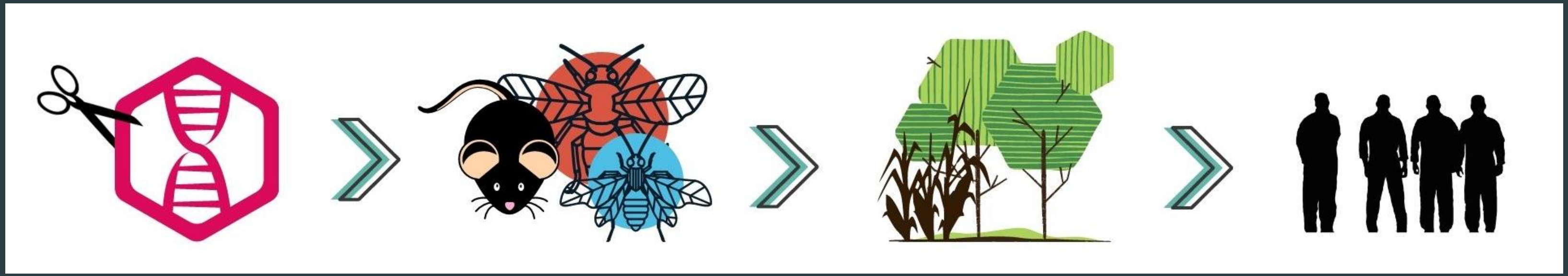
Challenges of the application

Depth of intervention (power and range of the technology)

- Residence time (perseverance and invasiveness)
  - designed to spread
- Confinement- geographical and species
  - Locally confined and species specific drives under development BUT uncertain, horizontal gene transfer
- Step-by-step release
  - Field trial could be irreversible
- Recall, rescue drives

Uncertainty

- Knowledge gaps
- Delayed effects
- Mutations, unforeseen recombination
- Rare mating events
- Horizontal gene transfer
- Behavioural change



Gene drives in Risk Assessment

- In the EU gene drives fall under the GMO Directives 2001/18/EC, 2015/412
- Approval authority EFSA- November 2020 Opinion report on adequacy and sufficiency for EFSA regulations on insects engineered with gene drives

Summary

The European Commission has requested the European Food Safety Authority (EFSA) to assess, through a problem formulation exercise, whether: (1) the deliberate release of genetically modified organisms (GMOs) containing engineered gene drives (termed hereafter as gene drive modified organisms [GDMOs]) could pose risks and potential novel hazards to human/animal health and the environment, considering relevant comparators; (2) the scientific considerations/requirements given in its previously published guidelines for the risk assessment of genetically modified animals (GMAs) (EFSA, 2012, 2013) are adequate and sufficient for GDMOs; and (3) there is a need for updated guidance in relation to previous documents (EFSA, 2012, 2013). Under this mandate, EFSA was not requested to develop risk assessment guidelines for GDMOs.

Fragment of the summary of EFSA Panel on GMOs 2020. Adequacy and sufficiency evaluation of existing EFSA guidelines for the molecular characterisation, environmental risk assessment and post-market environmental monitoring of genetically modified insects containing engineered gene drives

Prospective assessment

Ecological Vulnerability analysis

Current regulation provides scope for a broader range of prospective analysis

Broaden the scope of the classical risk assessment to include socioeconomic, ethic and legal aspects into the research when considering the effects of a new technology

Given the depth of intervention, there is a need to understand vulnerabilities across systems

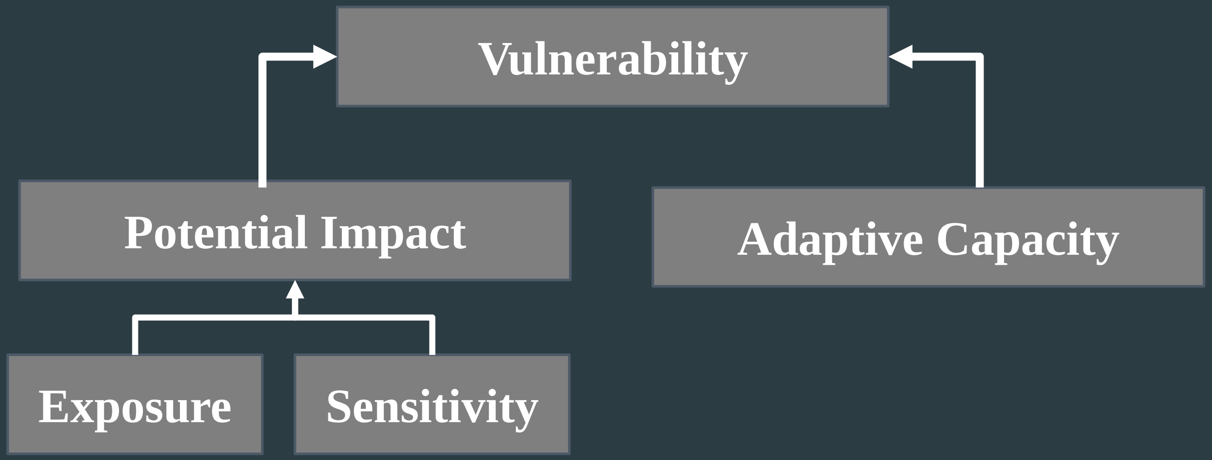
Ecological Vulnerability Analysis (eVA)

A priori analysis to determine the ecosystem's weaknesses and it's adaptive capacity

It is a function of exposure, sensitivity and adaptive capacity

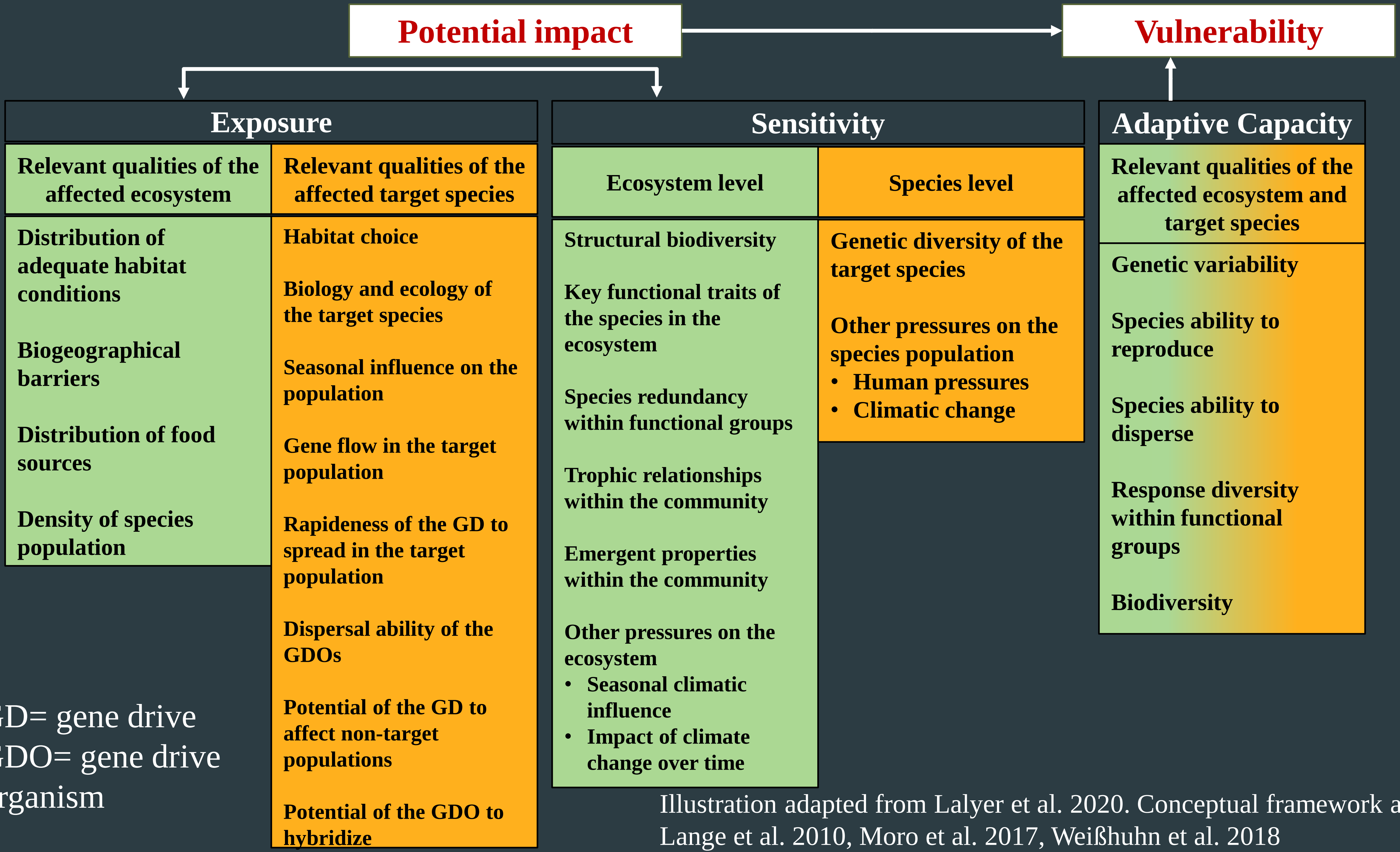
The analysis of a vulnerable ecosystem requires investigations at different levels:

- *species characterization,*
- *species' genetics*
- *species-environment interactions,*
- *abiotic elements*
- *landscape*



Elements of eVA. Adapted after Adger, 2006; De Lange et al., 2010; Gößling-Reisemann et al., 2013; IPCC, 2007, p. 27

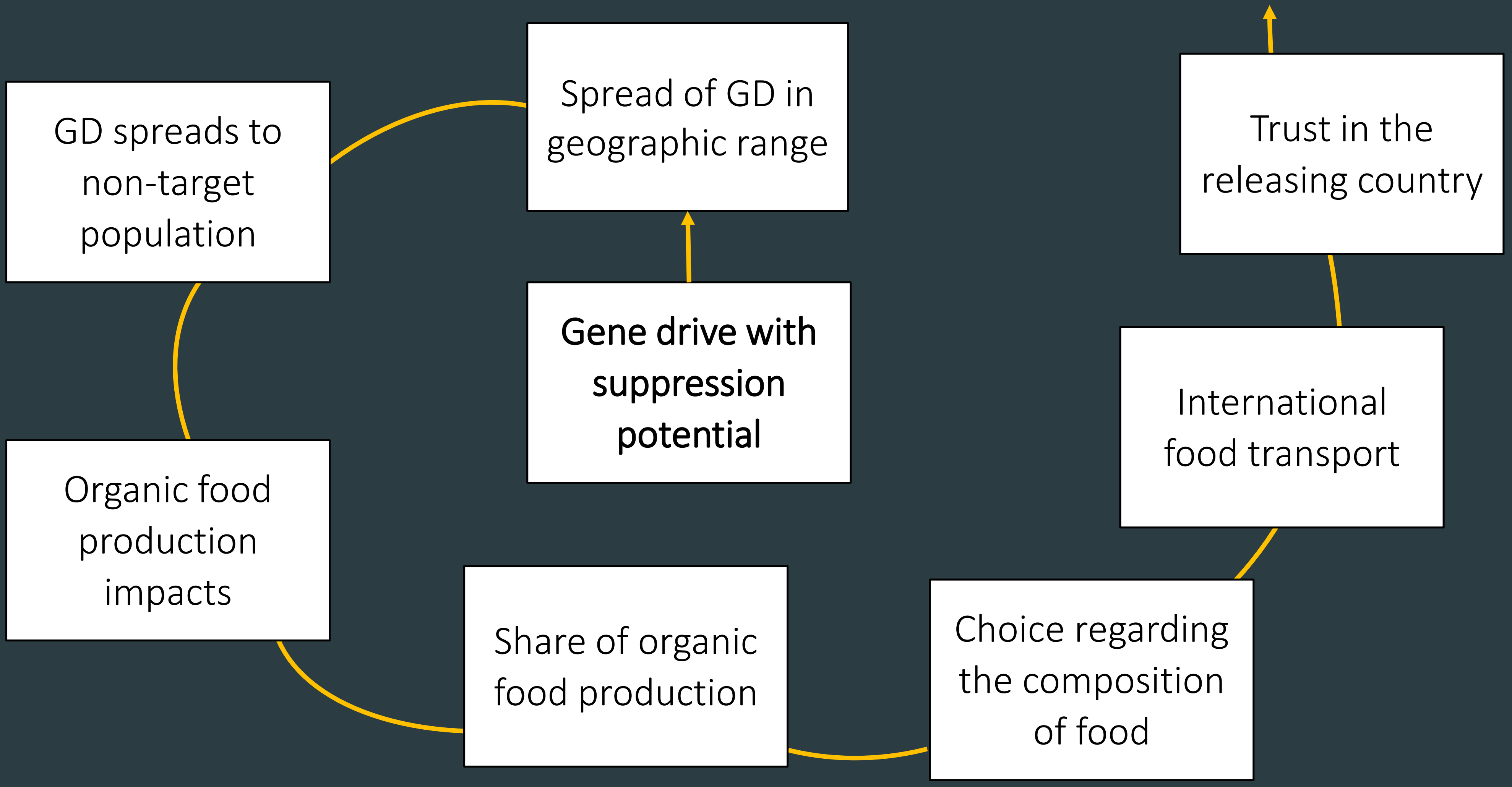
System-based approach



GD= gene drive
GDO= gene drive organism

Illustration adapted from Lalyer et al. 2020. Conceptual framework after de Lange et al. 2010, Moro et al. 2017, Weißhuhn et al. 2018

In what ways can gene drives become socio-economically relevant?



Case study

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Drosophila suzukii **(Matsumura, 1931)**

- fruit fly native to East Asia
- invasive pest of stone and berry fruits
- gene drive was recently developed for it by Buchman et al. (2018)
- closely related species: *D. pulchrella* , *D. subpulchrella* (possible competitors)
- Specialized parasitoids: the ”suzukii-specialised” type of *Ganaspis xanthopoda*, *Asobara sp*. TK1 type

Suppression of non-target (native) population of *Drosophila suzukii*

Take home message

- Gene drives have potential novel negative impacts at the ecosystem and societal level
- There is a need for a system-based and prospective approach
- As early as possible in the stage of the technology
- Ecological vulnerability analysis can be a complimentary approach to:
    - Take into account the exposure, sensitivity and adaptive capacity of an ecosystem
    - Uncover knowledge gaps
    - understand the susceptibility of an ecosystem to potentially unintended and irreversible harm
    - Reveal the potential cascading effects to the societal level

Thank you for your attention

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