

Evolution of biopesticide resistance with agent-based modelling in the resevol package

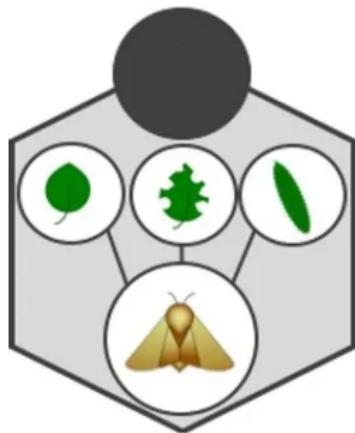
Brad Duthie

https://bradduthie.github.io/talks/BCB_talk.pdf

Pesticide resistance evolution

Pesticide resistance evolution

Impact on agriculture



- ▶ Resistance wicked & widespread¹
- ▶ Obstacle to food security²

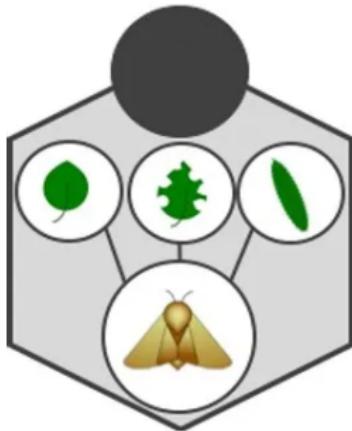
¹Gould et al. 2018. *Ecol. Appl.* 13:1791-1805.

²Bradshaw et al. 2016. *Nat. Commun.* 7:12986.

³Carroll et al. 2014. *Science* 346:1245993.

⁴Saikai et al. 2021. *Pest Manag. Sci.* 77:273-284.

Pesticide resistance evolution



Impact on agriculture

- ▶ Resistance wicked & widespread¹
- ▶ Obstacle to food security²

Manage resistance evolution

- ▶ Weaken selection for resistance³
- ▶ Varying pesticide application⁴

¹Gould et al. 2018. *Ecol. Appl.* 13:1791-1805.

²Bradshaw et al. 2016. *Nat. Commun.* 7:12986.

³Carroll et al. 2014. *Science* 346:1245993.

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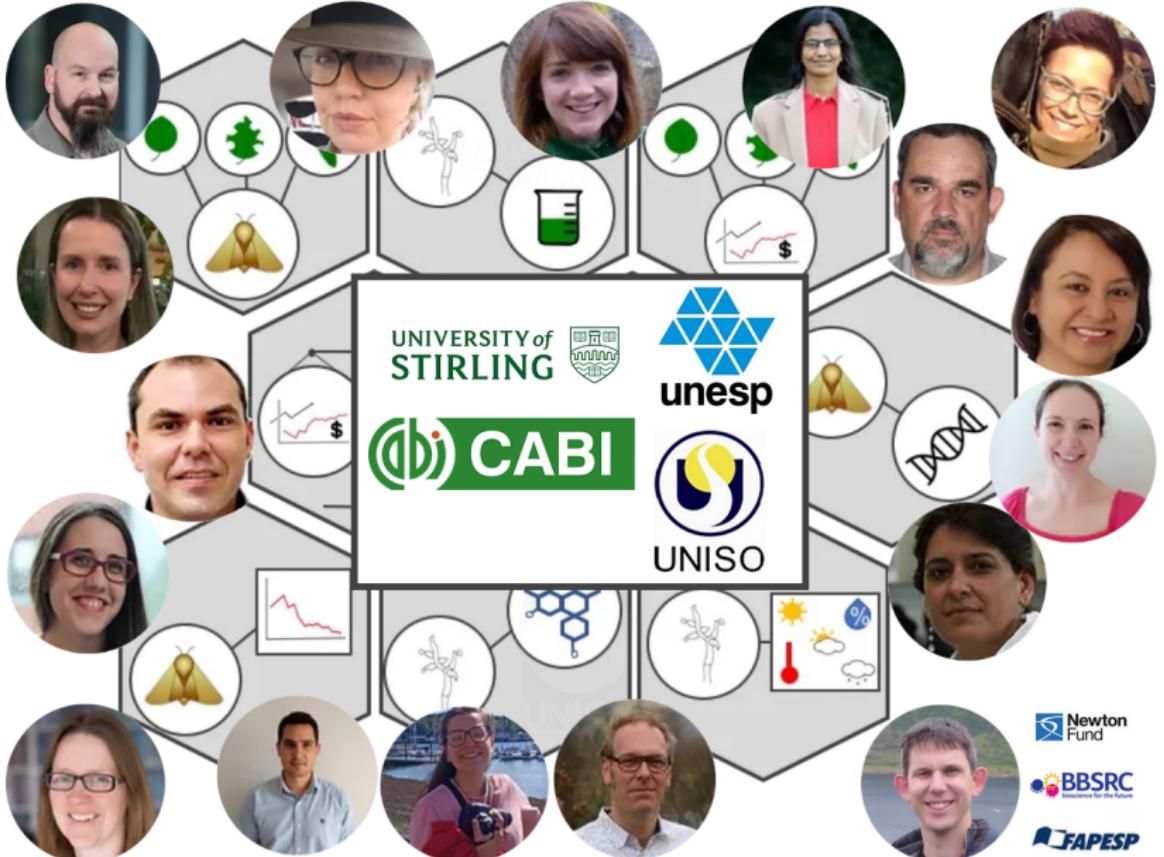




Newton Fund

BBSRC
Innovation for the Future

FAPESP

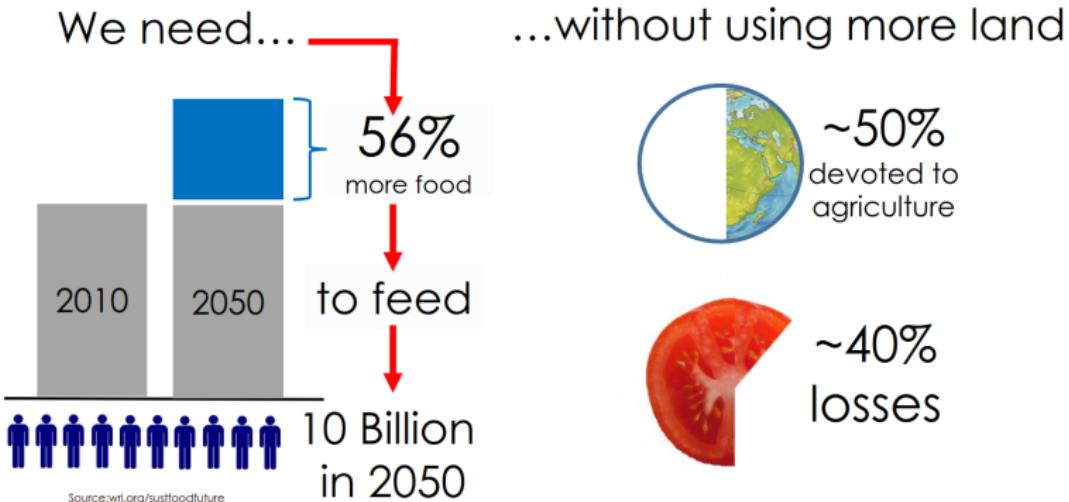


Newton Fund

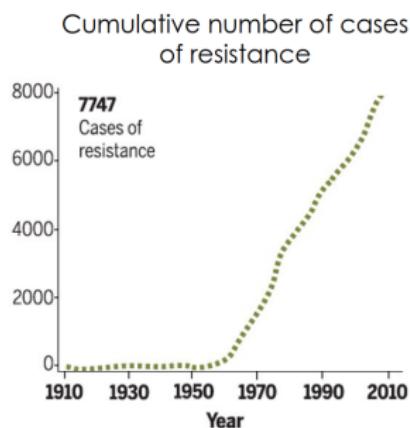
BBSRC
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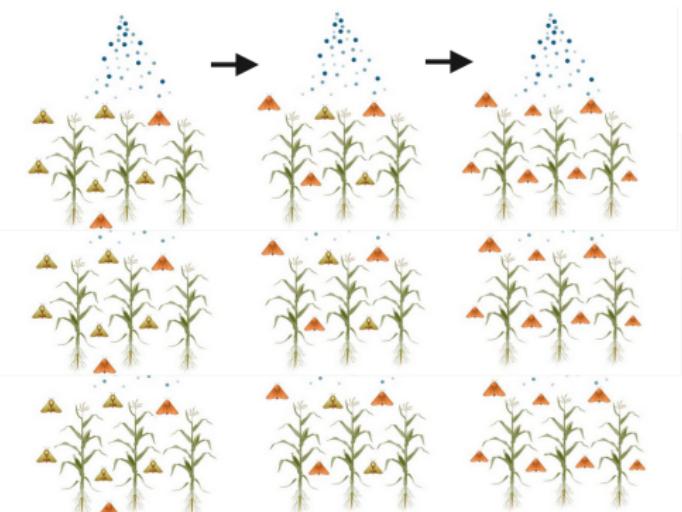
Food security requires agricultural innovation



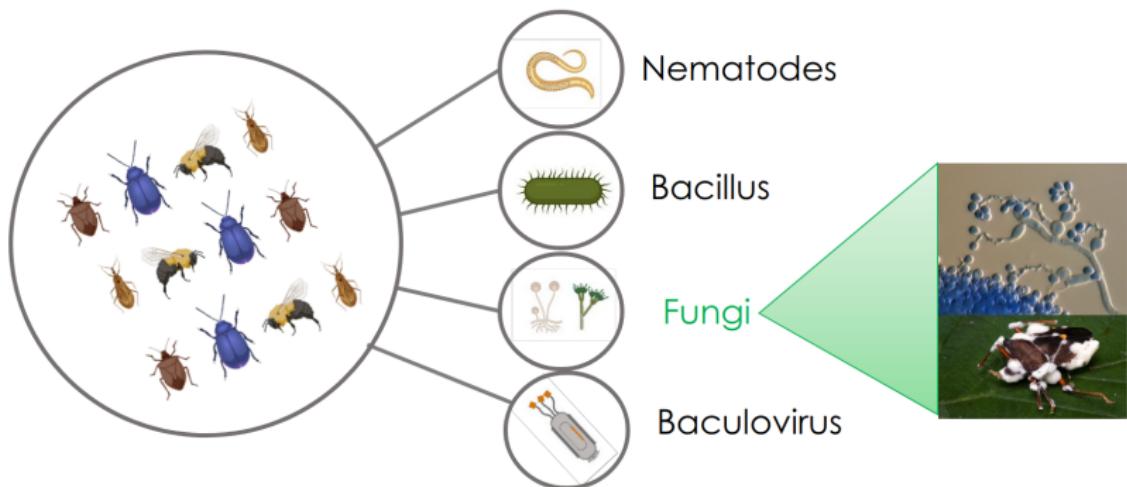
Synthetic pesticides suffer resistance evolution



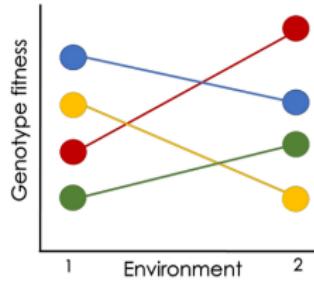
Gould et al., Science 360, 728–732 (2018)



Biopesticides offer a sustainable alternative



Genetic variation sustained in natural systems



Genotype by environment interactions provide one mechanism that maintains genetic variation

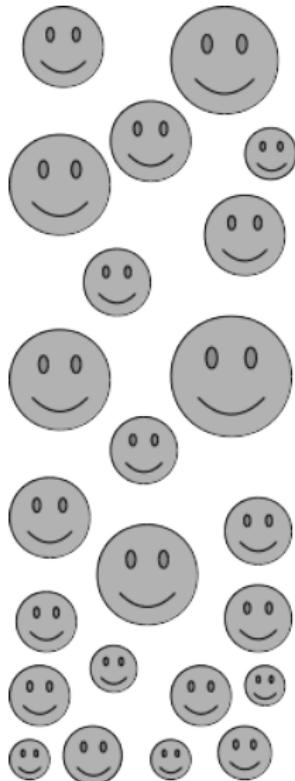
¹Chapman & Penman. 1979. *Nature* 281:298-299.

²Mangan et al. 2023. *Trends Ecol. Evol.* 38:605-614.

Measuring heritable variation

- ▶ Natural selection relies on heritable variation
- ▶ Quantitative genetics focuses on **variation** in phenotypes
- ▶ Not looking at specific genes

Measuring heritable variation



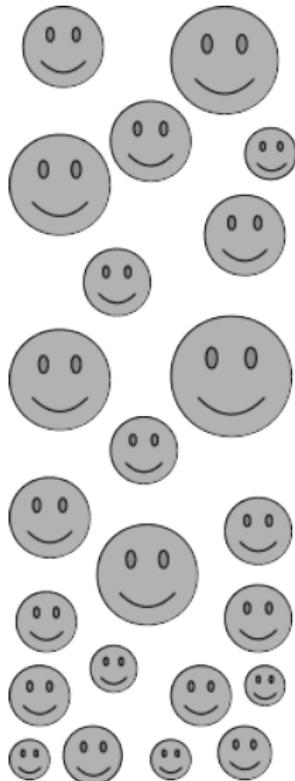
Components of phenotypic variation,

$$V_P = V_G + V_E.$$

- ▶ V_P = phenotypic variance
- ▶ V_G = genetic variance
- ▶ V_E = environmental variance

Total phenotypic variance is the sum of genetic variance and environmental variance.

Measuring heritable variation



Components of phenotypic variation,

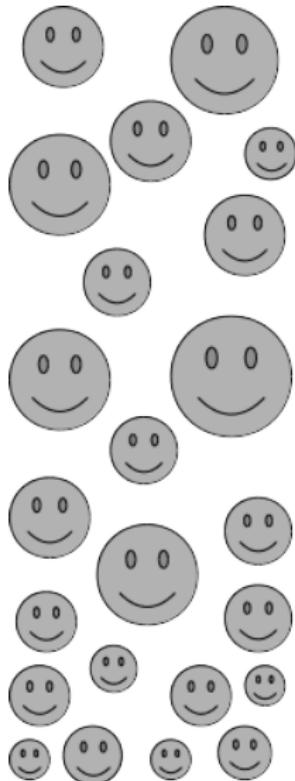
$$V_P = V_G + V_E.$$

We can break down V_G even further,

$$V_G = V_A + V_D + V_I.$$

- ▶ V_A = additive genetic variance
- ▶ V_G = dominance variance
- ▶ V_E = epistatic variance

Additive genetic variation



Additive genetic variation (V_A) is the variation in phenotype attributable to the summed effects of individual alleles.

- ▶ Summed effects of individual alleles are independent of other alleles (hence 'additive').
- ▶ Natural selection can only see additive variation because dominance and epistasis break down from parent to offspring.

Predicting evolutionary change

- ▶ Breeder's equation is foundational for food security
 - ▶ Increasing crop¹ & agricultural² yield
 - ▶ Increasing crop drought resistance³
- ▶ Can also look at multiple co-varying traits simultaneously (multivariate)

¹Cobb, J. N., et al. (2019). Enhancing the rate of genetic gain in public-sector plant breeding programs: lessons from the breeder's equation. *Theoretical and applied genetics* 132:627-645.

²Hill, W. G., & Kirkpatrick, M. (2010). What animal breeding has taught us about evolution. *Annual review of ecology, evolution, and systematics*, 41:1-19.

³Cooper, M., & Messina, C. D. (2023). Breeding crops for drought-affected environments and improved climate resilience. *The Plant Cell*, 35:162-186.

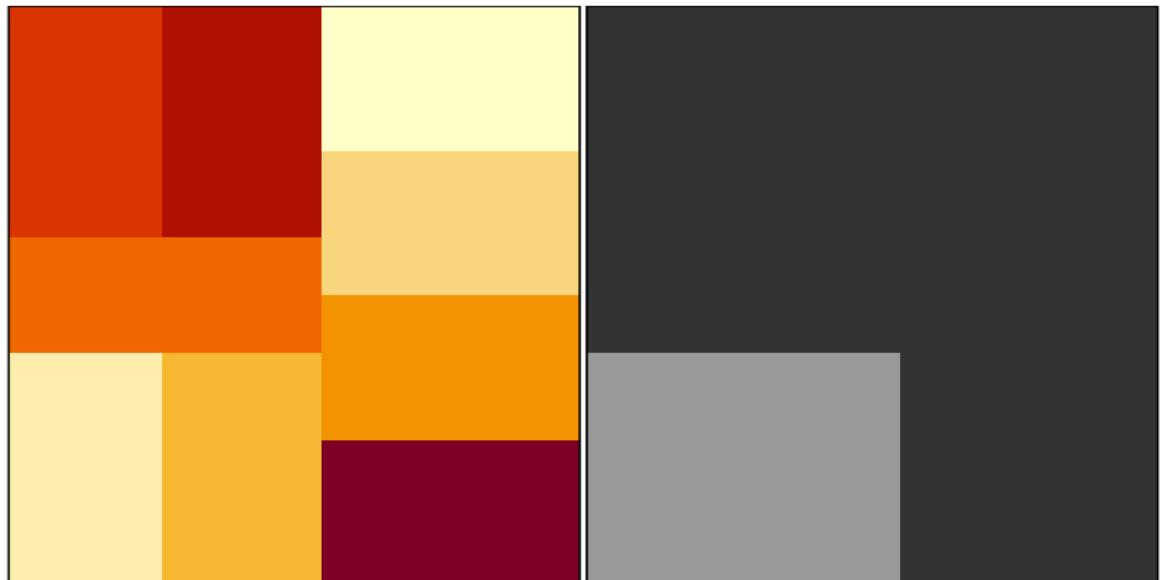
Agent-based modelling

Modelling as a proof of concept before scaling up



¹Image: [Public Domain](#)

Enhancing Diversity to Overcome Resistance Evolution

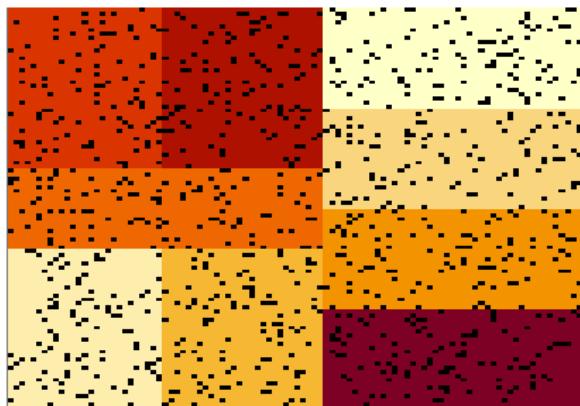


Unique farms

Pesticide applied

Agent-based modelling

Simulate a complex system *in silico* with code



- ▶ Simulate system *in silico*
- ▶ Agents as discrete entities
- ▶ Individual variation
- ▶ Spatially explicit landscapes
- ▶ Stochastic processes
- ▶ High model complexity

Advantages & disadvantages of using IBMs

Advantages

1. Very easy to model individual variation (genetic, phenotypic, environment, etc.)
2. Key biological processes are inherent to the model (e.g., drift, mutation, demography)
3. Models can often be more detailed and therefore more targeted

Advantages & disadvantages of using IBMs

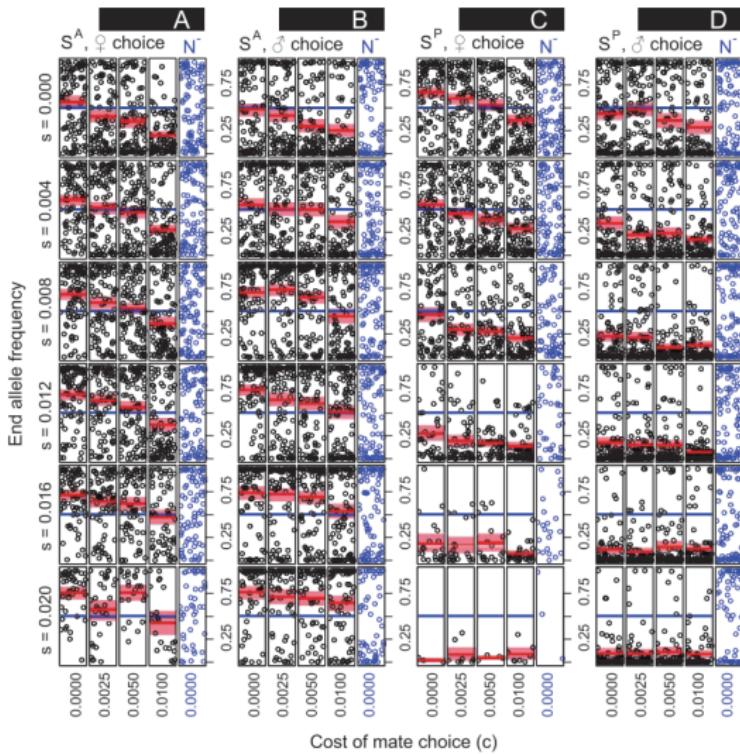
Advantages

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Disadvantages

1. Computational power can be limiting
2. Sometimes difficult to see the link between model assumptions and model predictions (i.e., difficult to interpret results)

Advantages & disadvantages of using IBMs



¹Duthie, A. B., & Reid, J. M. (2016). *Am. Nat.* 186, 651-667.

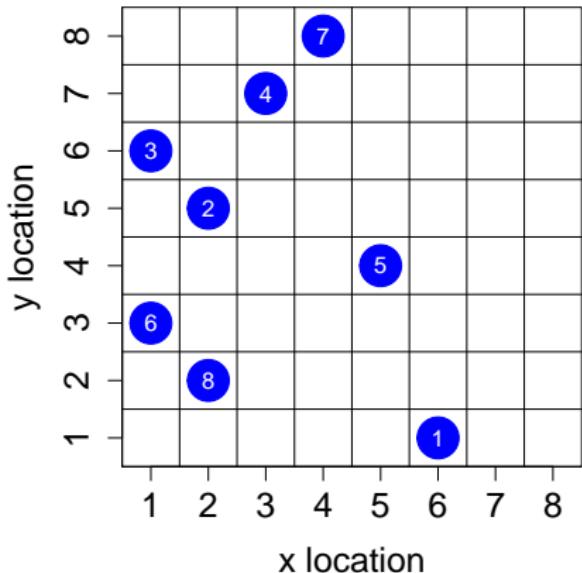
One way to model individuals in an IBM

Rows are individuals & columns are individual characteristics

ind_ID	x_loc	y_loc	body_mass	age
1	6	1	35.51	4
2	2	5	39.49	4
3	1	6	30.85	2
4	3	7	41.54	5
5	5	4	26.23	1
6	1	3	38.16	6
7	4	8	37.65	6
8	2	2	29.59	5

The process of modelling is then to do something to the individuals and their characteristics – have them interact, change, be removed, have more added. Models are as complex as we are willing to code.

Individual-based models are often spatially explicit



- ▶ Individual locations can be mapped to a landscape, with rules for movement
- ▶ Movement entails rules for changing x and y locations
- ▶ Landscape need not be represented in code, but can be used to define landscape properties

Simulate individuals over multiple time steps

Define individuals

```
inds      <- array(data = 0, dim = c(5, 3));
inds[, 1] <- 1:5;
inds[, 2] <- sample(x = 1:8, size = 5, replace = TRUE);
inds[, 3] <- sample(x = 1:8, size = 5, replace = TRUE);
```

Move individuals to the right 5 times

```
ts      <- 0;
time_steps <- 5;
while(ts < time_steps){
  inds[, 2] <- inds[, 2] + 1;
  ts    <- ts + 1;
}
```

resevol: An R package for modelling agricultural
pests

resevol: An R package for modelling agricultural pests



Resistance Evolution (resevol) simulation package

The `resevol` R package is a tool for simulating social-ecological individual-based models (IBMs) for the ecology and evolution of agricultural pest species. Simulations model a spatially explicit landscape broken down into one or more independent farms on which one of up to 10 crops can be grown and one of up to 10 pesticides can be applied. Crop and pesticide application can be rotated during a simulation at different spatial and temporal scales to simulate the effects of heterogeneity of pest environment. Haploid or diploid pest genomes are modelled explicitly with an arbitrary number of loci that map to any number of traits. This mapping of loci to traits can be set with a pre-specified trait correlation structure, which is found using an evolutionary algorithm run using the `mine_gmatrix()` function. Individual pest traits can affect movement, reproduction, feeding, pesticide tolerance, metabolism, and other individual characteristics. Simulations of pest populations dynamics run with the `run_sim_farm()` function can track individual pest locations, pedigree, behaviour, and trait evolution.

Links

- [View on CRAN](#)
- [Browse source code](#)
- [Report a bug](#)

License

GPL (>=2)

Citation

[Citing resevol](#)

Developers

- A. Bradley Duthie
Author, maintainer
- Rose McKeon
Author, contractor

[More about authors...](#)

¹Duthie AB, McKeon CR (2022). `resevol`: Simulate Agricultural Production and Evolution of Pesticide Resistance. R package version 0.3.3.0, <https://bradduthie.github.io/resevol/>.

resevol: An R package for modelling agricultural pests

Complex individuals

- ▶ Complete genomes
- ▶ Highly polygenic traits
- ▶ Set trait covariances
- ▶ Flexible life-history
- ▶ Flexible mating system

¹Duthie AB, McKeon CR (2022). resevol: Simulate Agricultural Production and Evolution of Pesticide Resistance. R package version 0.3.3.0, <https://bradduthie.github.io/resevol/>.

²Duthie, AB, R Mangan, CR McKeon, MC Tinsley, LF Bussière. 2022. resevol: an R package for spatially explicit models of pesticide resistance given evolving pest genomes. bioRxiv 2022.08.22.504740; doi: <https://doi.org/10.1101/2022.08.22.504740>

resevol: An R package for modelling agricultural pests

Complex individuals

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Dynamic landscapes

- ▶ Custom land dimensions
- ▶ Custom pesticide rotation
- ▶ Custom crop rotation
- ▶ Individual farms tracked
- ▶ Raster landscape maps

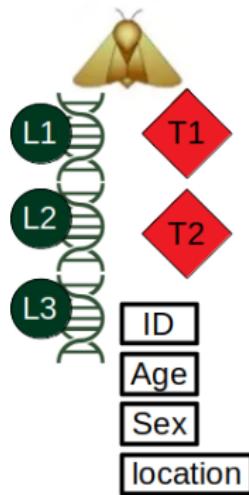
¹Duthie AB, McKeon CR (2022). *resevol: Simulate Agricultural Production and Evolution of Pesticide Resistance*. R package version 0.3.3.0, <https://bradduthie.github.io/resevol/>.

²Duthie, AB, R Mangan, CR McKeon, MC Tinsley, LF Bussière. 2022. *resevol: an R package for spatially explicit models of pesticide resistance given evolving pest genomes*. bioRxiv 2022.08.22.504740; doi: <https://doi.org/10.1101/2022.08.22.504740>

resevol: An R package for modelling agricultural pests

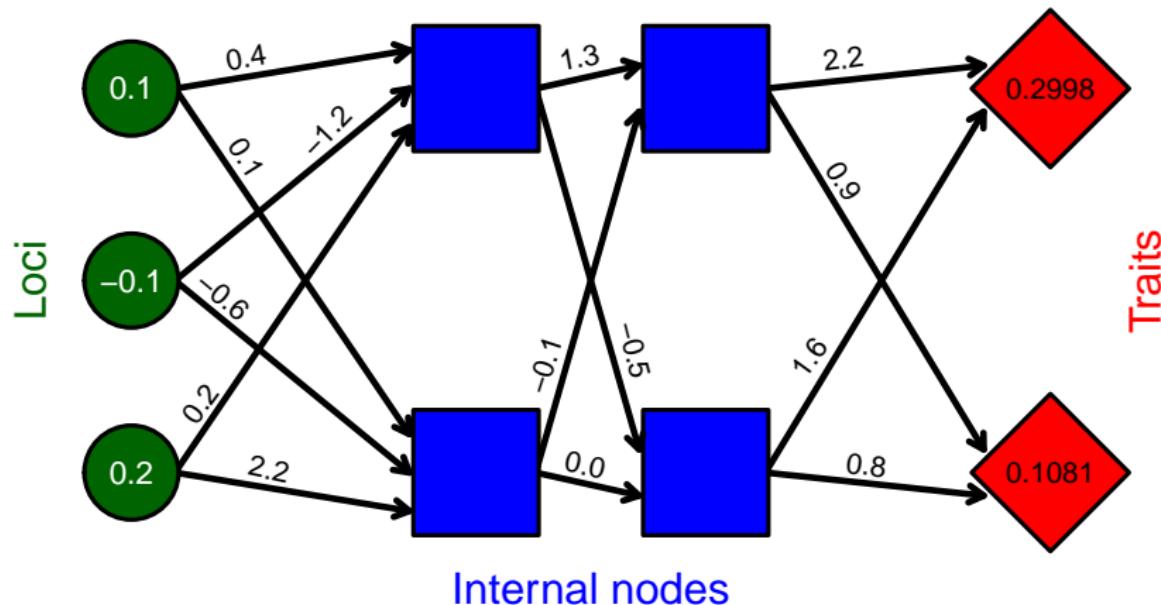
Complex individuals

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¹Image: Public domain

A genetic architecture for pre-specified trait covariances



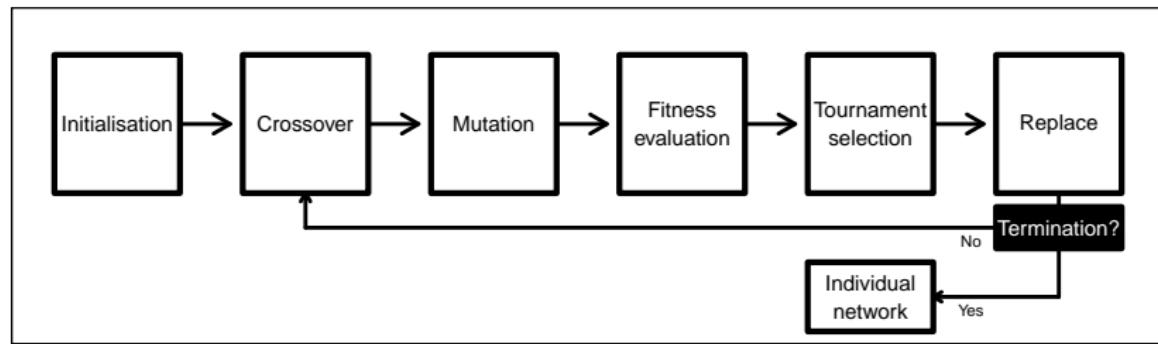
$$\begin{pmatrix} 0.1, & -0.1, & 0.2 \end{pmatrix} \begin{pmatrix} 0.4, & 0.1 \\ -1.2, & -0.6 \\ 0.2, & 2.2 \end{pmatrix} \begin{pmatrix} 1.3, & -0.5 \\ -0.1, & 0.0 \end{pmatrix} \begin{pmatrix} 2.2, & 0.9 \\ 1.6, & 0.8 \end{pmatrix} = \begin{pmatrix} 0.2998, & 0.1081 \end{pmatrix}$$

¹resevol R package vignette:

https://bradduthie.github.io/resevol/articles/evolutionary_algorithm.html

Evolutionary algorithm to find genetic architecture

Initialise a population of multiple potential networks from loci to traits.



Evolve values between nodes, mapping loci to traits.

¹resevol R package vignette:

https://bradduthie.github.io/resevol/articles/evolutionary_algorithm.html

Evolutionary algorithm to find genetic architecture

```
gmt <- matrix(data = c( 1.0, -0.5, -0.5, 2.0),  
               nrow = 2);
```

```
mg  <- mine_gmatrix(gmatrix = gmt,  
                     loci = 3,  
                     indivs = 2000, npsize = 12000,  
                     max_gen = 5400, sampleK = 1200,  
                     chooseK = 6, layers = 4,  
                     mu_pr = 0.2, pr_cross = 0.2,  
                     mu_sd = 0.004, term_cri = -8);
```

Evolutionary algorithm to find genetic architecture

**Pre-specified
covariances**

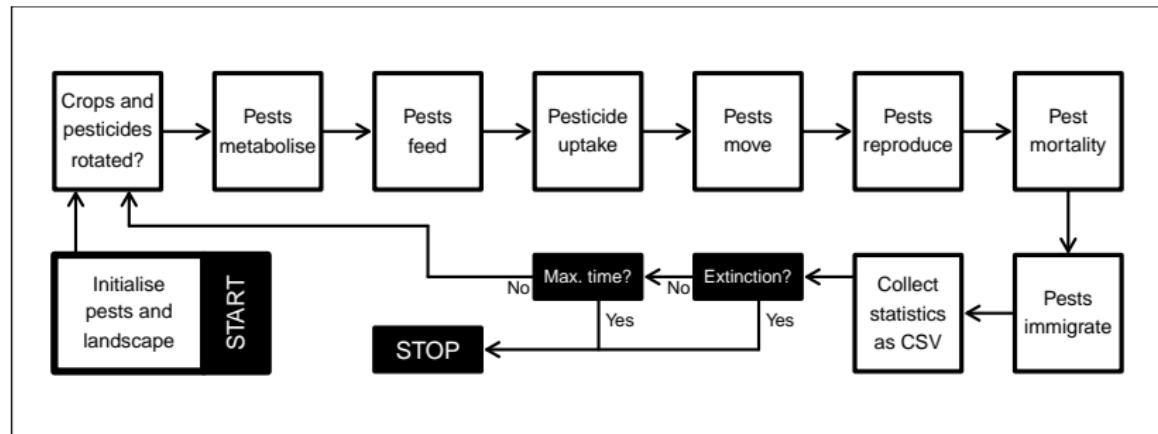
$$\begin{bmatrix} 1.0 & -0.5 \\ -0.5 & 2.0 \end{bmatrix} \quad (1)$$

**Covariances
produced**

$$\begin{bmatrix} 1.007 & -0.436 \\ -0.436 & 1.906 \end{bmatrix} \quad (2)$$

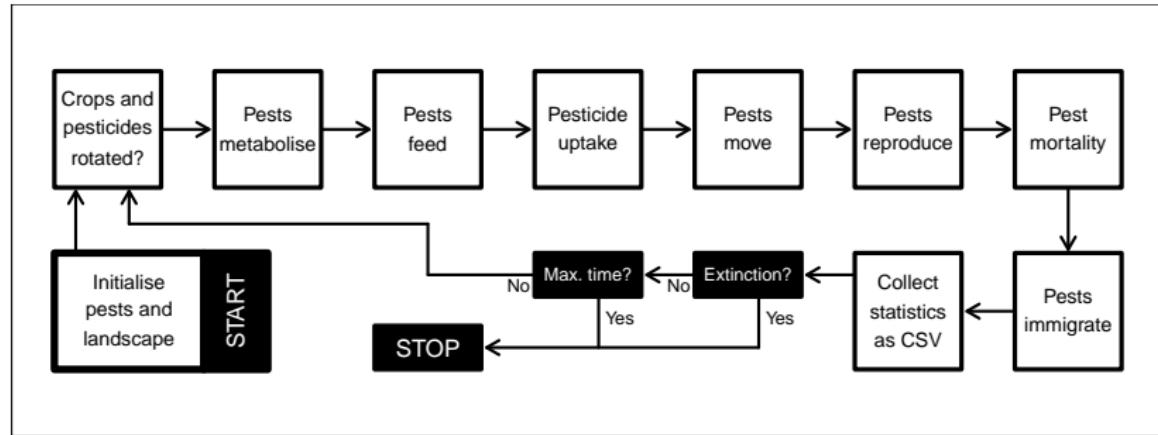
Pest life-history events defined within an age range

Within a time step, order of events are specified.



Pest life-history events defined within an age range

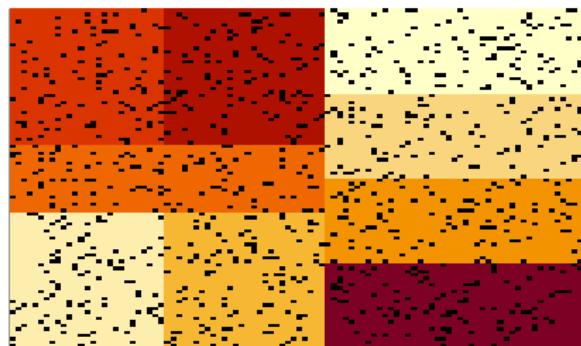
Within a time step, order of events are specified.



Specific events can be restricted to age ranges:

Feed: 0-2, Move: 3-8, Mate: 7-9

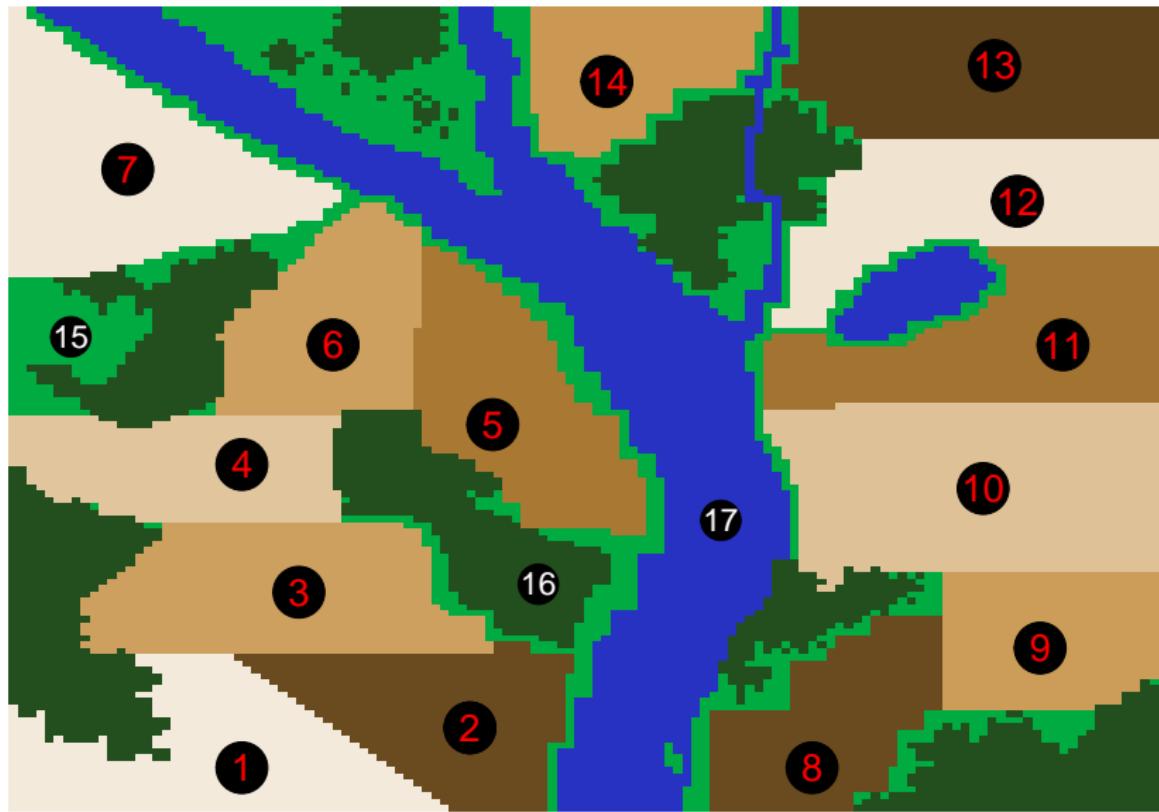
Constructing a landscape: Default options



- ▶ Specify 'farms', 'xdim', 'ydim'.
- ▶ Shortest splitline algorithm
- ▶ Land edge: torus, leaky, reflect

Each farm can use up to one crop and one pesticide, and the timing and rotation rules for crops and pesticide allow any Markov process.

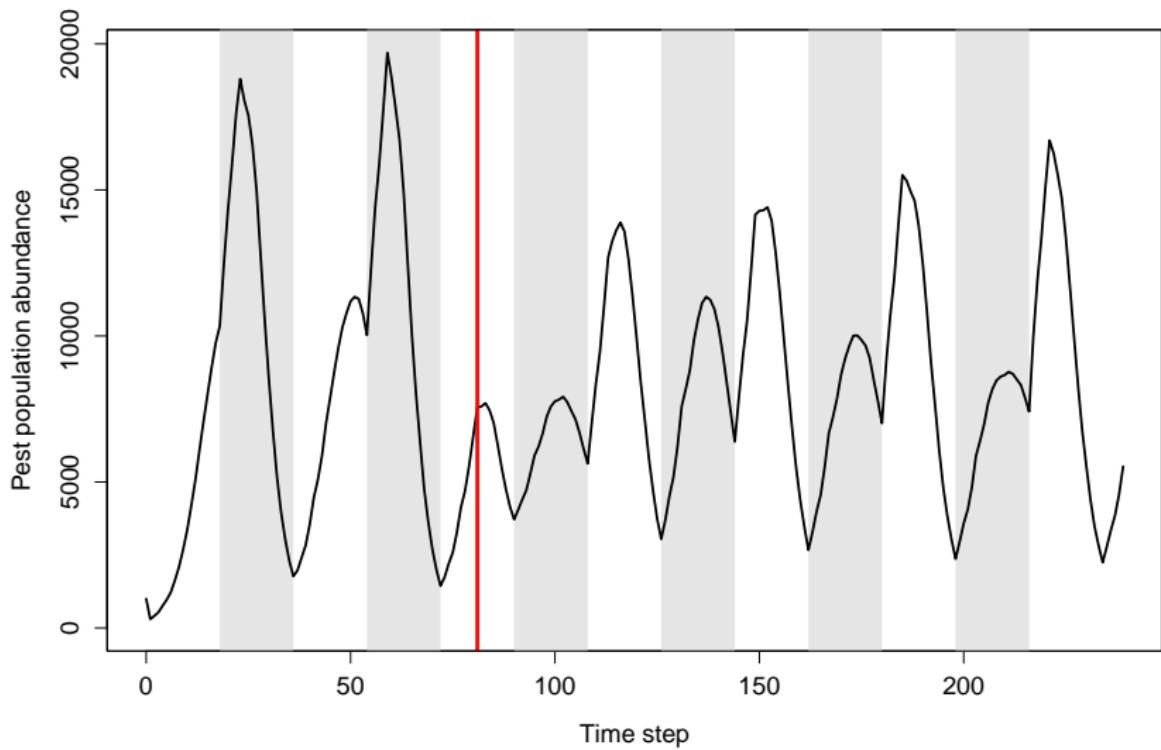
Constructing a landscape: Advanced options



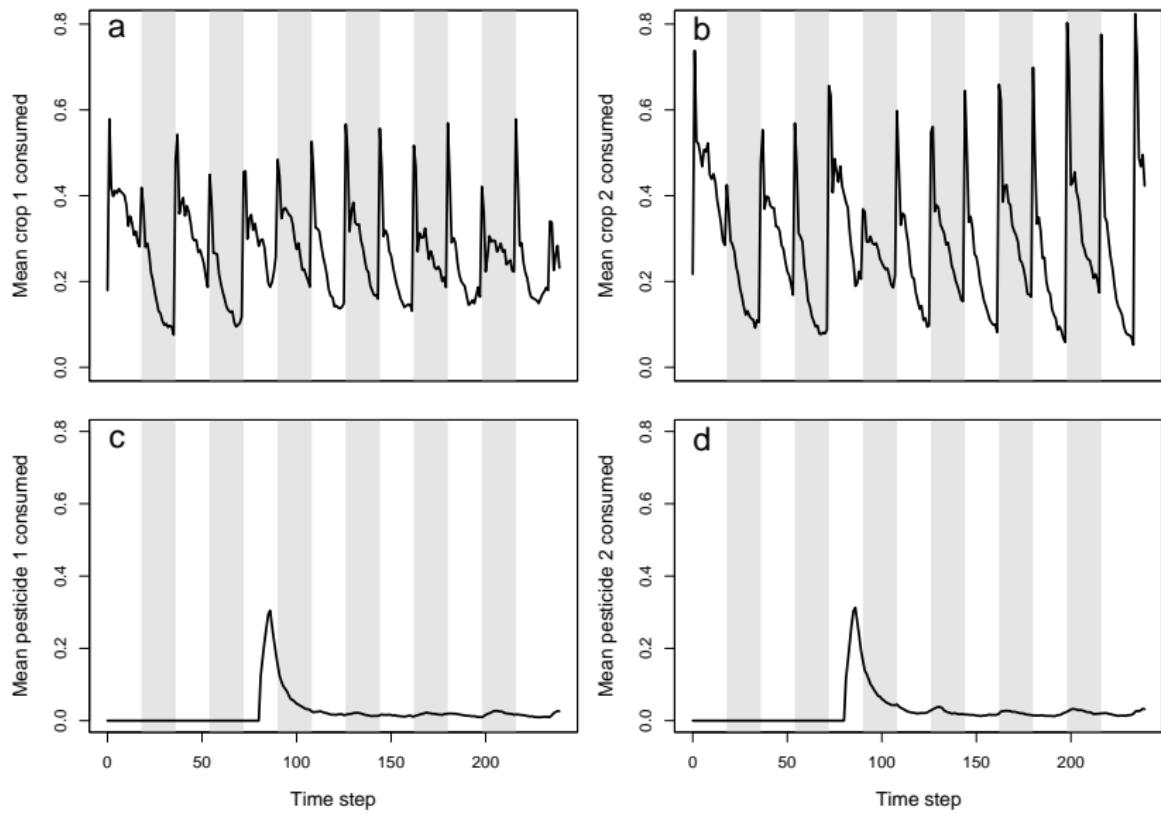
Running a simulation in resevol

```
run_farm_sim(mine_output = mg, repro = "asexual",
              pesticide_number = 2, time_steps = 160,
              farms = 9, pesticide_init = "random",
              pesticide_consume = c("T1", "T2"),
              pesticide_rotation_time = 16, xdim = 64,
              pesticide_rotation_type = 3, ydim = 64,
              pesticide_tolerated_surv = 0, max_age = 4,
              pesticide_per_cell = 1, crop_number = 1,
              crop_rotation_time = 16, crop_per_cell = 4,
              food_consume = 1, food_needed_surv = 1,
              reproduction_type = "food_based",
              food_needed_repr = 1, land_edge = "torus",
              min_age_feed = 0, max_age_feed = 2,
              min_age_move = 3, max_age_move = 4,
              min_age_reproduce = 4, print_gens = FALSE,
              max_age_reproduce = 4, rand_age = TRUE,
              age_pesticide_threshold = 2,
              immigration_rate = 10, move_distance = 2,
              print_last = TRUE, trait_means = c(0.1, 0.1));
```

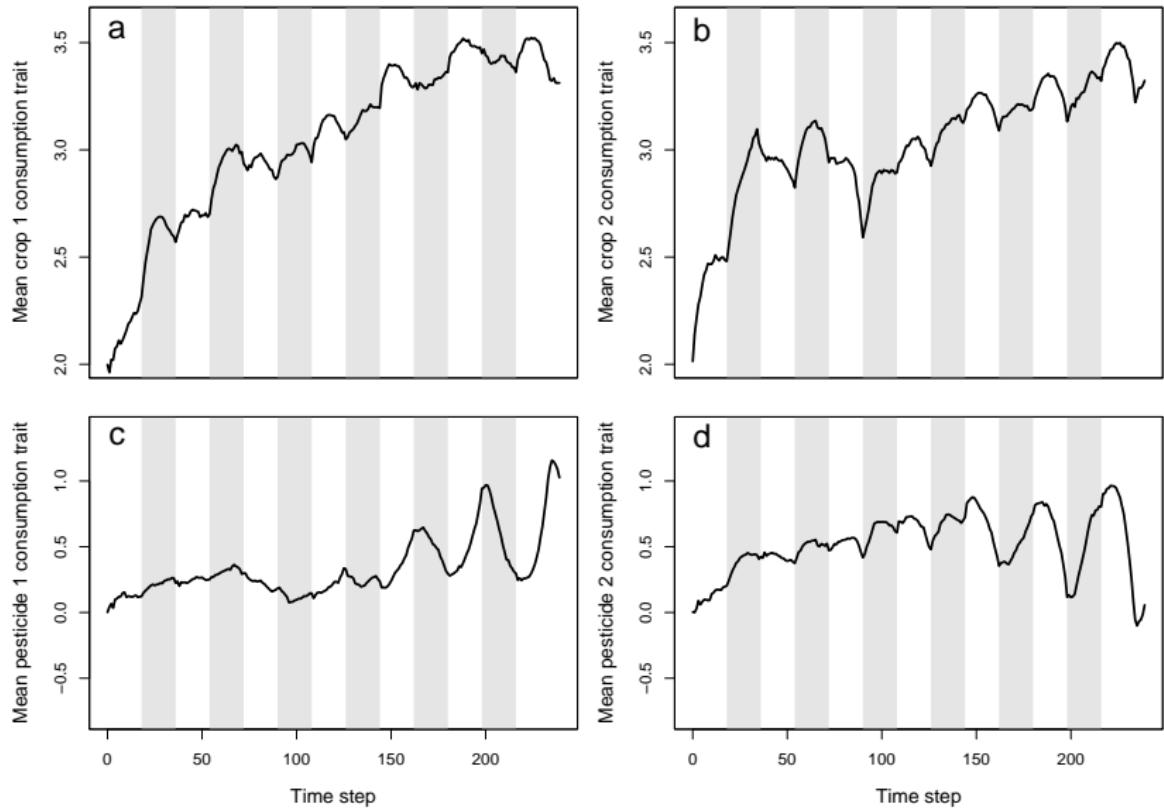
Simulating ecology, evolution, crop yields



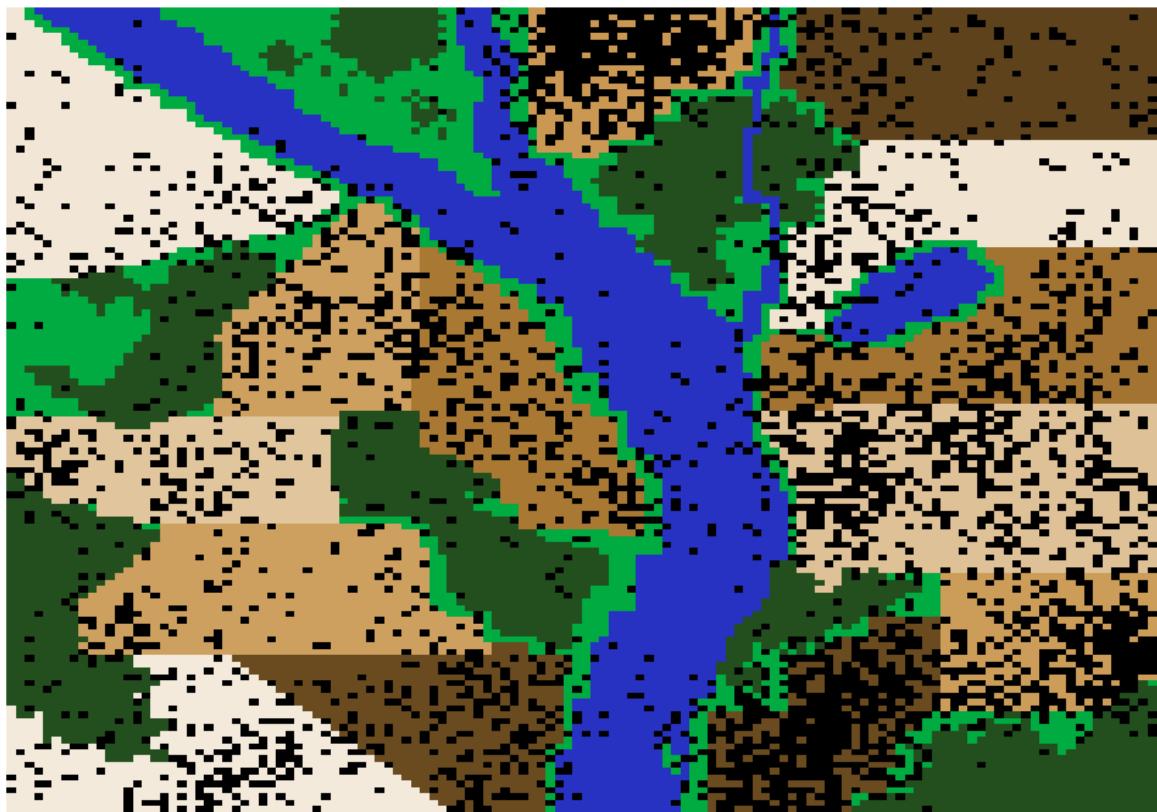
Simulating ecology, evolution, crop yields



Simulating ecology, evolution, crop yields



Simulating ecology, evolution, crop yields



The resevol R package: summary

- ▶ Rapidly develop and simulation models of pest ecology and resistance evolution
- ▶ Introduces a novel approach to modelling complex pest genetic architecture
- ▶ Flexible pest life-histories, mating systems, trait covariances
- ▶ Highly customisable, detailed landscapes
- ▶ Free to use¹, open source² (GPL >= 2), documented^{1,3}

¹Website: <https://bradduthie.github.io/resevol/>

²Code: <https://github.com;bradduthie/resevol>

³Lab Notebook: <https://bradduthie.github.io/resevol/notebook/>

Install the resevol R package

Install resevol:

```
install.packages("resevol")
```

Get started simulating:

<https://bradduthie.github.io/resevol>