




1 Mozzie: a computationally efficient simulator for the 2 spatio-temporal modelling of mosquitoes

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7 Summary

8 Mozzie enables simulation of the lifecycle and spatial spread of mosquitoes. Mozzie can be
9 used to assess risks associated with disease-control strategies at local, regional or continental
10 scales. Most particularly, strategies involving genetic alterations of mosquitoes to eliminate
11 malaria, are of prime interest.

12 More technically, Mozzie simulates a population-dynamics model that uses differential equations
13 or delay differential equations ([Bohner et al., 2018](#); [El-Hachem & Beeton, 2024](#)) to describe
14 the spread and persistence of mosquitoes that may be genetically altered. Genetic alterations
15 are flexibly modelled: these can involve any number of alleles; Mendelian or non-Mendelian
16 inheritance, including gene drives; they can be self-limiting or self-sustaining; and can include
17 the emergence of resistant alleles. The model allows simulation of N mosquito species.
18 It incorporates mate-choice, hybridisation and intra-specific competition that occur within
19 complexes of mosquito species ([Beeton et al., 2020](#)). This fills a gap that currently exists
20 among similar models, allowing researchers to assess potential transfer of the genetic alterations
21 between (sub-)species.

22 Mozzie supports spatial and temporal variations in lifecycle parameters, and local diffusion and
23 wind-assisted, long range, advection. For example, wind patterns and the capacity of the
24 landscape to support mosquitoes can vary spatially and temporally, reflecting daily variations,
25 seasonality, and local conditions.

26 Conversely, Mozzie does not contain human agents, nor does it consider the effect of genetic
27 control strategies on the prevalence of pathogens such as the malaria parasite, among human
28 or animal populations.

29 Mozzie has been used by the authors to simulate the spread across sub-Saharan Africa of
30 a theoretical, population-modifying, gene drive in *Anopheles gambiae s.s.* and *Anopheles*
31 *coluzzii* ([Beeton et al., 2022](#)) (that paper also describes the mathematics of a particular
32 mosquito lifecycle model that is contained in Mozzie). It has also been used to predict the
33 spread of Target Malaria's Paternal Male Bias construct ([Galizi et al., 2014](#)) following a
34 proposed field-release of genetically modified *Anopheles coluzzi* male mosquitoes in Burkina
35 Faso ([Hosack et al., 2023](#)).

36 State of the field

37 Alternatives to Mozzie include:

- 38 ▪ MIT's [HYDREMATS](#) software ([Bomblies et al., 2009](#)). HYDREMATS is a coupled
39 hydrology and entomology model that uses an agent-based approach for mosquito-human

- 40 dynamics, and focuses on high-resolution village-scale understanding of malaria without
41 genetically-modified mosquitoes.
- 42 ■ The well-established [SkeeterBuster](#) focuses on the *Aedes aegypti* species in order to
43 understand insecticidal control measures such as spraying ([Gunning et al., 2022](#); [Magori
44 et al., 2009](#)). A stochastic, mechanistic approach is employed.
 - 45 ■ [OpenMalaria](#) ([T. Smith et al., 2006](#)) is an open-source C++ program enabling simulation of
46 malaria epidemiology, typically at the village scale, in order to assess the efficacy of
47 non-genetic malaria interventions.
 - 48 ■ IDM's [EMOD](#) software can simulate malaria epidemiology using an agent-based approach,
49 with spatial structure based on a network ([Bershteyn et al., 2018](#)). Less emphasis is
50 spent on genetic modifications, and a single mosquito species is the focus.
 - 51 ■ The [dynamAedes](#) R package can be used to study the spatio-temporal evolution of a
52 single mosquito species, with particular attention paid to the impact of temperature
53 heterogeneity.
 - 54 ■ The [exDE](#) R package solves models of mosquito-borne pathogen dynamics and control
55 ([Wu et al., 2023](#)). Attention is paid to sophisticated representations of mosquito
56 lifecycles, including exogenous forcing by weather and vector control, as well as mosquito-
57 malaria-human interactions. Although a single mosquito species is the focus, the
58 framework allows for multiple species. The code centers on traditional vector controls,
59 rather than genetic controls.
 - 60 ■ Berkeley's [MGDrivE](#) is an open-source framework to study gene-drives in mosquito
61 populations ([Mondal et al., 2024](#); [Sánchez C. et al., 2019](#)), which is written in R. With
62 regards to lifecycle dynamics, MGDrivE has similar functionality to *Mozzie*, although
63 MGDrivE focuses on single species, in contrast to *Mozzie* where transfer of genetic
64 constructs between (sub-)species is of interest. MGDrivE's spatial structure is based on
65 a network, where each node in the network could be thought of as a household, house
66 block, or even a city. In terms of functionality, MGDrivE is the most similar to *Mozzie*,
67 although the numerical methods employed are quite different.

68 In addition to these publicly-available codes, many academic articles consider the lifecycle
69 and spatial spread of mosquitoes, for example ([Bruzzone & Utgés, 2022](#); [Dufourd & Dumont,
70 2013](#); [Dye & Cain, 2024](#); [Endo & Eltahir, 2018](#); [Fang et al., 2020](#); [Fernández-Carrión et al.,
71 2018](#); [Lutambi et al., 2013](#); [North et al., 2013](#); [Roques & Bonnefon, 2016](#); [Silva et al., 2020](#);
72 [N. R. Smith et al., 2018](#); [Yamashita, Takahashi, et al., 2018](#); [Yamashita, Das, et al., 2018](#)),
73 but few have published their code. Most appear to rely on unpublished scripts in codes such as
74 MATLAB ([Fernández-Carrión et al., 2018](#); [Lutambi et al., 2013](#); [Yamashita, Das, et al., 2018](#)),
75 or concentrate on specialised scenarios ([Bruzzone & Utgés, 2022](#); [Roques & Bonnefon, 2016](#)).

76 If spatially explicit, the aforementioned codes model spatial structure using a network. In
77 contrast, *Mozzie* uses a continuous-space (diffusion-advection equation) approach, deliberately
78 incorporating long-range dispersal in a way that is ecologically interpretable ([Hosack et al.,
79 2023](#)). In addition, *Mozzie* does not focus on single species, but concentrates on the interaction
80 of multiple (sub-)species. Many of the aforementioned alternatives contain human agents and
81 the malaria parasite, which *Mozzie* does not.

82 Statement of need

83 *Mozzie* is designed to solve problems involving:

- 84 ■ interacting (sub-)species of mosquitoes, with
- 85 ■ complicated lifecycle dynamics including transfers of genetic modifications between the
86 (sub-)species, in
- 87 ■ spatially-extensive settings (such as continental scales) including the spatio-temporal
88 dispersal of individuals (such as advection via wind).

89 It is anticipated that users of *Mozzie* will be researchers interested in such aspects.

90 Importantly, the numerical implementation of Mozzie is:

- 91 ▪ ecologically interpretable (Hosack et al., 2023),
- 92 ▪ computationally and I/O efficient, and
- 93 ▪ well tested.

94 This allows rapid simulation at continental scales to investigate sensitivity to input parameters,
 95 as required in risk assessments. It is written in Cython (Behnel et al., 2011) (a mixture of
 96 Python and C), and simulations are run using Python. The test coverage of the Mozzie
 97 codebase is over 99%, meaning it is also suitable for risk assessments that could be subject to
 98 considerable scrutiny.

99 Example

100 **Figure 1** shows results from Mozzie simulations when using 2 inter-breeding, hybridising and
 101 competing mosquito species (Beeton et al., 2022). A gene-drive is introduced into one of these
 102 species, and the modified individuals are released from one of 15 sites throughout sub-Saharan
 103 Africa. The script and data to reproduce this result can be found on [CSIRO's data access](#)
 104 [portal](#).

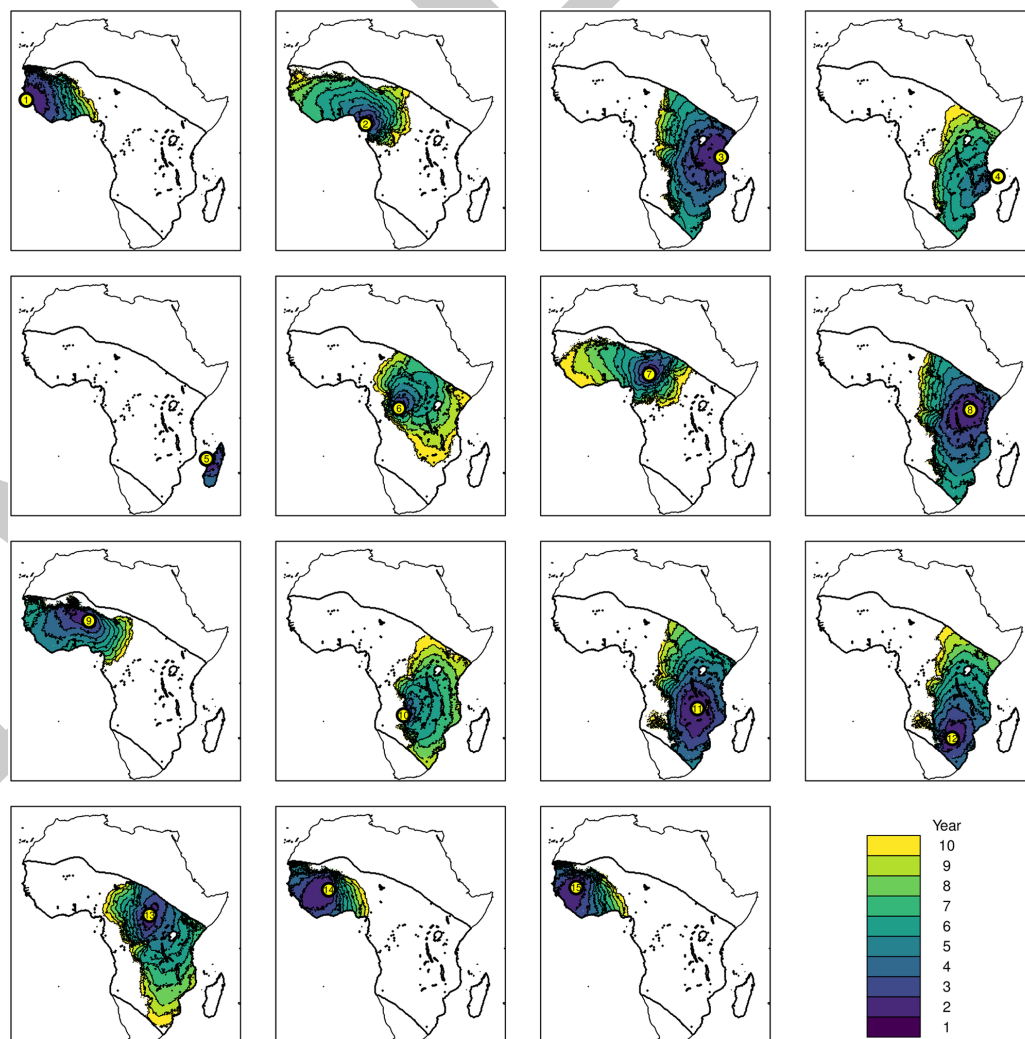


Figure 1: The invasion front of genetically-modified mosquito species, released from different points (Beeton et al., 2022). Figure used under the [Creative Commons Attribution License](#).

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