Universität Bremen

TEST BIOTECH
Testbiotech e. V.
Institute for Independent Impact Assessment in Biotechnology

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Gene Tip

Modelling of Gene Drives to identify bottlenecks and tipping points

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Different Population Dynamics Model Approaches

- Stock-flow model
  - Olive fly life stages
- Differential/Recurrence equation-based models
  - Iterative gene drive inheritance and invasiveness
  - Olive fly population dynamics with gene drive
  - Olive flies with gene drive and bottlenecks
- Individual-based model
- Olive fly life stages with gene drive

Model Organism: Olive Fly (*Bactrocera oleae)*

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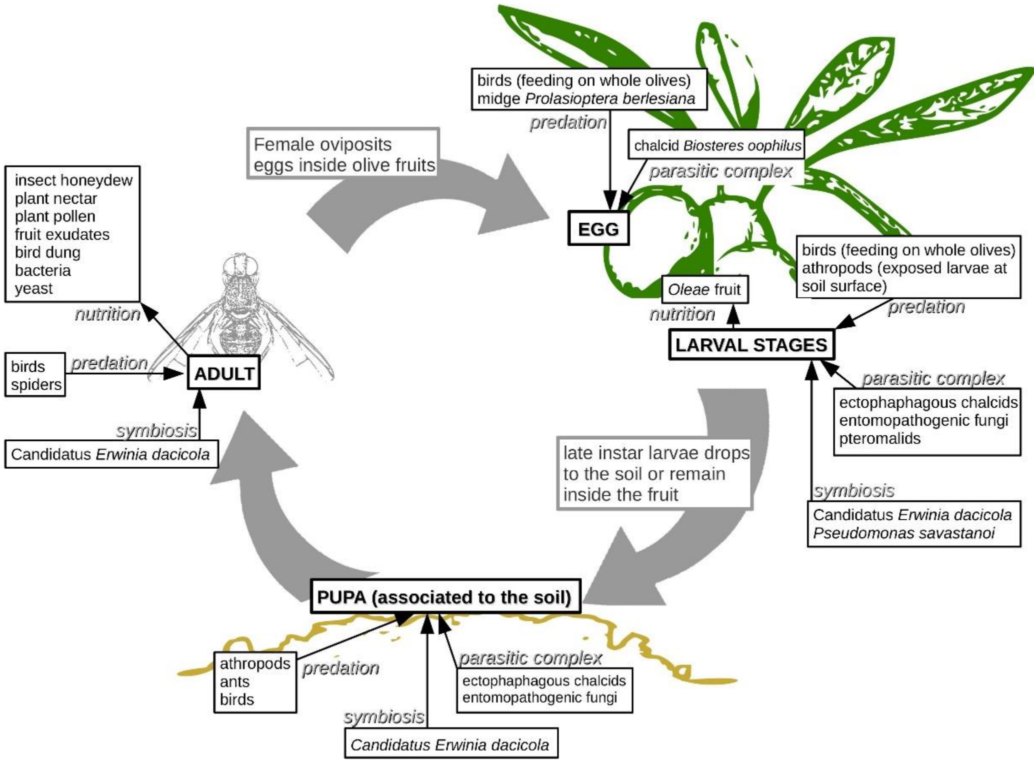
- Pest in the olive production
- Female lays 250-400 eggs
- 1 Larva per olive
- Monodietary larval stage
- 2-4 Generations per year
- Net damage of $ 3 billion
- in a $ 9 billion industry



Stock-Flow Model Approach - Introduction

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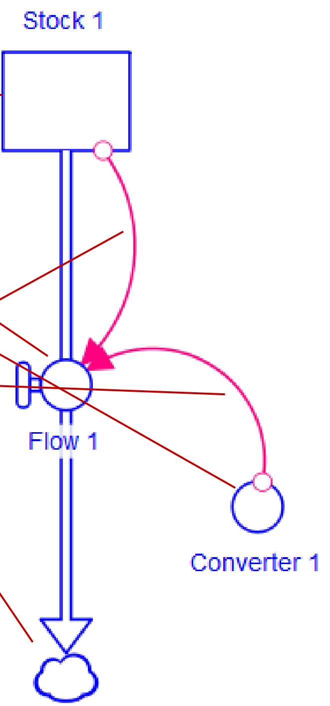
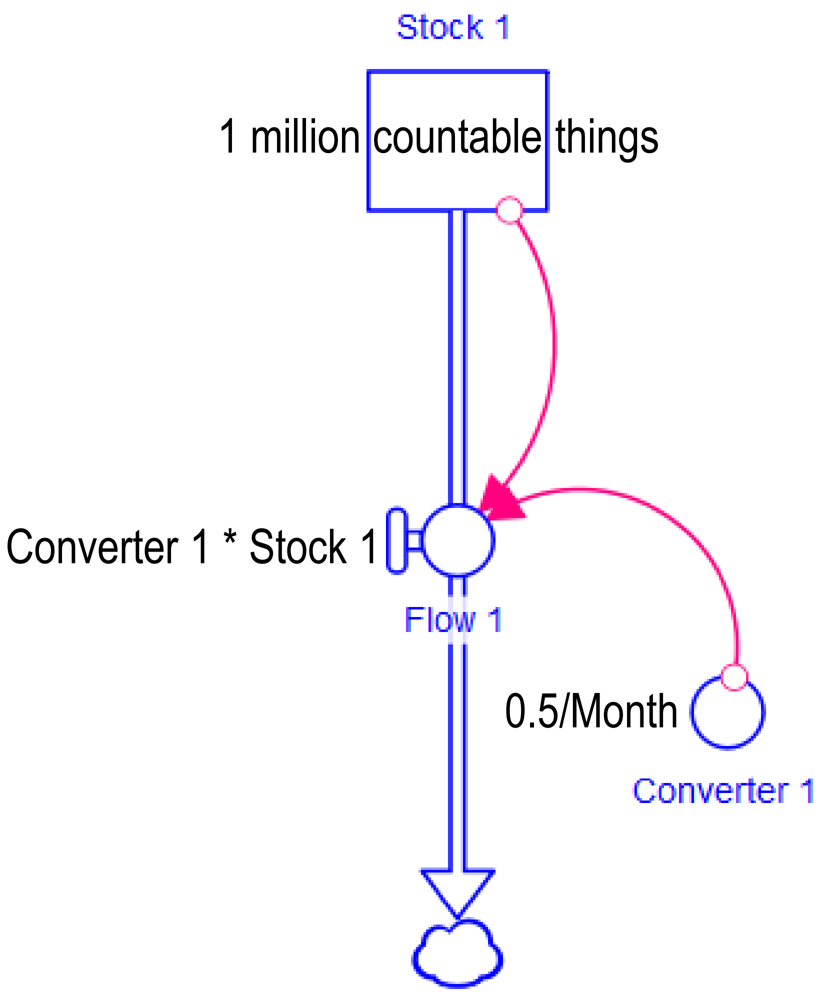
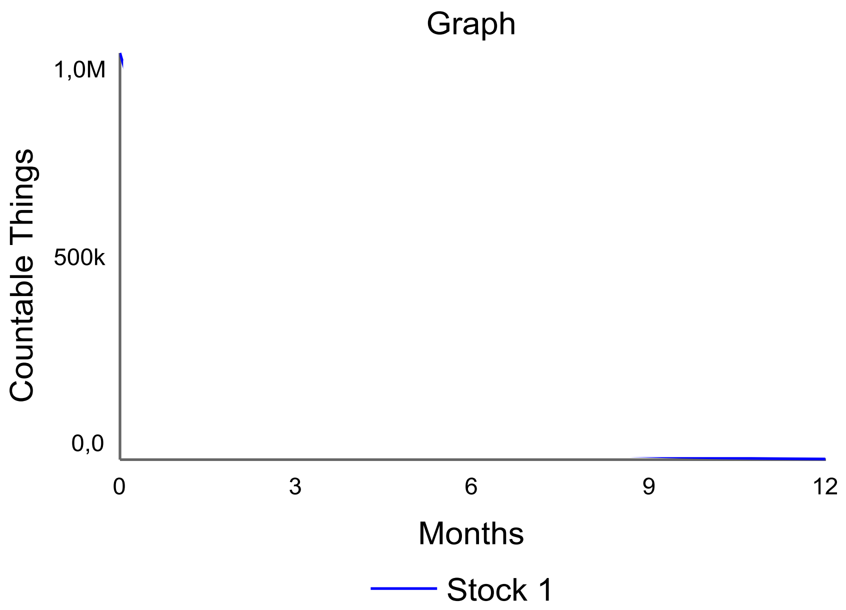
- Often used in economics
- Suitable for classic population dynamics

- Stocks
- Flows
- Operators
- Connectors
- Source/Sink



Stock-Flow Model Approach - Example





Deterministic Invasiveness Study – Gene Drive Inheritance

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- Invasiveness of a gene drive technique depends on its:
  - Inheritance scheme
  - Fitness penalty
  - Population percentage at release

Example: Inheritance scheme of Medea gene drive

+/+♀	+/+	M/+	M/M
+/+♂	1	0	0
M/+♂	0.5	0.5	0
M/M♂	0	1	0

M/+♀	+/+	M/+	M/M
+/+♂	0	0.5	0
M/+♂	0	0.5	0.25
M/M♂	0	0.5	0.5

M/M♀	+/+	M/+	M/M
+/+♂	0	1	0
M/+♂	0	0.5	0.5
M/M♂	0	0	1

maternal genotype, paternal genotype, offspring genotype

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Example: Inheritance scheme of Medea gene drive

+/+♀	+/+	M/+	M/M
+/+♂	1	0	0
M/+♂	0.5	0.413	0
M/M♂	0	0.826	0

M/+♀	+/+	M/+	M/M
+/+♂	0	0.413	0
M/+♂	0	0.413	0.2065
M/M♂	0	0.413	0.413

M/M♀	+/+	M/+	M/M
+/+♂	0	0.826	0
M/+♂	0	0.413	0.413
M/M♂	0	0	0.826

maternal genotype, paternal genotype, offspring genotype

- Fitness penalty 17.4%

Deterministic Approach - Olive Fly Population with Gene Drive

Model assumptions:

<u>Population:</u>

- Exponential growth with environmental capacity limit
- Exponential decline
- Equal preference for wildtype and gene drive males
- Sex ratio 1:1

<u>Gene drive:</u>

- If one partner carries the gene drive, all offspring inherit it
- Males carrying a gene drive have fertile male offspring.
- Females carrying gene drive die

Olive Fly Population Dynamics with Gene Drive - Equations

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Wildtype population

FF = 0.1 … 0.9

$$\frac{dW}{dt} = r * W * \frac{0.5\,W}{0.5\,W + Mg} * \frac{K - (W + Mg)}{K} - mf * FF * W$$

Fitness factor

Exp. growth

Share of wildtype/gene drive males

Limiting environment capacity

Exponential decline

Gene drive males

$$\frac{dMg}{dt} = r * W * \frac{Mg}{0.5\,W + Mg} * \frac{K - (W + Mg)}{K} - mf * Mg$$

r = 0.5

K = 2000

mf = 0.1

Stochastic Model Approach - Olive flies with gene drive and bottlenecks

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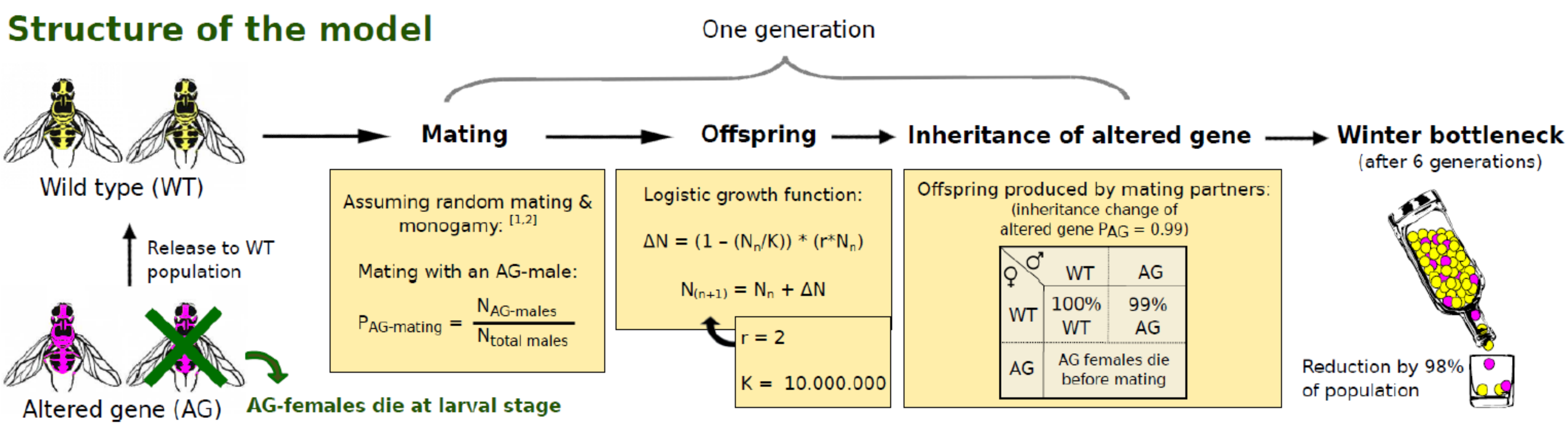
- Olive fruit fly population with a gene drive and bottlenecks



- Same gene drive as before
- Logistic growth (r = 2; K = $10^{7)}$
- 98% of population dies during winter bottlenecks every 6 generations

Stochastic Model Approach - Olive flies with gene drive

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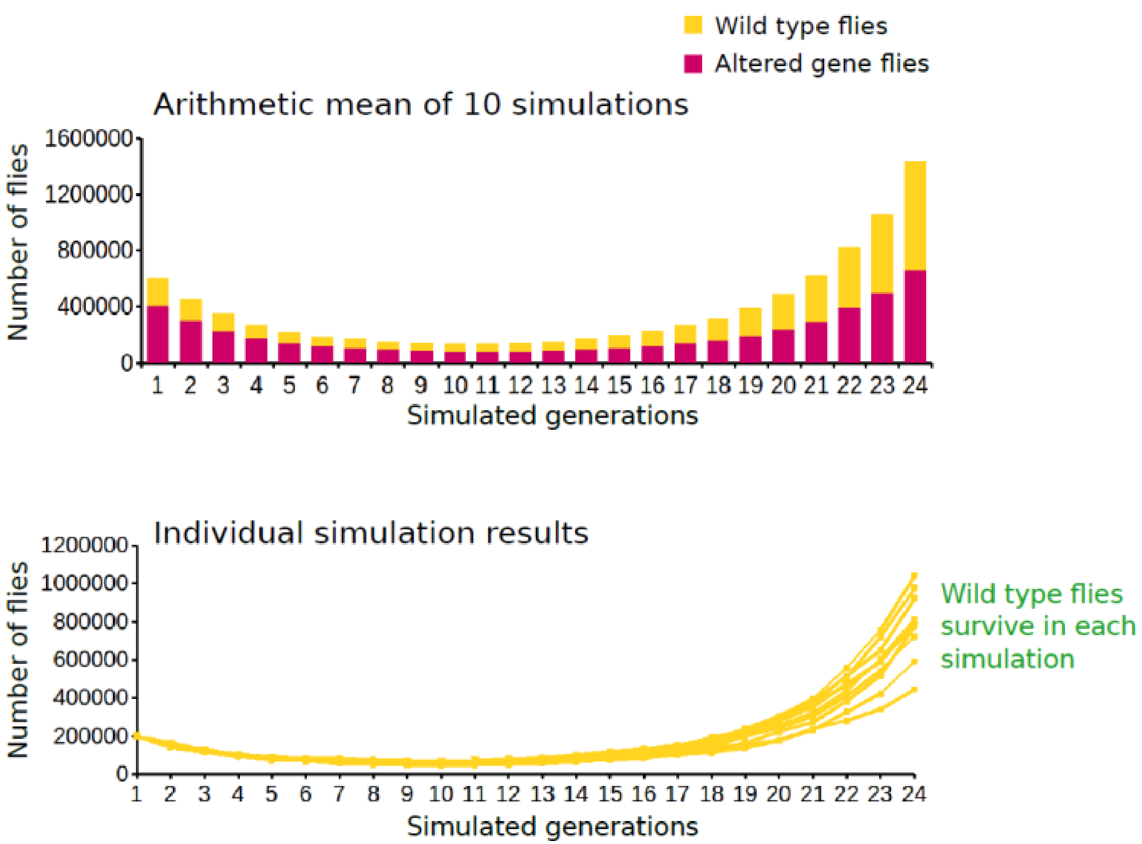
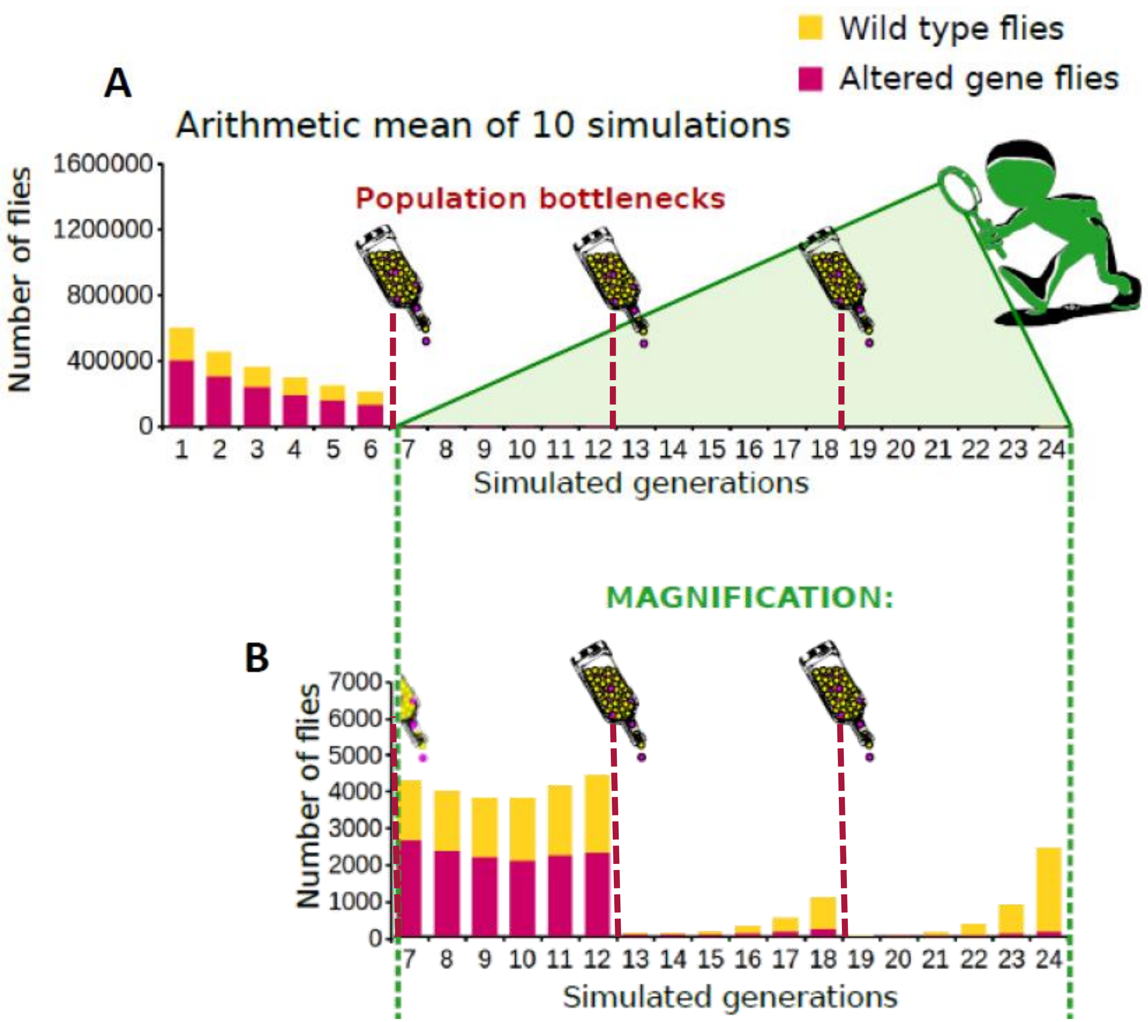
- Population without bottlenecks
- Release ratio 2:1
- WT sex ratio 1:1
- WT persists in each simulation



Stochastic Model Approach - Olive flies with gene drive and bottlenecks

- 98% of population dies during bottlenecks every 6 generations
- Release ratio 2:1
- 600k total population



Stochastic Model Approach - Olive flies with gene drive and bottlenecks

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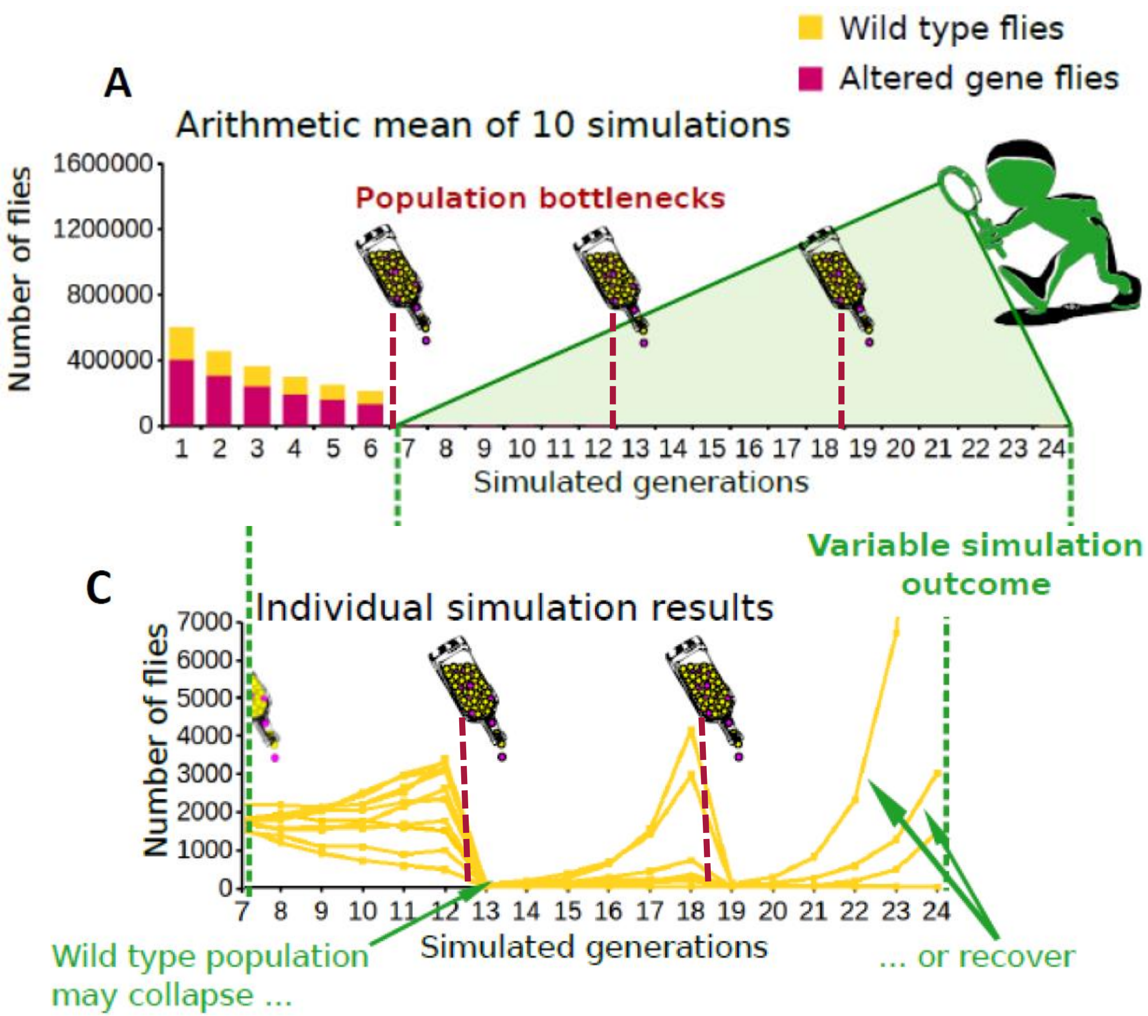
- Winter bottlenecks enhance the variability of the simulation outcome
- Ecological processes play an important role for the propagation of altered genes in natural populations



Individual-based Model – Prototypic description of individual flies

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- Process Class Olive Fly, Begin
  - Variables

    age, location, biomass, …
  - Activity procedures

    movement, mating, reproduction, …
  - Life Loop

    Execution of activity procedures according to current individual state and state of perceived environment, updating characterizing variables

    and possibly external (environmental) states
- End of Olive Fly

Individual-based Model – Class Structure

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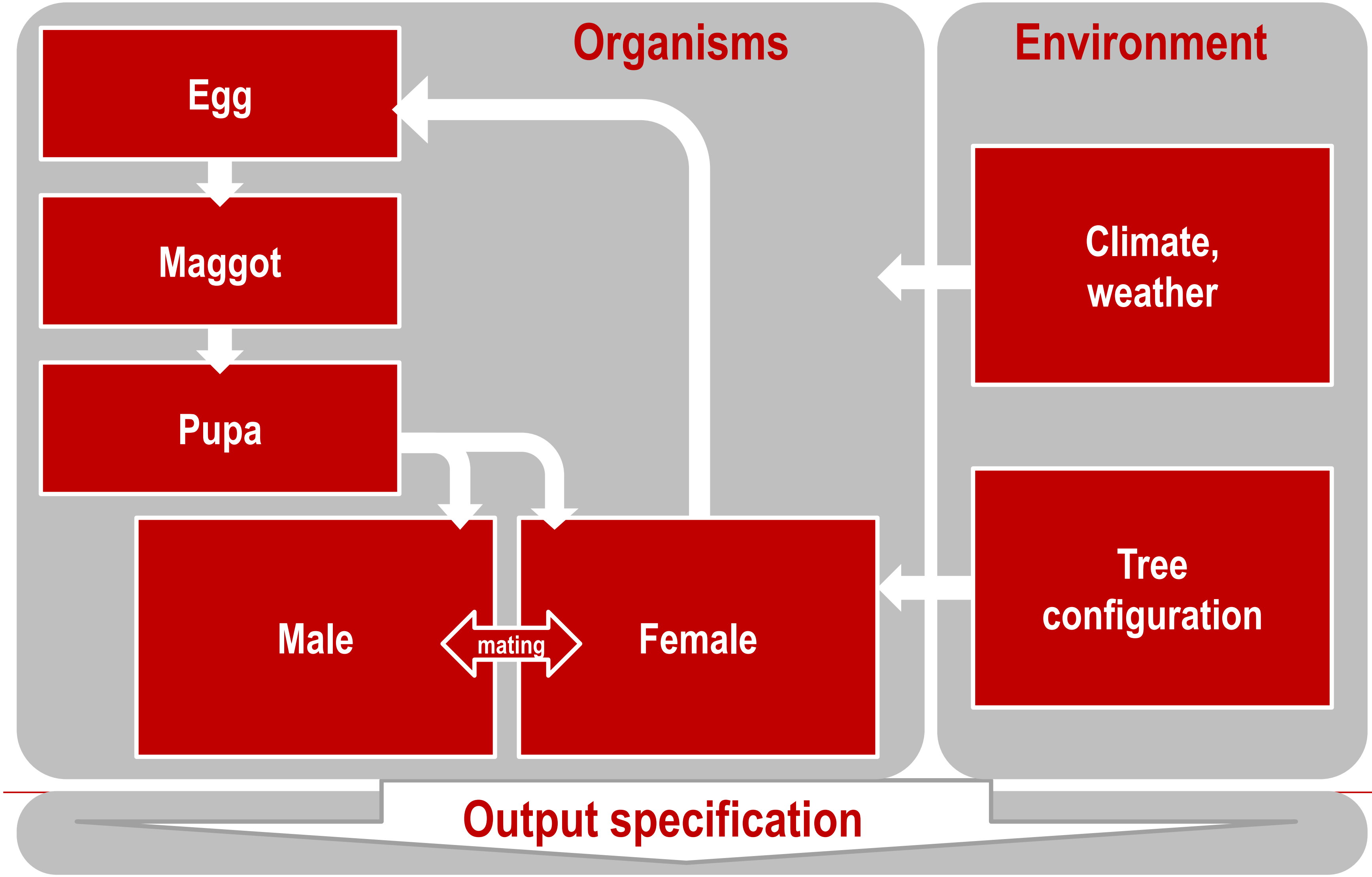

Individual-based Model – Test Model Assumptions

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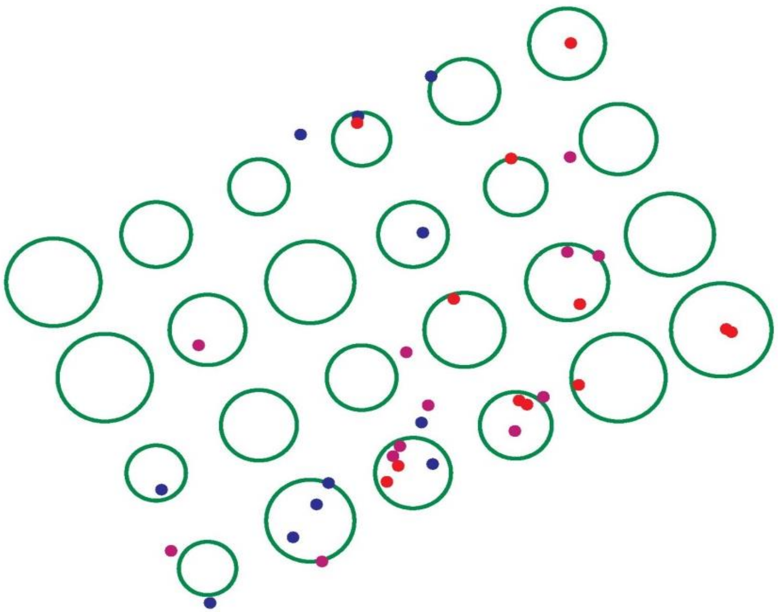

Initial setting

Initial conditions:

- 24 “trees”
- 10 “ WT females”
- 10 “WT males”
- 10 “gene drive males”

Fly ontogeny:

- 5 days egg development
- 5 days larval development
- 5 days pupa stage
- 18 days adult lifetime

Summary

- Models may give insights into various aspects of gene drives and population dynamics.
- Models are simplifications of complex processes.
- Each model has its focal points and does not represent reality
- Models facilitate analyses and implications of what was built into them.
- Therefore, we approached the topic from various sides, focusing on different key aspects.
- Nevertheless, models allow insights into complex dynamic processes.
- They help to discover emergent properties that would remain undisclosed otherwise.

Thank you!

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Let's discuss
about that!