

# Package ‘MGDrivE’

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**Type** Package

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**Maintainer** Héctor Manuel Sánchez Castellanos <sanchez.hmsc@berkeley.edu>

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[https://marshalllab.github.io/MGDrivE/docs\\_v1/](https://marshalllab.github.io/MGDrivE/docs_v1/)

**BugReports** <https://github.com/MarshallLab/MGDrivE/issues>

**Description** Provides a model designed to be a reliable testbed where various gene drive interventions for mosquito-borne diseases control. It is being developed to accommodate the use of various mosquito-specific gene drive systems within a population dynamics framework that allows migration of individuals between patches in landscape. Previous work developing the population dynamics can be found in Deredec et al. (2001) <[doi:10.1073/pnas.1110717108](https://doi.org/10.1073/pnas.1110717108)> and Hancock & Godfray (2007) <[doi:10.1186/1475-2875-6-98](https://doi.org/10.1186/1475-2875-6-98)>, and extensions to accommodate CRISPR homing dynamics in Marshall et al. (2017) <[doi:10.1038/s41598-017-02744-7](https://doi.org/10.1038/s41598-017-02744-7)>.

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**Author** Héctor Manuel Sánchez Castellanos [aut, cre],  
 Jared Bennett [aut],  
 Sean Wu [aut],  
 John M. Marshall [aut]

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---

aggregateFemales      *Aggregate Female Output by Genotype*

---

**Description**

Aggregate over male mate genotype to convert female matrix output into vector output.

**Usage**

```

aggregateFemales(
  readDir,
  writeDir = NULL,
  genotypes,
  remFile = TRUE,
  verbose = TRUE
)

```

**Arguments**

readDir	Directory to read input from
writeDir	Directory to write output to. Default is readDir
genotypes	Character vector of possible genotypes; found in driveCube\$genotypesID
remFile	Boolean flag to remove original (unaggregated) file
verbose	Chatty? Default is TRUE

**Examples**

```

## Not run:
# This example assumes user has already run MGDrive and generated output.
# This also assumes that the user has already split output by patch.
# See vignette for complete example.

# set read/write directory
fPath <- "path/to/data/containing/folder"

# Need genotypes from the cube run in the simulation
# This is dependent on the simulation run
# Using Mendelian cube for this example
cube <- cubeMendelian()

# no return value from function
aggregateFemales(readDir= fPath, writeDir = NULL, genotypes = cube$genotypesID,
                 remFile = TRUE)

## End(Not run)

```

---

 aggregateOutput

*Aggregate Output Over Landscape*


---

**Description**

This function aggregates the output of a run over the entire output, i.e., all of the patches. It writes the output one level above the folder pointed to by readDir, if writeDir is NULL. Output consists of 2 csv files, one for males and one for females, "...M\_LandscapeAgg\_Run...csv".

**Usage**

```
aggregateOutput(readDir, writeDir=NULL)
```

**Arguments**

```
readDir      Directory where output was written to
writeDir     Directory to write output to. Default is one level above readDir
```

**Examples**

```
## Not run:
# This assumes user has run MGDriVE and output is in fPath.
# See vignette for examples on how to run MGDriVE

# read/write dirs
fPath <- "folder/containing/output"
oPath <- "folder/to/write/stuff"

# first, split output by patch and aggregate females by mate genotype
# remember, cube is for example and changes with simulation
# landscape aggregation will work if females are not aggregated, but it's slower
cube <- cubeMendelian()

splitOutput(readDir = fPath, writeDir = NULL, remFile = TRUE)
aggregateFemales(readDir= fPath, writeDi = NULL, genotypes = cube$genotypesID,
                 remFile = TRUE)

# aggregate mosquitoes over entire landscape
# no return value
aggregateOutput(readDir = fPath, writeDir = NULL)

## End(Not run)
```

---

```
basicBatchMigration  Make List of Batch Migration Parameters
```

---

**Description**

Sets up a list containing the probability of a batch migration, the fractional amount of males/females that migrate, and the weighted probabilities for where to migrate. The default weights for migration are equal for all patches. These can be changed after running the function. This is only used in [oneDay\\_Migration\\_Stochastic\\_Network](#).

**Usage**

```
basicBatchMigration(
  batchProbs = 1e-05,
  sexProbs = c(0.01, 0.01),
  numPatches = 1
)
```

**Arguments**

batchProbs	Probability of a batch migration, either 1 number or a vector of length equal to the number of patches
sexProbs	Population fraction of males and females that migrate. Either a vector c(M,F) or matrix of 2 columns
numPatches	Number of patches in the simulation

**Examples**

```
# to setup for 3 patches
batchMigration = basicBatchMigration(batchProbs = 1e-5, sexProbs = c(0.1, 0.01), numPatches = 3)
```

---

 calcCos

---

*Calculate Geodesic Distance - Cosine Method*


---

**Description**

This function calculates geodesic distance using the cosine method.

**Usage**

```
calcCos(latLongs, r = 6378137)
```

**Arguments**

latLongs	Two column matrix of latitudes/longitudes
r	Earth radius. Default is WGS-84 radius

**Examples**

```
# two-column matrix with latitude/longitude, in degrees
latLong = cbind(runif(n = 5, min = 0, max = 90),
  runif(n = 5, min = 0, max = 180))

# cosine distance formula
distMat = calcCos(latLongs = latLong)
```

---

calcExpKernel	<i>Calculate Exponential Stochastic Matrix</i>
---------------	--

---

### Description

Given a distance matrix from [calcVinEll](#), calculate a stochastic matrix where one step movement probabilities follow an exponential density.

### Usage

```
calcExpKernel(distMat, rate)
```

### Arguments

distMat	Distance matrix from <a href="#">calcVinEll</a>
rate	Rate parameter of <a href="#">Exponential</a> distribution

### Details

The distribution and density functions for the exponential kernel are given below:

$$F(x) = 1 - e^{-\lambda x}$$

$$f(x) = \lambda e^{-\lambda x}$$

where  $\lambda$  is the rate parameter of the exponential distribution.

### Examples

```
# setup distance matrix
# two-column matrix with latitude/longitude, in degrees
latLong = cbind(runif(n = 5, min = 0, max = 90),
                runif(n = 5, min = 0, max = 180))

# Vincenty Ellipsoid distance formula
distMat = calcVinEll(latLongs = latLong)

# calculate exponential distribution over distances
# rate is just for example
kernMat = calcExpKernel(distMat = distMat, rate = 10)
```

---

calcGammaKernel	<i>Calculate Gamma Stochastic Matrix</i>
-----------------	--

---

### Description

Given a distance matrix from [calcVinEll](#), calculate a stochastic matrix where one step movement probabilities follow a gamma density.

### Usage

```
calcGammaKernel(distMat, shape, rate)
```

### Arguments

distMat	Distance matrix from <a href="#">calcVinEll</a>
shape	Shape parameter of <a href="#">GammaDist</a> distribution
rate	Rate parameter of <a href="#">GammaDist</a> distribution

### Details

The distribution and density functions for the gamma kernel are given below:

$$F(x) = \frac{1}{\Gamma(\alpha)} \gamma(\alpha, \beta x)$$

$$f(x) = \frac{\beta^\alpha}{\Gamma(\alpha)} x^{\alpha-1} e^{-\beta x}$$

where  $\Gamma(\alpha)$  is the Gamma function,  $\gamma(\alpha, \beta x)$  is the lower incomplete gamma function, and  $\alpha, \beta$  are the shape and rate parameters, respectively.

### Examples

```
# setup distance matrix
# two-column matrix with latitude/longitude, in degrees
latLong = cbind(runif(n = 5, min = 0, max = 90),
                runif(n = 5, min = 0, max = 180))

# Vincenty Ellipsoid distance formula
distMat = calcVinEll(latLongs = latLong)

# calculate gamma distribution over distances
# shape and rate are just for example
kernMat = calcGammaKernel(distMat = distMat, shape = 1, rate = 1)
```

---

calcHaversine	<i>Calculate Geodesic Distance - Haversine Method</i>
---------------	---

---

**Description**

This function calculates geodesic distance using the Haversine method.

**Usage**

```
calcHaversine(latLongs, r = 6378137)
```

**Arguments**

latLongs	Two column matrix of latitudes/longitudes
r	Earth radius. Default is WGS-84 radius

**Examples**

```
# two-column matrix with latitude/longitude, in degrees
latLong = cbind(runif(n = 5, min = 0, max = 90),
                runif(n = 5, min = 0, max = 180))

# Haversine distance formula
distMat = calcHaversine(latLongs = latLong)
```

---

calcHurdleExpKernel	<i>Calculate Zero-inflated Exponential Stochastic Matrix</i>
---------------------	--

---

**Description**

Given a distance matrix from [calcVinEll](#), calculate a stochastic matrix where one step movement probabilities follow an zero-inflated exponential density with a point mass at zero. The point mass at zero represents the first stage of a two-stage process, where mosquitoes decide to stay at their current node or leave anywhere. This parameter can be calculated from lifetime probabilities to stay at the current node with the helper function [calcZeroInflation](#).

**Usage**

```
calcHurdleExpKernel(distMat, rate, p0, eps = 1e-20)
```

**Arguments**

distMat	Distance matrix from <a href="#">calcVinEll</a>
rate	Rate parameter of <a href="#">Exponential</a> distribution
p0	Point mass at zero
eps	Cutoff for extremely small probabilities, default is 1e-20

**Details**

If a mosquito leaves its current node, with probability  $1 - p_0$ , it then chooses a destination node according to a standard exponential density with rate parameter *rate*.

The distribution and density functions for the zero inflated exponential kernel are given below:

$$F(x) = p_0\theta(x) + (1 - p_0)(1 - e^{-\lambda x})$$

$$f(x) = p_0\delta(x) + (1 - p_0)\lambda e^{-\lambda x}$$

where  $\lambda$  is the rate parameter of the exponential distribution,  $\theta(x)$  is the Heaviside step function and  $\delta(x)$  is the Dirac delta function.

**Examples**

```
# setup distance matrix
# two-column matrix with latitude/longitude, in degrees
latLong = cbind(runif(n = 5, min = 0, max = 90),
                runif(n = 5, min = 0, max = 180))

# Vincenty Ellipsoid distance formula
distMat = calcVinEll(latLongs = latLong)

# calculate hurdle exponential distribution over distances
# rate and point mass are just for example
kernMat = calcHurdleExpKernel(distMat = distMat, rate = 1/1e6, p0 = 0.1)
```

---

calcLognormalKernel    *Calculate Lognormal Stochastic Matrix*

---

**Description**

Given a distance matrix from [calcVinEll](#), calculate a stochastic matrix where one step movement probabilities follow a lognormal density.

**Usage**

```
calcLognormalKernel(distMat, meanlog, sdlog)
```

**Arguments**

distMat	Distance matrix from <a href="#">calcVinEll</a>
meanlog	Log mean of <a href="#">Lognormal</a> distribution
sdlog	Log standard deviation of <a href="#">Lognormal</a> distribution

**Details**

The distribution and density functions for the lognormal kernel are given below:

$$F(x) = \frac{1}{2} + \frac{1}{2} \operatorname{erf}\left[\frac{\ln x - \mu}{\sqrt{2}\sigma}\right]$$

$$f(x) = \frac{1}{x\sigma\sqrt{2\pi}} \exp\left(-\frac{(\ln x - \mu)^2}{2\sigma^2}\right)$$

where  $\mu$  is the mean on the log scale, and  $\sigma$  is the standard deviation on the log scale.

**Examples**

```
# setup distance matrix
# two-column matrix with latitude/longitude, in degrees
latLong = cbind(runif(n = 5, min = 0, max = 90),
                runif(n = 5, min = 0, max = 180))

# Vincenty Ellipsoid distance formula
distMat = calcVinEll(latLongs = latLong)

# calculate lognormal distribution over distances
# mean and standard deviation are just for example
kernMat = calcLognormalKernel(distMat = distMat, meanlog = 100, sdlog = 10)
```

---

 calcOmega

*Solve for Omega (additional genotype-specific mortality)*


---

**Description**

Solves for root of equation of geometrically-distributed lifespan for value of omega.

**Usage**

```
calcOmega(mu, lifespanReduction)
```

**Arguments**

```
mu           Daily mortality probability (discrete-time hazard, called muAd in code)
lifespanReduction Target reduced lifespan, between 0 and 1 (target average lifespan will be  $\frac{1}{\mu_{Ad}} \times$ 
lifespanReduction)
```

**Examples**

```
# reduce lifespan by 10%
# Example mu is an average for Aedes
newOmega <- calcOmega(mu = 0.11, lifespanReduction = 0.90)
```

---

 calcQuantiles

*Summary Statistics for Stochastic MGDriVE*


---

### Description

This function reads in all repetitions for each patch and calculates either the mean, quantiles, or both. User chooses the quantiles, up to 4 decimal places, and enters them as a vector. Quantiles are calculated empirically. (order does not matter)

### Usage

```
calcQuantiles(readDir, writeDir, mean = TRUE, quantiles = NULL, verbose = TRUE)
```

### Arguments

readDir	Directory to find repetition folders in
writeDir	Directory to write output
mean	Boolean, calculate mean or not. Default is TRUE
quantiles	Vector of quantiles to calculate. Default is NULL
verbose	Chatty? Default is TRUE

### Details

Given the readDir, this function assumes the follow file structure:

- readDir
  - repetition 1
    - \* patch 1
    - \* patch 2
    - \* patch 3
  - repetition 2
    - \* patch 1
    - \* patch 2
    - \* patch 3
  - repetition 3
  - repetition 4
  - ...

Output files are \*.csv contain the mean or quantile in the file name, i.e. {M/F}*Mean*(patchNum).csv and {M/F}*Quantile*(quantNum)\_(patchNum).csv.

**Value**

Writes output to files in writeDir

**Examples**

```
## Not run:
# This function assumes network$multRun() has been performed, or several
# network$oneRun() have been performed and all of the data has been split
# and aggregated.

# read/write paths
fPath <- "path/to/folder/ofFolders/with/data"
oPath <- "my/path/output"

# here, only calculate mean, no quantiles
# no return value
calcQuantiles(readDir = fPath, writeDir = oPath, mean = TRUE,
              quantiles = NULL)

# here, calculate 2.5% and 97.5% quantiles
calcQuantiles(readDir = fPath, writeDir = oPath, mean = FALSE,
              quantiles = c(0.025, 0.975))

## End(Not run)
```

---

 calcVinEll

---

*Calculate Geodesic Distance - Vincenty Ellipsoid Method*


---

**Description**

This function calculates geodesic distance using the original Vincenty Ellipsoid method.

**Usage**

```
calcVinEll(
  latLongs,
  a = 6378137,
  b = 6356752.3142,
  f = 1/298.257223563,
  eps = 1e-12,
  iter = 100
)
```

**Arguments**

latLongs	Two column matrix of latitudes/longitudes
a	Equatorial radius of the earth, default is WGS-84 radius

b	Polar radius of the earth, default is WGS-84 radius
f	Flattening or inverse eccentricity, default eccentricity is WGS-84
eps	Convergence criteria
iter	Maximum number of iterations to attempt convergence

### Examples

```
# two-column matrix with latitude/longitude, in degrees
latLong = cbind(runif(n = 5, min = 0, max = 90),
                runif(n = 5, min = 0, max = 180))

# Vincenty Ellipsoid distance formula
distMat = calcVinEll(latLongs = latLong)
```

---

calcVinSph

*Calculate Geodesic Distance - Vincenty Sphere Method*

---

### Description

This function calculates geodesic distance using the Vincenty sphere method.

### Usage

```
calcVinSph(latLongs, r = 6378137)
```

### Arguments

latLongs	Two column matrix of latitudes/longitudes
r	Earth radius. Default is WGS-84 radius

### Examples

```
# two-column matrix with latitude/longitude, in degrees
latLong = cbind(runif(n = 5, min = 0, max = 90),
                runif(n = 5, min = 0, max = 180))

# Vincenty Sphere distance formula
distMat = calcVinSph(latLongs = latLong)
```

---

calcZeroInflation	<i>Calculates the zero-inflation part of a hurdle exponential kernel.</i>
-------------------	---

---

**Description**

Given the probability of an adult mosquito to stay in the same patch throughout its whole lifespan, and its mortality, it calculates the height of the pulse-density part of the hurdle kernel.

**Usage**

```
calcZeroInflation(stayThroughLifespanProbability, adultMortality)
```

**Arguments**

```
stayThroughLifespanProbability
    Probability of a mosquito to spend its whole lifespan in the same node
adultMortality Adult mortality rate
```

**Examples**

```
# setup distance matrix
# two-column matrix with latitude/longitude, in degrees
latLong = cbind(runif(n = 5, min = 0, max = 90),
                runif(n = 5, min = 0, max = 180))

# Vincenty Ellipsoid distance formula
distMat = calcVinEll(latLongs = latLong)

# get hurdle height
# Lets assume 80% stay probs and adult mortality of 0.1
hHeight <- calcZeroInflation(stayThroughLifespanProbability = 0.80,
                             adultMortality = 0.1)

# calculate hurdle exponential distribution over distances
kernMat = calcHurdleExpKernel(distMat = distMat, rate = 10, p0 = hHeight)
```

---

cube2csv	<i>Export a Cube to .csv</i>
----------	------------------------------

---

**Description**

Export a cube as multiple .csv files (one for each genotype; slices of z-axis). This function will create the directory if it doesn't exist. Files are stored as slice\_(z-slice)\_(genotype).csv

**Usage**

```
cube2csv(cube, directory, digits = 3)
```

**Arguments**

cube	A cube object (see <a href="#">MGDrivE-Cube</a> for options)
directory	Directory to write .csv files to
digits	Number of significant digits to retain in .csv output

**Examples**

```
## Not run:
# output directory
oPath <- "path/to/write/output"

# setup inheritance cube for export, using Mendelian as the example
cube <- cubeMendelian()

# write out
cube2csv(cube = cube, directory = oPath, digits = 3)

## End(Not run)
```

---

cubeAlleleSail

*Inheritance Cube: 3-Piece Allele Sail*


---

**Description**

A generalized implementation of the Allele Sail ([doi:10.1038/s41467024509929](https://doi.org/10.1038/s41467024509929)) idea.

**Usage**

```
cubeAlleleSail(
  cMM = 0,
  crMM = 0,
  cPM = 0,
  crPM = 0,
  cMF = 0,
  crMF = 0,
  cPF = 0,
  crPF = 0,
  dMW = 0,
  dMrW = 0,
  dPW = 0,
  dPrW = 0,
  crF12 = 0.5,
```

```

    crM12 = 0.5,
    crF23 = 0.5,
    crM23 = 0.5,
    eta = NULL,
    phi = NULL,
    omega = NULL,
    xiF = NULL,
    xiM = NULL,
    s = NULL
)

```

### Arguments

cMM	Cutting efficacy of maternally-inherited Cas9 in males
crMM	Resistance rate of maternally-inherited Cas9 in males
cPM	Cutting efficacy of paternally-inherited Cas9 in males
crPM	Resistance rate of paternally-inherited Cas9 in males
cMF	Cutting efficacy of maternally-inherited Cas9 in females
crMF	Resistance rate of maternally-inherited Cas9 in females
cPF	Cutting efficacy of paternally-inherited Cas9 in females
crPF	Resistance rate of paternally-inherited Cas9 in females
dMW	Female deposition cutting rate, maternal Cas9
dMrW	Female deposition functional resistance rate, maternal Cas9
dPW	Female deposition (HH) cutting rate, paternal Cas9
dPrW	Female deposition (HH) functional resistance rate, paternal Cas9
crF12	Female crossover rate between loci 1 and 2, 0 is completely linked, 0.5 is unlinked, 1.0 is complete divergence
crM12	Male crossover rate between loci 1 and 2, 0 is completely linked, 0.5 is unlinked, 1.0 is complete divergence
crF23	Female crossover rate between loci 2 and 3, 0 is completely linked, 0.5 is unlinked, 1.0 is complete divergence
crM23	Male crossover rate between loci 2 and 3, 0 is completely linked, 0.5 is unlinked, 1.0 is complete divergence
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

## Details

This is an autosomal, 3-locus system. The first locus contains the Cas9 allele, the second locus carries the gRNA, and the third locus is the target. All loci can be linked/unlinked to the locus before it (so, 1 to 2 or 2 to 3). Cas9 efficacy due to provenance (mother vs father) is included.

This construct is very similar to our [2-locus Cleave and Rescue](https://doi.org/10.1101/2020.07.09.196253) design for Oberhofer et. al.(doi:10.1101/2020.07.09.196253).

This construct has 3 alleles at the first locus, 2 alleles at the second locus, and 3 alleles at the third locus.

- Locus 1
  - W: Wild-type
  - P: Paternal Cas9
  - M: Maternal Cas9
- Locus 2
  - W: Wild-type
  - G: gRNAs
- Locus 3
  - W: Wild-type
  - R: Resistant 1
  - B: Resistant 2

Female deposition is implemented incorrectly. Right now, it is performed on male alleles prior to zygote formation - it should happen post-zygote formation. Since this construct doesn't have HDR, this should be fine.

## Value

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeASmidler

*Inheritance Cube: Split-Drive for Andrea Smidler*

---

## Description

This is a modified split-drive construct for split-suppression drives. This is an autosomal, 2-locus drive. The first locus contains the Cas9 allele and the second locus has the gRNA construct. Cas9 efficacy in each sex is dependent upon parent of inheritance. This construct has 3 alleles at the first locus and 4 alleles at the second.

- Locus 1
  - W: Wild-type
  - P: Paternal Cas9

- M: Maternal Cas9
- Locus 2
  - W: Wild-type
  - G: gRNAs
  - R: Resistant 1
  - B: Resistant 2

### Usage

```
cubeASmidler(
  cMM = 0,
  chMM = 0,
  crMM = 0,
  cPM = 0,
  chPM = 0,
  crPM = 0,
  cMF = 0,
  chMF = 0,
  crMF = 0,
  cPF = 0,
  chPF = 0,
  crPF = 0,
  crF = 0.5,
  crM = 0.5,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

### Arguments

cMM	Cutting efficacy of maternally-inherited Cas9 in males
chMM	Homing efficacy of maternally-inherited Cas9 in males
crMM	Resistance rate of maternally-inherited Cas9 in males
cPM	Cutting efficacy of paternally-inherited Cas9 in males
chPM	Homing efficacy of paternally-inherited Cas9 in males
crPM	Resistance rate of paternally-inherited Cas9 in males
cMF	Cutting efficacy of maternally-inherited Cas9 in females
chMF	Homing efficacy of maternally-inherited Cas9 in females
crMF	Resistance rate of maternally-inherited Cas9 in females
cPF	Cutting efficacy of paternally-inherited Cas9 in females
chPF	Homing efficacy of paternally-inherited Cas9 in females

crPF	Resistance rate of paternally-inherited Cas9 in females
crF	Female crossover rate, 0 is completely linked, 0.5 is unlinked, 1.0 is complete divergence
crM	Male crossover rate, 0 is completely linked, 0.5 is unlinked, 1.0 is complete divergence
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeCLEAVRMF

*Inheritance Cube: CLEAVR - Cleave and Rescue*

---

**Description**

This is a novel cube from the Akbari lab. There are 2 loci: the first is a female fertility locus (e.g. doubleSex), where the Cas, gRNAs, and a recoded essential gene go. This locus is inherited in a Mendelian fashion, but is also targeted for destruction by the homing allele. The second locus involves an essential gene, for both males and females, and this is the target of the gRNAs at the first locus. No homing is performed, it is simply destroyed. There is different cutting rates in males and females, with no possibility for a rescuing resistant allele. Females homozygous for the H or B alleles at locus 1 are viable but infertile, while males are unaffected. All animals homozygous at locus two must contain the recoded copy at locus 1 to be viable. This version corresponds to the homing construct being autosomal.

**Usage**

```
cubeCLEAVRMF(
  cM1 = 1,
  cM2 = 1,
  cF1 = 1,
  cF2 = 1,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

cM1	Male cutting rate at first locus
cM2	Male cutting rate at second locus
cF1	Female cutting rate at first locus
cF2	Female cutting rate at second locus
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeCLEAVRX

*Inheritance Cube: CLEAVR - Cleave and Rescue*

---

**Description**

This is a novel cube from the Akbari lab. There are 2 loci: the first is a female fertility locus (e.g. doubleSex), where the Cas, gRNAs, and a recoded essential gene go. This locus is inherited in a Mendelian fashion, but is also targeted for destruction by the homing allele. The second locus involves an essential gene, for both males and females, and this is the target of the gRNAs at the first locus. No homing is performed, it is simply destroyed. There is different cutting rates in males and females, with no possibility for a rescuing resistant allele. Females homozygous for the H or B alleles at locus 1 are viable but infertile, while males are unaffected. All animals homozygous at locus two must contain the recoded copy at locus 1 to be viable. This corresponds to the homing construct being X-linked.

**Usage**

```
cubeCLEAVRX(
  cM1 = 1,
  cM2 = 1,
  cF1 = 1,
  cF2 = 1,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

cM1	Male cutting rate at first locus IS NOT USED IN THIS CUBE
cM2	Male cutting rate at second locus
cF1	Female cutting rate at first locus
cF2	Female cutting rate at second locus
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeClvR	<i>Inheritance Cube: ClvR (Cleave and Rescue)</i>
----------	---

---

**Description**

Based on the Cleave-and-Rescue system of Oberhofer et. al. ([doi:10.1073/pnas.1921698117](https://doi.org/10.1073/pnas.1921698117)), this is a 2-locus Cas9-based toxin-antidote system. The first locus carries the Cas9, gRNAs, and a recoded copy of an essential gene. The second locus is the targeted essential gene. This gene can be completely haplosufficient ( $hSuf = 1$ ) or completely haploinsufficient ( $hSuf = 0$ ). It is assumed that having 2 copies of the gene (be it wild-type at the second locus or recoded at the first) confers complete viability.

**Usage**

```
cubeClvR(
  cF = 1,
  crF = 0,
  ccF = cF,
  ccrF = crF,
  cM = 1,
  crM = 0,
  ccM = cM,
  ccrM = crM,
  dW = 0,
  drW = 0,
  ddW = dW,
  ddrW = drW,
```

```

hSuf = 1,
eta = NULL,
phi = NULL,
omega = NULL,
xiF = NULL,
xiM = NULL,
s = NULL
)

```

### Arguments

cF	Female cutting rate, one ClvR allele
crF	Female functional resistance rate, one ClvR allele
ccF	Female cutting rate, two ClvR alleles
ccrF	Female functional resistance rate, two ClvR alleles
cM	Male cutting rate, one ClvR allele
crM	Male functional resistance rate, one ClvR allele
ccM	Male cutting rate, two ClvR alleles
ccrM	Male functional resistance rate, two ClvR alleles
dW	Female deposition cutting rate
drW	Female deposition functional resistance rate
ddW	Female deposition (HH) cutting rate
ddrW	Female deposition (HH) functional resistance rate
hSuf	Haplosufficiency level, default is completely sufficient
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

### Value

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

cubeClvR2

*Inheritance Cube: 2-Locus ClvR (Cleave and Rescue)***Description**

Based on the Cleave-and-Rescue system of Oberhofer et. al. ([doi:10.1101/2020.07.09.196253](https://doi.org/10.1101/2020.07.09.196253)), this is a 3-locus Cas9-based toxin-antidote system. The first locus carries the Cas9, the second locus carries the gRNAs, and a recoded copy of an essential gene. The third locus is the targeted essential gene. This gene can be completely haplosufficient ( $hSuf = 1$ ) or completely haploinsufficient ( $hSuf = 0$ ). It is assumed that having 2 copies of the gene (be it wild-type at the second locus or recoded at the first) confers complete viability. Additionally, loci 1 and 2 can be linked, given crM and crF, imitating the original 2-locus ClvR system. For this construct, the first locus will have 2 alleles, the second will have 2 alleles, and the third will have 3 alleles:

- Locus 1
  - W: Wild-type
  - C: Cas9
- Locus 2
  - W: Wild-type
  - G: gRNAs and recoded essential gene
- Locus 3
  - W: Wild-type
  - R: Functional resistant
  - B: Non-functional resistant

**Usage**

```
cubeClvR2(
  cF = 1,
  crF = 0,
  ccF = cF,
  ccrF = crF,
  cM = 1,
  crM = 0,
  ccM = cM,
  ccrM = crM,
  dW = 0,
  drW = 0,
  ddW = dW,
  ddrW = drW,
  hSuf = 1,
  crossF = 0.5,
  crossM = 0.5,
  eta = NULL,
  phi = NULL,
```

```

    omega = NULL,
    xiF = NULL,
    xiM = NULL,
    s = NULL
)

```

### Arguments

cF	Female cutting rate, one CivR allele
crF	Female functional resistance rate, one CivR allele
ccF	Female cutting rate, two CivR alleles
ccrF	Female functional resistance rate, two CivR alleles
cM	Male cutting rate, one CivR allele
crM	Male functional resistance rate, one CivR allele
ccM	Male cutting rate, two CivR alleles
ccrM	Male functional resistance rate, two CivR alleles
dW	Female deposition cutting rate
drW	Female deposition functional resistance rate
ddW	Female deposition (HH) cutting rate
ddrW	Female deposition (HH) functional resistance rate
hSuf	Haplosufficiency level, default is completely sufficient
crossF	Crossover rate in females, 0 is completely linked, 0.5 is unlinked, 1.0 is complete divergence
crossM	Crossover rate in males, 0 is completely linked, 0.5 is unlinked, 1.0 is complete divergence
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

### Details

Female deposition is implemented incorrectly. Right now, it is performed on male alleles prior to zygote formation - it should happen post-zygote formation. Since this construct doesn't have HDR, this should be fine.

Additionally, it is assumed that deposition requires loaded Cas9-RNP complexes from the mother, having Cas9 and no maternal gRNA, even in the presence of paternal gRNA, will not result in maternal deposition mediated cleavage.

Copy-number dependent rates are based on Cas9, not gRNA. The assumption is that RNA is easier to produce, and therefore won't limit cleavage by Cas9.

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeConfinableHoming *Inheritance Cube: Confinable Homing*

---

**Description**

This function creates a confinable homing construct, it has 4 alleles at the first locus and 3 alleles at the second.

- W: Wild-type
- H: Homing allele
- A: Antidote allele
- R: No-cost resistance allele
- B: Detrimental resistance allele

**Usage**

```
cubeConfinableHoming(
  cF = 1,
  cM = 1,
  chF = 0,
  crF = 0,
  chM = 0,
  crM = 0,
  dR = 0,
  dB = 0,
  crossF = 0,
  crossM = 0,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

cF	Cutting efficiency of drive allele at locus 1 in females
cM	Cutting efficiency of drive allele at locus 1 in males
chF	Homing efficiency of drive allele at locus 1 in females
crF	Resistance allele generation rate at locus 1 in females

chM	Homing efficiency of drive allele at locus 1 in males
crM	Resistance allele generation rate at locus 1 in males
dR	Background mutation rate from W and H into R allele in males and females
dB	Background mutation rate from A into B allele in males and females
crossF	Female crossover rate
crossM	Male crossover rate
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeConfinableHomingJOHN

*Inheritance Cube: Confinable Homing Drive, John*

---

**Description**

write me

**Usage**

```
cubeConfinableHomingJOHN(
  eM = 1,
  eF = 1,
  prRF = 0,
  prRM = 0,
  r = 0,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

eM	Male homing rate
eF	Female homing rate
prRF	Female no-cost resistant allele generation rate
prRM	Male no-cost resistant allele generation rate
r	Crossover probability
eta	genotype-specific mating fitness
phi	genotype-specific sex ratio at emergence
omega	genotype-specific multiplicative modifier of adult mortality
xiF	genotype-specific female pupatory success
xiM	genotype-specific male pupatory success
s	genotype-specific fractional reduction(increase) in fertility

---

cubeConfinableHomingX *Inheritance Cube: Confinable Homing, X-Linked*

---

**Description**

This function creates an X-linked confinable homing construct, it has 5 alleles at the first locus and 4 alleles at the second. No crossovers or homing occurs into the y chromosome

- W: Wild-type
- H: Homing allele
- A: Antidote allele
- R: No-cost resistance allele
- B: Detrimental resistance allele
- Y: Male allele

**Usage**

```
cubeConfinableHomingX(
  cF = 1,
  chF = 0,
  crF = 0,
  dR = 0,
  dB = 0,
  crossF = 0,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

cF	Cutting efficiency of drive allele at locus 1 in females
chF	Homing efficiency of drive allele at locus 1 in females
crF	Resistance allele generation rate at locus 1 in females
dR	Background mutation rate from W and H into R allele in males and females
dB	Background mutation rate from A into B allele in males and females
crossF	Female crossover rate.
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeECHACR

*Inheritance Cube: ECHACR*

---

**Description**

This function creates an ECHACR construct, it has 5 alleles at the first locus and 4 alleles at the second.

- W: Wild-type
- H: Homing allele
- E: Eraser allele
- R: No-cost resistance allele
- B: Detrimental resistance allele
- cHW: Rate of homing from H, W -> H transition
- cEH: Rate of homing from E, H -> E transition
- cEW: Rate of homing from E, W -> E transition

**Usage**

```

cubeECHACR(
  cHW = 1,
  cEW = 1,
  cEH = 1,
  chHW = 0,
  crHW = 0,
  ceEW = 0,
  crEW = 0,
  ceEH = 0,
  crEH = 0,
  d1 = 0,
  d2 = 0,
  d3 = 0,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)

```

**Arguments**

cHW	Cutting efficiency of drive allele at locus 1
cEW	Cutting efficiency of ECHACR element into W
cEH	Cutting efficiency of ECHACR element into H
chHW	Homing efficiency of drive allele at locus 1
crHW	Resistance allele efficiency of drive allele at locus 1
ceEW	Homing efficiency of ECHACR element into W
crEW	Resistance allele efficiency of ECHACR element into W
ceEH	Homing efficiency of ECHACR element into H
crEH	Resistance allele efficiency of ECHACR element into H
d1	Background mutation rate from W into R allele
d2	Background mutation rate from H into R allele
d3	Background mutation rate from E into R allele
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Details**

This inheritance pattern corresponds to the Active Genetic Neutralizing Elements for Halting or Deleting Gene Drives ([doi:10.1016/j.molcel.2020.09.003](https://doi.org/10.1016/j.molcel.2020.09.003)) publication.

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

 cubeECHACRX

*Inheritance Cube: ECHACRX*


---

**Description**

This function creates an X-linked ECHACR construct, it has 5 alleles at the first locus and 4 alleles at the second.

- W: Wild-type
- H: Homing allele
- E: Eraser allele
- R: No-cost resistance allele
- B: Detrimental resistance allele
- cHW: Rate of homing from H, W -> H transition
- cEH: Rate of homing from E, H -> E transition
- cEW2: Rate of homing from E, W -> E transition

**Usage**

```
cubeECHACRX(
  cHW = 1,
  cEHW = 1,
  cEW1 = 1,
  cEW2 = 1,
  cEH = 1,
  chHW = 0,
  crHW = 0,
  chEHW = 0,
  crEHW = 0,
  ceEW1 = 0,
  crEW1 = 0,
  ceEW2 = 0,
  crEW2 = 0,
  ceEH = 0,
  crEH = 0,
  d1 = 0,
```

```

d2 = 0,
d3 = 0,
dHW = 0,
dEH = 0,
dEW = 0,
drHW = 0,
drEH = 0,
drEW = 0,
crossF = 0,
eta = NULL,
phi = NULL,
omega = NULL,
xiF = NULL,
xiM = NULL,
s = NULL
)

```

### Arguments

cHW	Cutting efficiency of drive allele at locus 1
cEHW	Cutting efficiency of drive allele, in the presence of ECHACR element, at locus 1
cEW1	Cutting efficiency of ECHACR element into W at locus 1
cEW2	Cutting efficiency of ECHACR element into W at locus 2
cEH	Cutting efficiency of ECHACR element into H
chHW	Homing efficiency of drive allele at locus 1
crHW	Resistance allele efficiency of drive allele at locus 1
chEHW	Homing efficiency of drive allele, in the presence of ECHACR element, at locus 1
crEHW	Resistance allele efficiency of drive allele, in the presence of ECHACR element, at locus 1
ceEW1	Homing efficiency of ECHACR element into W at locus 1
crEW1	Resistance allele efficiency of ECHACR element into W at locus 1
ceEW2	Homing efficiency of ECHACR element into W at locus 2
crEW2	Resistance allele efficiency of ECHACR element into W at locus 2
ceEH	Homing efficiency of ECHACR element into H
crEH	Resistance allele efficiency of ECHACR element into H
d1	Background mutation rate from W into R allele
d2	Background mutation rate from H into R allele
d3	Background mutation rate from E into R allele
dHW	Female H deposition rate against W
dEH	Female E deposition rate against H
dEW	Female E deposition rate against W

drHW	Female resistance generation rate, from H allele
drEH	Female resistance generation rate, from E allele
drEW	Female resistance generation rate, from E allele
crossF	Female crossover rate. 0 is fully linked, 0.5 is unlinked, 1 is negatively linked
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

### Details

This inheritance pattern corresponds to the Active Genetic Neutralizing Elements for Halting or Deleting Gene Drives ([doi:10.1016/j.molcel.2020.09.003](https://doi.org/10.1016/j.molcel.2020.09.003)) publication.

### Value

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeHoming1RA

*Inheritance Cube: Homing Drive with 1 Resistance Allele*

---

### Description

This function creates an inheritance cube to model a homing gene drive (such as a CRISPR-Cas9 system) that creates 1 type of resistance allele. It assumes no sex-specific inheritance patterns and the construct is on an autosome.

### Usage

```
cubeHoming1RA(
  c = 1,
  ch = 0,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

c	Cutting rate
ch	Successful homing rate rate
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeHomingDrive	<i>Inheritance Cube: CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) with 2 Resistance Alleles and maternal deposition</i>
-----------------	---

---

**Description**

This is a sex-specific version of the original cube [cubeHoming1RA](#). It assumes that the construct is on an autosome and there can be different male/female homing rates. It also has maternal deposition, i.e., when the male provides a W allele to a female with a H allele, some portion are cut during oogenesis. If the maternal deposition parameters are zero (d\* parameters), this is a normal CRISPR drive.

**Usage**

```
cubeHomingDrive(
  cM = 1,
  cF = 1,
  dF = 0,
  chM = 0,
  crM = 0,
  chF = 0,
  crF = 0,
  dhF = 0,
  drF = 0,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

cM	Male homing rate
cF	Female homing rate
dF	Female deposition homing rate
chM	Male correct homing rate
crM	Male resistance generating rate
chF	Female correct homing rate
crF	Female resistance generating rate
dhF	Female correct deposition rate
drF	Female resistance deposition rate
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeHomingDriveSM	<i>Inheritance Cube: CRISPR-SM (Clustered Regularly Interspaced Short Palindromic Repeats) with Small-Molecule Induction and I Resistance Allele and Maternal Deposition</i>
-------------------	--

---

**Description**

This is a sex-specific version of CRISPR with small-molecule induced homing. It assumes that the construct is on an autosome and there can be different male/female homing rates. It also has maternal deposition, i.e., when the male provides a W allele to a female with a H allele, some portion are cut during oogenesis. Additionally, this cube is designed for small-molecule induction, i.e., with the SM branch of MGDriVE. It allows the homing (H) allele to be turned off into an O allele, which inherits stably, and so that all offspring of H individuals are O until turned on with the spray. If the maternal deposition parameters are zero (d\* parameters), this is a normal CRISPR drive.

**Usage**

```

cubeHomingDriveSM(
  cM = 1,
  cF = 1,
  dF = 0,
  chM = 0,
  chF = 0,
  dhF = 0,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)

```

**Arguments**

cM	Male homing rate
cF	Female homing rate
dF	Female deposition homing rate
chM	Male correct homing rate
chF	Female correct homing rate
dhF	Female correct deposition rate
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeImmunizingReversalMF

*Inheritance Cube: Immunizing Reversal/Basic Reversal*

---

**Description**

This function creates an Immunizing Reversal construct, it has 5 alleles at 1 locus

- W: Wild-type
- H: Homing allele
- E: Eraser allele
- R: No-cost resistance allele
- B: Detrimental resistance allele

**Usage**

```
cubeImmunizingReversalMF(  
  cHWM = 1,  
  cHWF = 1,  
  cEWM = 1,  
  cEWF = 1,  
  cEHM = 1,  
  cEHF = 1,  
  chHWM = 0,  
  chHWF = 0,  
  crHWM = 0,  
  crHWF = 0,  
  ceEWM = 0,  
  ceEWF = 0,  
  crEWM = 0,  
  crEWF = 0,  
  ceEHM = 0,  
  ceEHF = 0,  
  crEHM = 0,  
  crEHF = 0,  
  dHW = 0,  
  dEW = 0,  
  dEH = 0,  
  dhHW = 0,  
  drHW = 0,  
  deEW = 0,  
  drEW = 0,  
  deEH = 0,  
  drEH = 0,  
  eta = NULL,  
  phi = NULL,  
  omega = NULL,  
  xiF = NULL,  
  xiM = NULL,  
  s = NULL  
)
```

**Arguments**

cHWM	Cutting efficiency of H into W in males
cHWF	Cutting efficiency of H into W in females
cEWM	Cutting efficiency of E into W in males
cEWF	Cutting efficiency of E into W in females
cEHM	Cutting efficiency of E into H in males
cEHF	Cutting efficiency of E into H in females
chHWM	Homing efficiency of H into W in males
chHWF	Homing efficiency of H into W in females
crHWM	Resistance efficiency of H into W in males
crHWF	Resistance efficiency of H into W in females
ceEWM	Homing efficiency of E into W in males
ceEWF	Homing efficiency of E into W in females
crEWM	Resistance efficiency of E into W in males
crEWF	Resistance efficiency of E into W in females
ceEHM	Homing efficiency of E into H in males
ceEHF	Homing efficiency of E into H in females
crEHM	Resistance efficiency of E into H in males
crEHF	Resistance efficiency of E into H in females
dHW	Deposition cutting efficiency of H into W
dEW	Deposition cutting efficiency of E into W
dEH	Deposition cutting efficiency of E into H
dhHW	Deposition homing efficiency of H into W
drHW	Deposition resistance efficiency of H into W
deEW	Deposition homing efficiency of E into W
drEW	Deposition resistance efficiency of E into W
deEH	Deposition homing efficiency of E into H
drEH	Deposition resistance efficiency of E into H
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Details**

This is the general form for an immunizing reversal drive. If the *EW* terms are 0, then this simplifies to a basic reversal drive. This drive handles different male and female homing rates, and female deposition from each allele, signifying differential expression from an autosome.

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeImmunizingReversalX

*Inheritance Cube: Immunizing Reversal*

---

**Description**

This function creates an Immunizing Reversal construct, it has 5 alleles at 1 locus

- W: Wild-type
- H: Homing allele
- E: Eraser allele
- R: No-cost resistance allele
- B: Detrimental resistance allele

**Usage**

```
cubeImmunizingReversalX(  
  cHW = 1,  
  cEW = 1,  
  cEH = 1,  
  chHW = 0,  
  crHW = 0,  
  ceEW = 0,  
  crEW = 0,  
  ceEH = 0,  
  crEH = 0,  
  dHW = 0,  
  dEW = 0,  
  dEH = 0,  
  dhHW = 0,  
  drHW = 0,  
  deEW = 0,  
  drEW = 0,  
  deEH = 0,  
  drEH = 0,  
  eta = NULL,  
  phi = NULL,  
  omega = NULL,  
  xiF = NULL,  
  xiM = NULL,  
  s = NULL  
)
```

**Arguments**

cHW	Cutting efficiency of H into W
cEW	Cutting efficiency of E into W
cEH	Cutting efficiency of E into H
chHW	Homing efficiency of H at W
crHW	Resistance generation efficiency of H at W
ceEW	Homing efficiency of E at W
crEW	Resistance generation efficiency of E at W
ceEH	Homing efficiency of E at H
crEH	Resistance efficiency of E at H
dHW	H deposition efficiency against W
dEW	E deposition efficiency against W
dEH	E deposition efficiency against H
dhHW	H deposition homing efficiency against W
drHW	H deposition resistance efficiency against W
deEW	E deposition homing efficiency against W
drEW	E deposition resistance efficiency against W
deEH	E deposition homing efficiency against H
drEH	E deposition resistance efficiency against H
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Details**

This is the general form for an immunizing reversal drive. If the  $c_{EW}$  and  $d_{EW}$ , parameters are all 0, then this simplifies to a basic reversal drive. This drive represents an X-linked IR drive.

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeKillerRescue      *Inheritance Cube: Killer-Rescue System*

---

### Description

This function creates an inheritance cube to model a Killer-Rescue system. Killer-Rescue is a 2-locus system: one locus has a toxin and the other locus contains the antidote. The loci are assumed independent and are non-homing.

This drive has 3 alleles at locus 1 and 2 alleles and locus 2:

- Locus 1
  - T: Wild-type allele
  - K: "Killer" toxin allele
  - R: Broken toxin allele
- Locus 2
  - W: Wild-type allele
  - A: Antidote allele

### Usage

```
cubeKillerRescue(
  eR = 0,
  Keff = 1,
  Aeff = 1,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

### Arguments

eR	Conversion of K allele to R allele, a basal mutation rate
Keff	Toxin efficacy
Aeff	Antidote efficacy
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeMEDEA	<i>Inheritance Cube: MEDEA (Maternal Effect Dominant Embryonic Arrest)</i>
-----------	--

---

**Description**

This function creates an inheritance cube to model a MEDEA drive system. This system was first discovered in flour beetles. It biases inheritance by expressing a maternal toxin such that offspring die unless they express a zygotic antidote.

This drive has 3 alleles at 1 locus:

- W: Wild-type allele
- M: MEDEA allele
- R: Resistance allele

**Usage**

```
cubeMEDEA(
  rM = 0,
  rW = 0,
  Teff = 1,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

rM	Breakdown of MEDEA allele, no homing/toxin/antidote, M -> R conversion
rW	De novo resistance generation, W -> R conversion
Teff	Efficacy of the toxin
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeMendelian	<i>Inheritance Cube: Mendelian</i>
---------------	------------------------------------

---

**Description**

This function creates a Mendelian Inheritance Cube. It only handles simple, alphabetic genotypes. The default is 3 alleles at 1 locus, this can be extended to however many alleles one is interested in, but only at 1 locus.

**Usage**

```
cubeMendelian(
  gtype = c("AA", "Aa", "aa"),
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

gtype	Vector of genotypes, with the wild-type in the first position
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

 cubeOneLocusTA

*Inheritance Cube: 1 Locus Maternal-Toxin/Zygotic-Antidote System*


---

### Description

This function creates a 1 locus maternal-toxin/zygotic-antidote system. This is similar to the construct called UDMel. There is no resistance generation in this model.

This drive has 3 alleles at 1 locus:

- A: Maternal-toxin 1, zygotic-antidote 2
- B: Maternal-toxin 2, zygotic-antidote 1
- W: Wild-type allele

### Usage

```
cubeOneLocusTA(
  TAEfficacy = 1,
  TBEfficacy = 1,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

### Arguments

TAEfficacy	Maternal toxin A efficacy
TBEfficacy	Maternal toxin B efficacy
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

### Value

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

 cubeReciprocalTranslocations

*Inheritance Cube: Reciprocal Translocation*


---

### Description

This function creates an inheritance cube to model a reciprocal translocation. This technology was the original form of underdominant system. It involves 2 chromosomes, each with two alleles. This drive has 4 alleles at 2 loci:

- a: Wild-type at locus A
- A: Translocation at locus A
- b: Wild-type at locus B
- B: Translocation at locus B

### Usage

```
cubeReciprocalTranslocations(
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

### Arguments

eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

### Value

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

 cubeRIDL

*Inheritance Cube: RIDL (Release of Insects with Dominant Lethality)*


---

### Description

This function creates a RIDL system. RIDL (Release of Insects with Dominant Lethality), is a form of SIT. Created by Oxitec, this is based on a positive feedback loop using the toxic tTAV gene, controlled under lab conditions by the TetO promoter. This has 2 alleles at 1 locus

- W: Wild-type allele
- R: OX513 RIDL allele

### Usage

```
cubeRIDL(
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

### Arguments

eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

### Value

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

cubeSplitDrive

*Inheritance Cube: Split CRISPR Drive with 2 Resistance Alleles and male/female specific homing***Description**

This is a sex-specific version of a split CRISPR drive. At one locus is the Cas9, inherited in a Mendelian fashion. At a second, unlinked, locus are the gRNAs. When the two loci occur together, the gRNAs drive, with potential damaged alleles, but the Cas9 remains Mendelian. It is assumed that this is an autosomal drive. This drive corresponds to the **confinable gene drive system** developed by the Akbari lab.

**Usage**

```
cubeSplitDrive(
  cM = 1,
  chM = 0,
  crM = 0,
  ccM = cM,
  cchM = chM,
  ccrM = crM,
  cF = 1,
  chF = 0,
  crF = 0,
  ccF = cF,
  cchF = chF,
  ccrF = crF,
  dW = 0,
  dhW = 0,
  drW = 0,
  ddW = dW,
  ddhW = dhW,
  ddrW = drW,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

cM	Cutting efficiency in males, one Cas9 allele
chM	Homing efficiency in males, one Cas9 allele
crM	Resistance efficiency in males, one Cas9 allele

ccM	Cutting efficiency in males, two Cas9 alleles
cchM	Homing efficiency in males, two Cas9 alleles
ccrM	Resistance efficiency in males, two Cas9 alleles
cF	Cutting efficiency in females, one Cas9 allele
chF	Homing efficiency in females, one Cas9 allele
crF	Resistance efficiency in females, one Cas9 allele
ccF	Cutting efficiency in females, two Cas9 alleles
cchF	Homing efficiency in females, two Cas9 alleles
ccrF	Resistance efficiency in females, two Cas9 alleles
dW	Maternal deposition cutting, one Cas9 allele
dhW	Maternal deposition homing, one Cas9 allele
drW	Maternal deposition resistance, one Cas9 allele
ddW	Maternal deposition cutting, two Cas9 alleles
ddhW	Maternal deposition homing, two Cas9 alleles
ddrW	Maternal deposition resistance, two Cas9 alleles
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

### Value

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeSplitDriveX	<i>Inheritance Cube: X-linked Split CRISPR Drive with 2 Resistance Alleles and male/female specific homing</i>
-----------------	--

---

### Description

This is a X-linked, sex-specific version of a split CRISPR drive. At the X locus is the Cas9, inherited in a Mendelian fashion. At a second, unlinked, autosomal locus are the gRNAs. When the two loci occur together, the gRNAs drive, with potential damaged alleles, but the Cas9 remains Mendelian. Deposition in this cube is performed when both pieces come together in females. This drive has 2 loci:

- "Locus" 1, sex chromosomes, has 3 alleles
  - X: Wild-type X chromosome

- C: X-chromosome carrying a Cas9 construct
- Y: Wild-type Y chromosome
- Locus 2, autosomal locus, has 4 alleles:
  - W: Wild-type allele
  - G: gRNA allele
  - R: Functional or low-cost resistance allele
  - B: Non-functional or high-cost resistance allele

### Usage

```
cubeSplitDriveX(
  cM = 1,
  chM = 0,
  crM = 0,
  cF = 1,
  chF = 0,
  crF = 0,
  ccF = cF,
  cchF = chF,
  ccrF = crF,
  dW = 0,
  dhW = 0,
  drW = 0,
  ddW = dW,
  ddhW = dhW,
  ddrW = drW,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

### Arguments

cM	Cutting efficiency in males
chM	Homing efficiency in males
crM	Resistance efficiency in males
cF	Cutting efficiency in females, one Cas9 allele
chF	Homing efficiency in females, one Cas9 allele
crF	Resistance efficiency in females, one Cas9 allele
ccF	Cutting efficiency in females, two Cas9 alleles
cchF	Homing efficiency in females, two Cas9 alleles
ccrF	Resistance efficiency in females, two Cas9 alleles

dw	Maternal deposition cutting, one Cas9 allele
dhw	Maternal deposition homing, one Cas9 allele
drw	Maternal deposition resistance, one Cas9 allele
ddw	Maternal deposition cutting, two Cas9 alleles
ddhw	Maternal deposition homing, two Cas9 alleles
ddrw	Maternal deposition resistance, two Cas9 alleles
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

### Value

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeSplitDriveY	<i>Inheritance Cube: Y-linked Split CRISPR Drive with 2 Resistance Alleles</i>
-----------------	--

---

### Description

This is a Y-linked version of a split CRISPR drive. At the Y-locus is the Cas9, inherited in a Mendelian fashion. At a second, unlinked, autosomal locus are the gRNAs. When the two loci occur together (i.e. in males), the gRNAs drive, with potential damaged alleles, but the Cas9 remains Mendelian. This drive has 2 loci:

- "Locus" 1, sex chromosomes, has 3 alleles:
  - X: Wild-type X chromosome
  - Y: Wild-type Y chromosome
  - C: Y chromosome with Cas9
- Locus 2, autosomal locus, has 4 alleles:
  - W: Wild-type allele
  - G: gRNA allele
  - R: Functional or low-cost resistance allele
  - B: Non-functional or high-cost resistance allele

**Usage**

```
cubeSplitDriveY(
  cM = 1,
  chM = 0,
  crM = 0,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

cM	Cutting efficiency in males
chM	Homing efficiency in males
crM	Resistance efficiency in males
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

 cubeTGD

*Inheritance Cube: tGD*


---

**Description**

The trans-complementing Gene Drive (tGD) is a 1-locus, 2 target site drive. The first target site corresponds to the Cas protein, the second to an effector gene and the gRNAs. There are two sets of gRNAs, because each target site may have different cutting/homing/resistance rates, and each sex can have different rates for all of those things. Additionally, the parent that you receive your Cas from dictates its efficiency. Therefore, this construct has 5 alleles at the first locus and 4 alleles at the second.

- Locus 1
  - W: Wild-type

- P: Paternal Cas9
- M: Maternal Cas9
- R: Resistant allele 1
- B: Resistant allele 2
- Locus 2
  - W: Wild-type
  - G: gRNAs
  - R: Resistant 1
  - B: Resistant 2

### Usage

```
cubeTGD(
  cM1 = 0,
  cM2 = 0,
  cP1 = 0,
  cP2 = 0,
  hM1 = 0,
  hM2 = 0,
  hP1 = 0,
  hP2 = 0,
  rM1 = 0,
  rM2 = 0,
  rP1 = 0,
  rP2 = 0,
  crM = 0,
  crP = 0,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

### Arguments

cM1	Maternally inherited Cas9 cutting rate at locus 1
cM2	Maternally inherited Cas9 cutting rate at locus 2
cP1	Paternally inherited Cas9 cutting rate at locus 1
cP2	Paternally inherited Cas9 cutting rate at locus 2
hM1	Maternally inherited Cas9 homing efficiency at locus 1
hM2	Maternally inherited Cas9 homing efficiency at locus 2
hP1	Paternally inherited Cas9 homing efficiency at locus 1
hP2	Paternally inherited Cas9 homing efficiency at locus 2

rM1	Maternally inherited Cas9 resistance efficiency at locus 1
rM2	Maternally inherited Cas9 resistance efficiency at locus 2
rP1	Paternally inherited Cas9 resistance efficiency at locus 1
rP2	Paternally inherited Cas9 resistance efficiency at locus 2
crM	Maternal crossover rate, 0 is completely linked, 0.5 is unlinked, 1.0 is complete divergence
crP	Paternal crossover rate, 0 is completely linked, 0.5 is unlinked, 1.0 is complete divergence
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

### Details

This drive corresponds to the **transcomplementing gene drive** developed by the Gantz and Bier lab.

### Value

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeTGDX

*Inheritance Cube: tGDX*

---

### Description

The trans-complementing Gene Drive (tGD) is a 1-locus, 2 target site drive. The first target site corresponds to the Cas protein, the second to an effector gene and the gRNAs. There are two sets of gRNAs, because each target site may have different cutting/homing/resistance rates, and each sex can have different rates for all of those things. Additionally, the parent that you receive your Cas from dictates its efficiency. Therefore, this construct has 6 alleles at the first locus and 5 alleles at the second.

- Locus 1
  - W: Wild-type
  - P: Paternal Cas9
  - M: Maternal Cas9
  - R: Resistant allele 1
  - B: Resistant allele 2
  - Y: Y allele

- Locus 2
  - W: Wild-type
  - G: gRNAs
  - R: Resistant 1
  - B: Resistant 2
  - Y: Y allele

### Usage

```
cubeTGDX(
  cM1 = 0,
  cM2 = 0,
  cP1 = 0,
  cP2 = 0,
  hM1 = 0,
  hM2 = 0,
  hP1 = 0,
  hP2 = 0,
  rM1 = 0,
  rM2 = 0,
  rP1 = 0,
  rP2 = 0,
  crM = 0,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

### Arguments

cM1	Maternally inherited Cas9 cutting rate at locus 1
cM2	Maternally inherited Cas9 cutting rate at locus 2
cP1	Paternaly inherited Cas9 cutting rate at locus 1
cP2	Paternaly inherited Cas9 cutting rate at locus 2
hM1	Maternally inherited Cas9 homing efficiency at locus 1
hM2	Maternally inherited Cas9 homing efficiency at locus 2
hP1	Paternaly inherited Cas9 homing efficiency at locus 1
hP2	Paternaly inherited Cas9 homing efficiency at locus 2
rM1	Maternally inherited Cas9 resistance efficiency at locus 1
rM2	Maternally inherited Cas9 resistance efficiency at locus 2
rP1	Paternaly inherited Cas9 resistance efficiency at locus 1
rP2	Paternaly inherited Cas9 resistance efficiency at locus 2

crM	Maternal crossover rate, 0 is completely linked, 0.5 is unlinked, 1.0 is complete divergence
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

### Details

This drive corresponds to the **transcomplementing gene drive** developed by the Gantz and Bier lab.

### Value

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeTwoLocusTA

*Inheritance Cube: 2 Locus Maternal-Toxin/Zygotic-Antidote System*

---

### Description

This function creates a 2 locus maternal-toxin/zygotic-antidote system. This is similar to the construct called UDMel. There is no resistance generation in this model.

This drive has 2 unlinked alleles, 1 allele each at 2 loci:

- A: Maternal-toxin 1, zygotic-antidote 2
- a: Wild-type at locus A
- B: Maternal-toxin 2, zygotic-antidote 1
- b: Wild-type at locus B

### Usage

```
cubeTwoLocusTA(
  TAEfficacy = 1,
  TBEfficacy = 1,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

TAEfficacy	Maternal toxin A efficacy
TBEfficacy	Maternal toxin B efficacy
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeWolbachia	<i>Inheritance Cube: Wolbachia</i>
---------------	------------------------------------

---

**Description**

This function creates an inheritance cube to model a Wolbachia infection. Wolbachia is a parasite that can infect mosquitoes. It biases its inheritance through cytoplasmic incompatibility. This drive has 2 alleles at 1 locus:

- W: has Wolbachia
- w: does not have Wolbachia

**Usage**

```
cubeWolbachia(
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Details**

Cytoplasmic Incompatibility:

- male W cross female w -> all offspring die (complete penetrance)
- male w cross female W -> all offspring inherit Wolbachia

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeXHomingDeposition *Inheritance Cube: CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) X-linked with 2 Resistance Allele and Maternal Deposition*

---

**Description**

This is an X-linked version of the 2 allele cube. It assumes that the construct is on the X chromosome and there is no male homing. It also has maternal deposition, i.e., when the male provides a W allele to a female with an H allele, some portion are cut during oogenesis. If the deposition parameters are zero (\*D parameters), this is just an X-linked drive.

**Usage**

```
cubeXHomingDeposition(
  cF = 1,
  chF = 0,
  crF = 0,
  dF = 0,
  dhF = 0,
  drF = 0,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

cF	Female cutting rate
chF	Female proper homing rate
crF	Female no-cost resistance generation rate
dF	Female deposition cutting rate

dhF	Female deposition proper homing rate
drF	Female deposition no-cost resistance generation rate
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

### Value

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeXShredderMF	<i>Inheritance Cube: Autosomal X-Shredder</i>
-----------------	---

---

### Description

This function creates an inheritance cube to model an autosomal X-Shredder construct. This construct resides on an autosomal chromosome, and chops the X chromosome into many pieces during gametogenesis, destroying the X chromosome. Thus, males may only produce Y gametes and females can become sterile.

This drive has 2 loci:

- Locus 1, the autosomal locus, has 3 alleles:
  - W: Wild-type allele
  - A: Attacking allele, contains the shredder construct
  - B: Broken attacking allele, shredder construct is defunct
- Locus 2, the sex locus, has 3 alleles:
  - X: Wild-type X allele
  - R: X-allele resistant to cleavage
  - Y: Wild-type Y allele

### Usage

```
cubeXShredderMF(
  cM = 1,
  cF = 1,
  crM = 0,
  crF = 0,
  cbM = 0,
  cbF = 0,
  eta = NULL,
```

```

    phi = NULL,
    omega = NULL,
    xiF = NULL,
    xiM = NULL,
    s = NULL
)

```

### Arguments

cM	Rate of X shredding in males (default is 1, complete shredding)
cF	Rate of X shredding in females (default is 1, complete shredding)
crM	Rate of resistance chromosome generation in males (default is 0)
crF	Rate of resistance chromosome generation in females (default is 0)
cbM	Rate of shredder construct breakdown in males (default is 0)
cbF	Rate of shredder construct breakdown in females (default is 0)
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

### Value

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

cubeXShredderY

*Inheritance Cube: Y-Linked X-Shredder*

---

### Description

This function creates an inheritance cube to model a Y-linked X-Shredder construct. This construct resides on the Y chromosome, and chops the X chromosome into many pieces during male spermatogenesis, destroying the X chromosome. Thus, males only produce Y gametes.

This drive has 5 alleles at 1 locus:

- X: Wild-type X chromosome
- R: X chromosome resistant to destruction by the shredder construct
- Y: Wild-type Y chromosome
- A: Attacking Y chromosome, a Y chromosome with the shredder construct
- B: Broken Y chromosome, a Y chromosome with a defunct shredder construct

**Usage**

```
cubeXShredderY(
  cX = 1,
  crX = 0,
  cB = 0,
  eta = NULL,
  phi = NULL,
  omega = NULL,
  xiF = NULL,
  xiM = NULL,
  s = NULL
)
```

**Arguments**

cX	Rate of X shredding (default is 1, complete shredding)
crX	Rate of resistance chromosome generation (default is 0)
cB	Rate of shredder construct breakdown (default is 0)
eta	Genotype-specific mating fitness
phi	Genotype-specific sex ratio at emergence
omega	Genotype-specific multiplicative modifier of adult mortality
xiF	Genotype-specific female pupatory success
xiM	Genotype-specific male pupatory success
s	Genotype-specific fractional reduction(increase) in fertility

**Value**

Named list containing the inheritance cube, transition matrix, genotypes, wild-type allele, and all genotype-specific parameters.

---

eraseDirectory	<i>Erase all files in a directory</i>
----------------	---------------------------------------

---

**Description**

Given a directory path, check that it exists, and if so, delete all its contents.

**Usage**

```
eraseDirectory(directory, verbose = TRUE)
```

**Arguments**

directory	Directory whose contents will be deleted
verbose	Chatty? Default is TRUE

**Examples**

```
## Not run:
# Path to directory, can tilde expand
myPath <- "~/path/to/write/output"

# Erase directory
# No return value
eraseDirectory(directory = myPath)

## End(Not run)
```

---

generateReleaseVector *Make List of Modified Mosquito Releases*

---

**Description**

Sets up a release schedule for a single patch, calls [basicRepeatedReleases](#) internally.

**Usage**

```
generateReleaseVector(driveCube, releasesParameters, nameGenotypes = NULL)
```

**Arguments**

driveCube	Gene-drive cube
releasesParameters	A list containing the releasesStart, releasesNumber releasesInterval, and release-Proportion named values.
nameGenotypes	Optional list to specify different genotypes for egg/male/female releases. This is required for mated female releases. This parameter overrides the default release type.

**Examples**

```
# setup a drive cube, using Mendelian as the example
cube <- cubeMendelian()

# setup release parameter list
# releasesStart is the time of first release
# releasesNumber is the number of releases
# releasesInterval is the number of days between releases
# releaseProportion is the number of mosquitoes released
relParams <- list(releasesStart = 25, releasesNumber = 1,
                  releasesInterval = 0, releaseProportion = 10)

# generate male releases
mRelVec <- generateReleaseVector(driveCube = cube,
```

```

releasesParameters = relParams)

# generate mated female releases
fRelVec <- generateReleaseVector(driveCube = cube,
                                releasesParameters = relParams,
                                nameGenotypes = list(c("AA", "AA", 10),
                                                       c("AA", "aa", 10)))

```

---

kernels

*Kernels Parameters*


---

### Description

A named list containing maximum likelihood fitted parameter values from mosquito dispersal estimates.

### Usage

```
data(kernels)
```

### Format

named list with 5 elements:

- lnorm\_mean** log mean of log-normal density
- lnorm\_sd** log standard deviation of log-normal density
- gamma\_shape** shape parameter of gamma density
- gamma\_sd** rate parameter of gamma density
- exp\_rate** rate parameter of exponential density

---

MGDrivE

*MGDrivE: Mosquito Gene Drive Explorer*


---

### Description

MGDrivE: Mosquito Gene Drive Explorer

## Introduction

Recent developments of CRISPR-Cas9 based homing endonuclease gene drive systems, for the suppression or replacement of mosquito populations, have generated much interest in their use for control of mosquito-borne diseases (such as dengue, malaria, Chikungunya and Zika). This is because genetic control of pathogen transmission may complement or even substitute traditional vector-control interventions, which have had limited success in bringing the spread of these diseases to a halt. Despite excitement for the use of gene drives for mosquito control, current modeling efforts have analyzed only a handful of these new approaches (usually studying just one per framework). Moreover, these models usually consider well-mixed populations with no explicit spatial dynamics. To this end, we are developing MGDrivE (Mosquito Gene DRivE Explorer), in cooperation with the 'UCI Malaria Elimination Initiative', as a flexible modeling framework to evaluate a variety of drive systems in spatial networks of mosquito populations. This framework provides a reliable testbed to evaluate and optimize the efficacy of gene drive mosquito releases. What separates MGDrivE from other models is the incorporation of mathematical and computational mechanisms to simulate a wide array of inheritance-based technologies within the same, coherent set of equations. We do this by treating the population dynamics, genetic inheritance operations, and migration between habitats as separate processes coupled together through the use of mathematical tensor operations. This way we can conveniently swap inheritance patterns whilst still making use of the same set of population dynamics equations. This is a crucial advantage of our system, as it allows other research groups to test their ideas without developing new models and without the need to spend time adapting other frameworks to suit their needs.

## Brief Description

MGDrivE is based on the idea that we can decouple the genotype inheritance process from the population dynamics equations. This allows the system to be treated and developed in three semi-independent modules that come together to form the system. The way this is done will be described later in this document but a reference diagram is shown here.

## Previous Work

The original version of this model was based on work by (Deredec et al. 2011; Hancock and Godfray 2007) and adapted to accommodate CRISPR homing dynamics in a previous publication by our team (Marshall et al. 2017). As it was described, we extended this framework to be able to handle a variable number of genotypes, and migration across spatial scenarios. We accomplish this by adapting the equations to work in a tensor-oriented manner, where each genotype can have different processes affecting their particular strain (death rates, mating fitness, sex-ratio bias, et cetera).

## Notation and Conventions

Before beginning the full description of the model we will define some of the conventions we followed for the notation of the written description of the system.

- Overlines are used to denote the dimension of a tensor.
- Subscript brackets are used to indicate an element in time. For example:  $L_{[t-1]}$  is the larval population at time:  $t - 1$ .
- Parentheses are used to indicate the parameter(s) of a function. For example:  $\overline{O(T_e + T_l)}$  represents the function  $O$  evaluated with the parameter:  $T_e + T_l$

- Matrices follow a 'row-first' indexing order (i: row, j: column)

In the case of one dimensional tensors, each slot represents a genotype of the population. For example, the male population is stored in the following way:

$$\overline{Am} = \begin{pmatrix} g_1 \\ g_2 \\ g_3 \\ \vdots \\ g_n \end{pmatrix}_i$$

All the processes that affect mosquitoes in a genotype-specific way are defined and stored in this way within the framework.

There are two tensors of squared dimensionality in the model: the adult females matrix, and the genotype-specific male-mating ability ( $\overline{\eta}$ ) In the case of the former the rows represent the females' genotype, whilst the columns represent the genotype of the male they mated with:

$$\overline{Af} = \begin{pmatrix} g_{11} & g_{12} & g_{13} & \cdots & g_{1n} \\ g_{21} & g_{22} & g_{23} & \cdots & g_{2n} \\ g_{31} & g_{32} & g_{33} & \cdots & g_{3n} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ g_{n1} & g_{n2} & g_{n3} & \cdots & g_{nn} \end{pmatrix}_{ij}$$

The genotype-specific male mating ability, on the other hand, stores the females' genotype in the rows, and the male genotypes in the columns of the matrix.

## References

- Deredec A, Godfray HCJ, Burt A (2011). "Requirements for effective malaria control with homing endonuclease genes." *Proceedings of the National Academy of Sciences of the United States of America*, **108**(43), E874–80. ISSN 1091-6490, doi:10.1073/pnas.1110717108, <https://www.pnas.org/content/108/43/E874>.
- Hancock PA, Godfray HCJ (2007). "Application of the lumped age-class technique to studying the dynamics of malaria-mosquito-human interactions." *Malaria journal*, **6**, 98. ISSN 1475-2875, doi:10.1186/14752875698, <https://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-6-98>.
- Marshall J, Buchman A, C. HMS, Akbari OS (2017). "Overcoming evolved resistance to population-suppressing homing-based gene drives." *Nature Scientific Reports*, 1–46. ISSN 2045-2322, doi:10.1038/s41598017027447, <https://www.nature.com/articles/s41598-017-02744-7>.

### Description

To model an arbitrary number of genotypes efficiently in the same mathematical framework, we use a 3-dimensional array structure (cube) where each axis represents the following information:

- x: female adult mate genotype
- y: male adult mate genotype
- z: proportion of the offspring that inherits a given genotype (layer)

### Details

The cube structure gives us the flexibility to apply tensor operations to the elements within our equations, so that we can calculate the stratified population dynamics rapidly; and within a readable, flexible computational framework. This becomes apparent when we define the equation we use for the computation of eggs laid at any given point in time:

$$\overline{O(T_x)} = \sum_{j=1}^n \left( \left( (\beta * \bar{s} * \overline{Af}_{[t-T_x]}) * \overline{Ih} \right) * \Lambda \right)_{ij}^{\top}$$

In this equation, the matrix containing the number of mated adult females ( $\overline{Af}$ ) is multiplied element-wise with each one of the layers containing the eggs genotypes proportions expected from this cross ( $\overline{Ih}$ ). The resulting matrix is then multiplied by a binary 'viability mask' ( $\Lambda$ ) that filters out female-parent to offspring genetic combinations that are not viable due to biological impediments (such as cytoplasmic incompatibility). The summation of the transposed resulting matrix returns us the total fraction of eggs resulting from all the male to female genotype crosses ( $\overline{O(T_x)}$ ).

Note: For inheritance operations to be consistent within the framework the summation of each element in the z-axis (this is, the proportions of each one of the offspring's genotypes) must be equal to one.

### Drive-specific Cubes

An inheritance cube in an array object that specifies inheritance probabilities (offspring genotype probability) stratified by male and female parent genotypes. MGDrivE provides the following cubes to model different gene drive systems:

- [cubeOneLocusTA](#): 1 Locus Maternal-Toxin/Zygotic-Antidote System
- [cubeTwoLocusTA](#): 2 Locus Maternal-Toxin/Zygotic-Antidote System
- [cubeAlleleSail](#): 3 Locus Allele Sail, similar to Oberhofer et. al.
- [cubeASmidler](#): Split drive design with significant parent-specific impacts
- [cubeCLEAVRMF](#): Cleave and Rescue
- [cubeCLEAVRX](#): Cleave and Rescue, X-Linked
- [cubeClvR](#): 1 Locus Cleave and Rescue (ClvR)
- [cubeClvR2](#): 2 Locus Cleave and Rescue (ClvR)
- [cubeConfinableHoming](#): Confinable Homing
- [cubeConfinableHomingX](#): Confinable Homing, X-Linked

- [cubeHoming1RA](#): Homing Drive with 1 Resistance Allele
- [cubeHomingDrive](#): CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) with 2 Resistance Allele
- [cubeHomingDriveSM](#): CRISPR with Small-Molecule Induction
- [cubeXHomingDeposition](#): CRISPR, X-Linked
- [cubeECHACR](#): 2 Locus Eraser/Chaser Construct, Autosomal
- [cubeECHACRX](#): 2 Locus Eraser/Chaser Construct, X-Linked
- [cubeImmunizingReversalMF](#): Immunizing Reversal/Basic Reversal
- [cubeImmunizingReversalX](#): Immunizing Reversal
- [cubeConfinableHomingJOHN](#): Original Cube Design (We DO NOT recommend using this)
- [cubeKillerRescue](#): Killer-Rescue System
- [cubeMEDEA](#): MEDEA (Maternal Effect Dominant Embryonic Arrest)
- [cubeReciprocalTranslocations](#): Reciprocal Translocation
- [cubeRIDL](#): RIDL (Release of Insects with Dominant Lethality)
- [cubeXShredderMF](#): X-Shredder, Autosomal
- [cubeXShredderY](#): X-Shredder, Y-Linked
- [cubeMendelian](#): Mendelian
- [cubeSplitDrive](#): Split CRISPR Drive
- [cubeSplitDriveX](#): Split CRISPR Drive, X-Linked
- [cubeSplitDriveY](#): Split CRISPR Drive, Y-Linked
- [cubeTGD](#): trans-complementing Gene Drive
- [cubeTGDX](#): trans-complementing Gene Drive, X-Linked
- [cubeWolbachia](#): Wolbachia

### Functions for Cubes

We provide one auxiliary function to operate on cube objects.

- [cube2csv](#): Export slices of a cube to .csv format

### Description

The original version of this model was based on work by (Deredec et al. 2011; Hancock and Godfray 2007) and adapted to accommodate CRISPR homing dynamics in a previous publication by our team (Marshall et al. 2017). As it was described, we extended this framework to be able to handle a variable number of genotypes, and migration across spatial scenarios. We did this by adapting the equations to work in a tensor-oriented manner, where each genotype can have different processes affecting their particular strain (death rates, mating fitness, sex-ratio bias, et cetera).

### Inheritance Cube and Oviposition

To allow the extension of the framework to an arbitrary number of genotypes, we transformed traditional inheritance matrices into inheritance cubes, where each of the axis represents the following information:

- x: female adult mate genotype
- y: male adult mate genotype
- z: proportion of the offspring that inherits a given genotype (slice)

The 'cube' structure gives us the flexibility to apply tensor operations to the elements within our equations, so that we can calculate the stratified population dynamics rapidly; and within a readable, flexible computational framework. This becomes apparent when we define the equation we use for the computation of eggs laid at any given point in time:

$$\overline{O(T_x)} = \sum_{j=1}^n \left( \left( (\beta * \bar{s} * \overline{Af}_{[t-T_x]}) * \overline{Ih} \right) * \Lambda \right)_{ij}^\top$$

In this equation, the matrix containing the number of mated adult females ( $\overline{Af}$ ) is multiplied element-wise with each one of the slices containing the eggs genotypes proportions expected from this cross ( $\overline{Ih}$ ). The resulting matrix is then multiplied by a binary 'viability mask' ( $\Lambda$ ) that filters out female-parent to offspring genetic combinations that are not viable due to biological impediments (such as cytoplasmic incompatibility). The summation of the transposed resulting matrix returns us the total fraction of eggs resulting from all the male to female genotype crosses ( $\overline{O(T_x)}$ ).

Note: For inheritance operations to be consistent within the framework, the summation of each element in the 'z' axis (this is, the proportions of each one of the offspring's genotypes) must be equal to one.

### Population Dynamics

During the three aquatic stages, a density-independent mortality process takes place:

$$\theta_{st} = (1 - \mu_{st})^{T_{st}}$$

Along with a density dependent process dependent on the number of larvae in the environment:

$$F(L[t]) = \left( \frac{\alpha}{\alpha + \sum \overline{L[t]}} \right)^{1/T_l}$$

where  $\alpha$  represents the strength of the density-dependent process. This parameter is calculated with:

$$\alpha = \left( \frac{1/2 * \beta * \theta_e * Ad_{eq}}{R_m - 1} \right) * \left( \frac{1 - (\theta_l/R_m)}{1 - (\theta_l/R_m)^{1/T_l}} \right)$$

in which  $\beta$  is the species' fertility in the absence of gene-drives,  $Ad_{eq}$  is the adult mosquito population equilibrium size, and  $R_m$  is the population growth in the absence of density-dependent mortality. This population growth is calculated with the average generation time ( $g$ ), the adult mortality rate ( $\mu_{ad}$ ), and the daily population growth rate ( $r_m$ ):

$$g = T_e + T_l + T_p + \frac{1}{\mu_{ad}} R_m = (r_m)^g$$

**Larval Stages:** The computation of the larval stage in the population is crucial to the model because the density dependent processes necessary for equilibrium trajectories to be calculated occur here. This calculation is performed with the following equation:

$$D(\theta_l, T_x) = \begin{cases} \theta'_{l[0]} = \theta_l & i = 0 \\ \theta'_{l[i+1]} = \theta'_{l[i]} * F(\overline{L}_{[t-i-T_x]}) & i \leq T_l \end{cases}$$

In addition to this, we need the larval mortality ( $\mu_l$ ):

$$\mu_l = 1 - \left( \frac{R_m * \mu_{ad}}{1/2 * \beta * (1 - \mu_m)} \right)^{\frac{1}{T_e + T_l + T_p}}$$

With these mortality processes, we are now able to calculate the larval population:

$$\overline{L}_{[t]} = \overline{L}_{[t-1]} * (1 - \mu_l) * F(\overline{L}_{[t-1]}) + \overline{O}(T_e) * \theta_e - \overline{O}(T_e + T_l) * \theta_e * D(\theta_l, 0)$$

where the first term accounts for larvae surviving one day to the other; the second term accounts for the eggs that have hatched within the same period of time; and the last term computes the number of larvae that have transformed into pupae.

**Adult Stages:** We are ultimately interested in calculating how many adults of each genotype exist at any given point in time. For this, we first calculate the number of eggs that are laid and survive to the adult stages with the equation:

$$\overline{E}' = \overline{O}(T_e + T_l + T_p) * \left( \overline{\xi}_m * (\theta_e * \theta_p) * (1 - \mu_{ad}) * D(\theta_l, T_p) \right)$$

With this information we can calculate the current number of male adults in the population by computing the following equation:

$$\overline{Am}_{[t]} = \overline{Am}_{[t-1]} * (1 - \mu_{ad}) * \overline{\omega}_m + (1 - \overline{\phi}) * \overline{E}' + \overline{\nu}m_{[t-1]}$$

in which the first term represents the number of males surviving from one day to the next; the second one, the fraction of males that survive to adulthood ( $\overline{E}'$ ) and emerge as males ( $1 - \overline{\phi}$ ); the last one is used to add males into the population as part of gene-drive release campaigns.

Female adult populations are calculated in a similar way:

$$\overline{Af}_{[t]} = \overline{Af}_{[t-1]} * (1 - \mu_{ad}) * \overline{\omega}_f + \left( \overline{\phi} * \overline{E}' + \overline{\nu}f_{[t-1]} \right)^\top * \left( \frac{\overline{\eta} * \overline{Am}_{[t-1]}}{\sum \overline{Am}_{[t-1]}} \right)$$

where we first compute the surviving female adults from one day to the next; and then we calculate the mating composition of the female fraction emerging from pupa stage. To do this, we obtain the surviving fraction of eggs that survive to adulthood ( $\overline{E}'$ ) and emerge as females ( $\overline{\phi}$ ), we then add the new females added as a result of gene-drive releases ( $\overline{\nu}f_{[t-1]}$ ). After doing this, we calculate the proportion of males that are allocated to each female genotype, taking into account their respective mating fitnesses ( $\overline{\eta}$ ) so that we can introduce the new adult females into the population pool.

### Gene Drive Releases and Effects

As it was briefly mentioned before, we are including the option to release both male and/or female individuals into the populations. Another important thing to emphasize is that we allow flexible releases sizes and schedules. Our model handles releases internally as lists of populations compositions so, it is possible to have releases performed at irregular intervals and with different numbers of mosquito genetic compositions as long as no new genotypes are introduced (which have not been previously defined in the inheritance cube).

$$\bar{v} = \left\{ \begin{pmatrix} g_1 \\ g_2 \\ g_3 \\ \vdots \\ g_n \end{pmatrix}_{t=1}, \begin{pmatrix} g_1 \\ g_2 \\ g_3 \\ \vdots \\ g_n \end{pmatrix}_{t=2}, \dots, \begin{pmatrix} g_1 \\ g_2 \\ g_3 \\ \vdots \\ g_n \end{pmatrix}_{t=x} \right\}$$

So far, however, we have not described the way in which the effects of these gene-drives are included into the mosquito populations dynamics. This is done through the use of various modifiers included in the equations:

- $\bar{\omega}$ : Relative increase in mortality (zero being full mortality effects and one no mortality effect)
- $\bar{\phi}$ : Relative shift in the sex of the pupating mosquitoes (zero biases the sex ratio towards males, whilst 1 biases the ratio towards females).
- $\bar{\eta}$ : Standardized mating fitness (zero being complete fitness ineptitude, and one being regular mating skills).
- $\bar{\beta}$ : Fecundity (average number of eggs laid).
- $\bar{\xi}$ : Pupation success (zero being full mortality and one full pupation success).

### Migration

To simulate migration within our framework we are considering patches (or nodes) of fully-mixed populations in a network structure. This allows us to handle mosquito movement across spatially-distributed populations with a transitions matrix, which is calculated with the tensor outer product of the genotypes populations tensors and the transitions matrix of the network as follows:

$$\overline{Am}_{(t)}^i = \sum \overline{A}_m^j \otimes \overline{\tau m}_{[t-1]} \overline{Af}_{(t)}^i = \sum \overline{A}_f^j \otimes \overline{\tau f}_{[t-1]}$$

In these equations the new population of the patch  $i$  is calculated by summing the migrating mosquitoes of all the  $j$  patches across the network defined by the transitions matrix  $\tau$ , which stores the mosquito migration probabilities from patch to patch. It is worth noting that the migration probabilities matrices can be different for males and females; and that there's no inherent need for them to be static (the migration probabilities may vary over time to accommodate wind changes due to seasonality).

### Parameters

This table compiles all the parameters required to run MGDrivE clustered in six categories:

- Life Stages: These deal with the structure of mosquito population.

- **Bionomics:** This set of parameters is related to the behavior of the specific mosquito species being modeled.
- **Gene Drive:** Genotype-specific vectors of parameters that affect how each gene-drive modifies the responses of populations to them.
- **Releases:** List of vectors that control the release of genetically-modified mosquitoes.
- **Population:** General mosquito-population parameters that control environmentally-determined variables.
- **Network:** Related to migration between nodes of population units

### Stochasticity

*MGDrivE* allows stochasticity to be included in the dynamics of various processes; in an effort to simulate processes that affect various stages of mosquitoes lives. In the next section, we will describe all the stochastic processes that can be activated in the program. It should be noted that all of these can be turned on and off independently from one another as required by the researcher.

#### Mosquito Biology: Oviposition

Stochastic egg laying by female/male pairs is separated into two steps: calculating the number of eggs laid by the females and then distributing laid eggs according to their genotypes. The number of eggs laid follows a Poisson distribution conditioned on the number of female/male pairs and the fertility of each female.

$$Poisson(\lambda = numFemales * Fertility)$$

Multinomial sampling, conditioned on the number of offspring and the relative viability of each genotype, determines the genotypes of the offspring.

$$Multinomial(numOffspring, p_1, p_2 \dots p_b) = \frac{numOffspring!}{p_1! p_2 \dots p_n} p_1^{n_1} p_2^{n_2} \dots p_n^{n_n}$$

#### Sex Determination

Sex of the offspring is determined by multinomial sampling. This is conditioned on the number of eggs that live to hatching and a probability of being female, allowing the user to design systems that skew the sex ratio of the offspring through reproductive mechanisms.

$$Multinomial(numHatchingEggs, p_{female}, p_{female})$$

**Mating** Stochastic mating is determined by multinomial sampling conditioned on the number of males and their fitness. It is assumed that females mate only once in their life, therefore each female will sample from the available males and be done, while the males are free to potentially mate with multiple females. The males' ability to mate is modulated with a fitness term, thereby allowing some genotypes to be less fit than others (as seen often with lab releases).

$$Multinomial(numFemales, p_1 f_1, p_2 f_2, \dots p_n f_n)$$

#### Hatching

**Other Stochastic Processes** All remaining stochastic processes (larval survival, hatching, pupating, surviving to adult hood) are determined by multinomial sampling conditioned on factors affecting the current life stage. These factors are determined empirically from mosquito population data.

**Migration:** Variance of stochastic movement (not used in diffusion model of migration).

## References

- Deredec A, Godfray HCJ, Burt A (2011). “Requirements for effective malaria control with homing endonuclease genes.” *Proceedings of the National Academy of Sciences of the United States of America*, **108**(43), E874–80. ISSN 1091-6490, doi:10.1073/pnas.1110717108, <https://www.pnas.org/content/108/43/E874>.
- Hancock PA, Godfray HCJ (2007). “Application of the lumped age-class technique to studying the dynamics of malaria-mosquito-human interactions.” *Malaria journal*, **6**, 98. ISSN 1475-2875, doi:10.1186/14752875698, <https://malariajournal.biomedcentral.com/articles/10.1186/1475-2875-6-98>.
- Marshall J, Buchman A, C. HMS, Akbari OS (2017). “Overcoming evolved resistance to population-suppressing homing-based gene drives.” *Nature Scientific Reports*, 1–46. ISSN 2045-2322, doi:10.1038/s41598017027447, <https://www.nature.com/articles/s41598-017-02744-7>.

---

 moveMatAll2

*Movement Matrix: All 2*


---

## Description

A movement matrix for simulation with 3 patches.

## Usage

```
data(moveMatAll2)
```

## Format

A matrix with 3 rows and 3 columns:

Patches 1 and 3 are sources for patch 2, which is a sink.

---

 moveMatCascade3

*Movement Matrix: Cascade 3*


---

## Description

A movement matrix for simulation with 3 patches.

## Usage

```
data(moveMatCascade3)
```

## Format

A matrix with 3 rows and 3 columns:

Mosquitoes in patch 1 have equal probability to stay or move to 2; mosquitoes in patch 2 have equal probability to stay or move to 3; mosquitoes in patch 3 stay there.

---

moveMatDiag	<i>Movement Matrix: Diagonal</i>
-------------	----------------------------------

---

**Description**

A movement matrix for simulation with 3 patches.

**Usage**

```
data(moveMatDiag)
```

**Format**

A matrix with 3 rows and 3 columns:  
3 independent patches.

---

moveMatDiagOneCity	<i>Movement Matrix: Diagonal One City</i>
--------------------	---

---

**Description**

A movement matrix for simulation with 1 patch.

**Usage**

```
data(moveMatDiagOneCity)
```

**Format**

A matrix with 1 rows and 1 columns:  
A 1 by 1 matrix with entry 1.

---

moveMatDie	<i>Movement Matrix: Die</i>
------------	-----------------------------

---

**Description**

A movement matrix for simulation with 3 patches.

**Usage**

```
data(moveMatDie)
```

**Format**

A matrix with 3 rows and 3 columns:  
All entries of matrix are 0 for testing that all mosquitoes will be killed.

---

moveMatIndependent3     *Movement Matrix: Independent 3*

---

**Description**

A movement matrix for simulation with 3 patches.

**Usage**

```
data(moveMatIndependent3)
```

**Format**

A matrix with 3 rows and 3 columns:

Mosquitoes in patch 1 stay with probability 0.975, move to patch 2 with probability 0.025, mosquitoes in patch 2 and 3 stay in their patches.

---

moveMatMixedSpil     *Movement Matrix: Mixed Spill*

---

**Description**

A movement matrix for simulation with 3 patches.

**Usage**

```
data(moveMatMixedSpil)
```

**Format**

A matrix with 3 rows and 3 columns:

Mosquitoes in patch 1 stay with probability 0.999, move to patch 2 with probability 0.001, mosquitoes in patch 2 and 3 stay in their patches.

---

`moveMatTaleOfTwoCities`*Movement Matrix: Tale of Two Cities*

---

**Description**

A movement matrix for simulation with 2 patches.

**Usage**

```
data(moveMatTaleOfTwoCities)
```

**Format**

A matrix with 2 rows and 2 columns:

Mosquitoes do not move between the two patches.

---

`moveMatTriDiagonal`*Movement Matrix: Tri-diagonal*

---

**Description**

A movement matrix for simulation with 12 patches.

**Usage**

```
data(moveMatTriDiagonal)
```

**Format**

A matrix with 12 rows and 12 columns:

Tri-diagonal matrix with approximately 0.985 probability on diagonal and rest of probability mass on  $k-1$  and  $k+1$  off-diagonal elements.

---

moveMatTriple	<i>Movement Matrix: Triple</i>
---------------	--------------------------------

---

**Description**

A movement matrix for simulation with 3 patches.

**Usage**

```
data(moveMatTriple)
```

**Format**

A matrix with 3 rows and 3 columns:

All entries of matrix are 1 for testing that mosquitoes will be produced.

---

multRun_Network	<i>Run Simulation</i>
-----------------	-----------------------

---

**Description**

Run multiple simulations on this network

**Usage**

```
multRun_Network(verbose = TRUE)
```

**Arguments**

verbose            Chatty? Default is TRUE

---

Network	<i>Network Class Definition</i>
---------	---------------------------------

---

**Description**

A Network class object stores all the information for a simulation on a defined landscape.

**Format**

An [R6Class](#) generator object

**Constructor**

- params: see [parameterizeMGDrive](#)
- driveCube: an inheritance cube
- patchReleases: see [basicRepeatedReleases](#) for examples on how to set up release schedules
- migrationMale: a stochastic matrix whose dimensions conform to the number of patches
- migrationFemale: a stochastic matrix whose dimensions conform to the number of patches
- migrationBatch: a list of batch migration parameters. See [basicBatchMigration](#)
- directory: character string of output directory
- verbose: Chatty? Default is TRUE

**Methods**

- get\_timeAq: see [get\\_timeAq\\_Network](#)
- get\_beta: see [get\\_beta\\_Network](#)
- get\_muAd: see [get\\_muAd\\_Network](#)
- get\_muAq: see [get\\_muAq\\_Network](#)
- get\_alpha: see [get\\_alpha\\_Network](#)
- get\_drivecubeindex: see [get\\_drivecubeindex\\_Network](#)
- get\_tau: see [get\\_tau\\_Network](#)
- get\_genotypesID: see [get\\_genotypesID\\_Network](#)
- get\_genotypesN: see [get\\_genotypesN\\_Network](#)
- get\_eta: see [get\\_eta\\_Network](#)
- get\_phi: see [get\\_phi\\_Network](#)
- get\_omega: see [get\\_omega\\_Network](#)
- get\_xiF: see [get\\_xiF\\_Network](#)
- get\_xiM: see [get\\_xiM\\_Network](#)
- get\_s: see [get\\_s\\_Network](#)
- get\_nPatch: see [get\\_nPatch\\_Network](#)
- get\_conADM: see [get\\_conM\\_Network](#)
- get\_conADF: see [get\\_conF\\_Network](#)
- get\_tNow: see [get\\_tNow\\_Network](#)
- get\_patchReleases: see [get\\_patchReleases\\_Network](#)
- oneDay\_Migration: see [oneDay\\_Migration\\_Deterministic\\_Network](#) or see [oneDay\\_Migration\\_Stochastic\\_Network](#)
- reset: see [reset\\_Network](#)
- oneDay: see [oneDay\\_Network](#)
- oneRun: see [oneRun\\_Network](#)
- multRun: see [multRun\\_Network](#)

## Fields

- parameters: see [parameterizeMGDrive](#)
- patches: a list of [Patch](#) objects
- nPatch: number of patches
- simTime: maximum time of simulation
- sampTime: how often to write output, tNow %% sampTime
- driveCube: an inheritance cube
- tNow: current time of simulation (time starts at 2 because time 1 is the initial equilibrium state)
- runID: an identifier for the current simulation run, useful for Monte Carlo simulation
- directory: a character string of where to store output
- conADM: a [connection](#) to write male population dynamics out to
- conADF: a [connection](#) to write female population dynamics out to
- migrationMale: a stochastic matrix whose dimensions conform to the number of patches
- migrationFemale: a stochastic matrix whose dimensions conform to the number of patches
- migrationBatch: list of items for batch migration in stochastic sim.
- mMoveMat: holder object for male migration
- fMoveArray: holder object for female migration
- patchReleases: a list of release schedules for each patch

## Examples

```
## Not run:  
# There are no simple examples for this, so looking at the vignettes would be  
# most useful.  
  
# Complete manual with examples, but none explored in depth.  
vignette("MGDrive-Examples", package = "MGDrive")  
  
# One example, explored in great detail. This is probably more helpful.  
vignette("MGDrive-Run", package = "MGDrive")  
  
## End(Not run)
```

---

oneRun_Network	<i>Run Simulation</i>
----------------	-----------------------

---

**Description**

Run a single simulation on this network.

**Usage**

```
oneRun_Network(verbose = TRUE)
```

**Arguments**

verbose	Chatty? Default is TRUE
---------	-------------------------

---

parameterizeMGDrive	<i>parameterizeMGDrive</i>
---------------------	----------------------------

---

**Description**

Generate parameters for simulation on a [Network](#). Parameters include: average generation time  $g$ , population growth rate  $R_m$ , aquatic mortality  $\mu_{Aq}$ , and aquatic survival  $\theta_{Aq}$ , which are shared between patches and calculated by [calcAverageGenerationTime](#), [calcPopulationGrowthRate](#), and [calcLarvalStageMortalityRate](#).

Patch-specific parameters  $\alpha$  and  $L_{eq}$  are calculated for each patch by [calcDensityDependentDeathRate](#) and [calcLarvalPopEquilibrium](#).

**Usage**

```
parameterizeMGDrive(
  runID = 1L,
  nPatch,
  simTime,
  sampTime = 1L,
  tEgg = 1L,
  tLarva = 14L,
  tPupa = 1L,
  beta = 32,
  muAd = 0.123,
  popGrowth = 1.096,
  AdPopEQ,
  LarPopRatio,
  AdPopRatio_F,
  AdPopRatio_M,
  inheritanceCube
)
```

**Arguments**

runID	Begin counting runs with this set of parameters from this value
nPatch	Number of <a href="#">Patch</a>
simTime	Maximum time to run simulation
sampTime	Times to sample, used as tNow %% sampTime, default is every day
tEgg	Length of egg stage
tLarva	Length of larval instar stage
tPupa	Length of pupal stage
beta	Female egg batch size of wild-type
muAd	Wild-type daily adult mortality (1/muAd is average wild-type lifespan)
popGrowth	Daily population growth rate (used to calculate equilibrium)
AdPopEQ	Single number or vector of adult population size at equilibrium (single number implies all patches have the same population)
LarPopRatio	May be empty; if not, a vector gives the wildtype gene frequencies among larval stages at the beginning of simulation or a matrix provides different initial frequencies for each patch (every row is a different patch, must have nrow = nPatch)
AdPopRatio_F	May be empty; if not, a vector gives the wildtype gene frequencies among adult females at the beginning of simulation or a matrix provides different initial frequencies for each patch (every row is a different patch, must have nrow = nPatch)
AdPopRatio_M	May be empty; if not, a vector gives the wildtype gene frequencies among adult males at the beginning of simulation or a matrix provides different initial frequencies for each patch (every row is a different patch, must have nrow = nPatch)
inheritanceCube	Inheritance cube to check/set population ratios at the beginning of the simulation

**Examples**

```
# using default parameters for 2 patches
# using different population sizes for patches
simPars <- parameterizeMGDrive(nPatch = 2, simTime = 365,
                               AdPopEQ = c(100,200), inheritanceCube = cubeMendelian())
```

---

Patch	<i>Patch Class Definition</i>
-------	-------------------------------

---

**Description**

A Patch is a single well-mixed population that is the smallest unit of simulation for MGDrive.

**Format**

An [R6Class](#) generator object

**Constructor**

- patchID: integer ID of this patch
- genotypesID: character vector of genotypes
- timeAq: integer vector of length 3 specifying the length of each aquatic stage
- numPatches: integer, total number of patches in this simulation
- adultEQ: integer, total adult population in this patch for the duration of the simulation
- larvalEQ: integer, total larval population in this patch for the duration of the simulation
- muAq: double vector, length 3, daily death rate for each aquatic stage
- alpha: double, density-dependent centering parameter, see [parameterizeMGDrive](#)
- adultRatioF: named double vector, distribution of adult female genotypes, see [parameterizeMGDrive](#)
- adultRatioM: named double vector, distribution of adult male genotypes, see [parameterizeMGDrive](#)
- larvalRatio: named double vector, distribution of all aquatic genotypes, see [parameterizeMGDrive](#)
- eggReleases: egg release schedule for this patch, see [basicRepeatedReleases](#)
- maleReleases: male release schedule for this patch, see [basicRepeatedReleases](#)
- femaleReleases: female release schedule for this patch, see [basicRepeatedReleases](#)
- matedFemaleReleases: mated females release schedule for this patch, see [basicRepeatedReleases](#)

**Methods**

- set\_NetworkPointer: see [set\\_NetworkPointer\\_Patch](#)
- get\_femalePopulation: see [get\\_femalePop\\_Patch](#)
- get\_malePopulation: see [get\\_malePop\\_Patch](#)
- initialPopulation: see [set\\_initialPopulation\\_Patch](#)
- setPopulation: see [set\\_population\\_deterministic\\_Patch](#) or [set\\_population\\_stochastic\\_Patch](#)
- reset: see [reset\\_Patch](#)
- oneDay\_initOutput: see [oneDay\\_initOutput\\_Patch](#)
- oneDay\_writeOutput: see [oneDay\\_writeOutput\\_Patch](#)
- oneDay\_migrationIn: see [oneDay\\_migrationIn\\_Patch](#)
- oneDay\_PopDynamics: see [oneDay\\_PopDynamics\\_Patch](#)
- oneDay\_adultD: see [oneDay\\_adultDeath\\_deterministic\\_Patch](#) or [oneDay\\_adultDeath\\_stochastic\\_Patch](#)
- oneDay\_pupaDM: see [oneDay\\_pupaDM\\_deterministic\\_Patch](#) or [oneDay\\_pupaDM\\_stochastic\\_Patch](#)
- oneDay\_larvaDM: see [oneDay\\_larvaDM\\_deterministic\\_Patch](#) or [oneDay\\_larvaDM\\_stochastic\\_Patch](#)
- oneDay\_eggDM: see [oneDay\\_eggDM\\_deterministic\\_Patch](#) or [oneDay\\_eggDM\\_stochastic\\_Patch](#)
- oneDay\_pupation: see [oneDay\\_pupation\\_deterministic\\_Patch](#) or [oneDay\\_pupation\\_stochastic\\_Patch](#)
- oneDay\_releases: see [oneDay\\_releases\\_Patch](#)
- oneDay\_releaseEggs: see [oneDay\\_eggReleases\\_Patch](#)
- oneDay\_mating: see [oneDay\\_mating\\_deterministic\\_Patch](#) or [oneDay\\_mating\\_stochastic\\_Patch](#)
- oneDay\_layEggs: see [oneDay\\_oviposit\\_deterministic\\_Patch](#) or [oneDay\\_oviposit\\_stochastic\\_Patch](#)

**Fields**

- patchID: integer ID of this patch
- popAquatic: matrix, nGenotype x sum(timeAquatic), holding all eggs, larva, and pupa
- popMale: vector, nGenotype x 1, holds adult males
- popFemale: matrix, nGenotype x nGenotype, holds mated adult females
- popHolder: vector, nGenotype x 1, temporary population storage
- popPupSex: vector, nGenotype x 1, used in stochastic pupation as another temporary population
- popUnmated: vector, nGenotype x 1, holds unmated females
- popAquatic0: matrix, nGenotype x sum(timeAquatic), holding all eggs, larva, and pupa for reset, see [reset\\_Patch](#)
- popMalet0: vector, nGenotype x 1, holds adult males for reset see [reset\\_Patch](#)
- popFemalet0: matrix, nGenotype x nGenotype, holds mated adult females for reset see [reset\\_Patch](#)
- eggReleases: list of egg releases for this patch. See [oneDay\\_eggReleases\\_Patch](#)
- maleReleases: list of adult male releases for this patch. See [oneDay\\_releases\\_Patch](#)
- femaleReleases: list of adult female releases for this patch. See [oneDay\\_releases\\_Patch](#)
- matedFemaleReleases: list of mated adult female releases for this patch. See [oneDay\\_releases\\_Patch](#)
- NetworkPointer: a reference to enclosing [Network](#)

---

plotMGDrivEMult

*Plot*


---

**Description**

Plots several traces from MGD<sub>DrivE</sub>, assuming each set is another repetition from the same experiment.

Given the readDir, this function assumes the follow file structure:

- readDir
  - repetition 1
    - \* patch 1
    - \* patch 2
    - \* patch 3
  - repetition 2
    - \* patch 1
    - \* patch 2
    - \* patch 3
  - repetition 3
  - repetition 4
  - ...

**Usage**

```
plotMGDriveMult(readDir, whichPatches = NULL, totalPop = FALSE,
                nonZeroGen = FALSE, lwd = 0.75, alpha = 0.75)
```

**Arguments**

readDir	Directory to find repetition folders in
whichPatches	Vector of patches to plot, must be less than 15. Default is NULL if less than 15 patches
totalPop	Boolean, to plot the total population or not. Default is FALSE
nonZeroGen	Boolean, to plot genotypes that are always zero in simulation
lwd	Double, specify the line width for plotting
alpha	Double, specify the opacity for plotting

**Details**

This function plots output from one run or one set of runs after being analyzed. Setting totalPop to FALSE keeps it from plotting the total population. NonZeroGen accounts for genotypes that could exist, but are not created in the simulation. Default is FALSE, as this is easier to read on a plot.

**Examples**

```
## Not run:
# Requires the user to have run MGDrive, logically stochastic, analyzed
# the data, and stored it in the directory shown below.
# See vignette for complete example

# Folder where single run is stored
fPath <- "path/to/data/containing/folder"

# plot output to see effect
plotMGDriveMult(readDir=fPath, totalPop = TRUE, lwd=3.5, alpha=1)

## End(Not run)
```

---

plotMGDriveSingle      *Plot*

---

**Description**

Plots one run from MGDrive

**Usage**

```
plotMGDriveSingle(readDir, whichPatches = NULL, totalPop = FALSE,
                  nonZeroGen = FALSE, lwd = 0.75, alpha = 0.75)
```

**Arguments**

readDir	Path to file from single-run of MGDriVE or from analysis function
whichPatches	Vector of patches to plot, must be less than 15. Default is NULL if less than 15 patches
totalPop	Boolean, to plot the total population or not.
nonZeroGen	Boolean, to plot genotypes that are always zero in simulation
lwd	Double, specify the line width for plotting
alpha	Double, specify the opacity for plotting

**Details**

This function plots output from one run or one set of runs after being analyzed. Setting totalPop to FALSE keeps it from plotting the total population. NonZeroGen accounts for genotypes that could exist, but are not created in the simulation. Default is FALSE, as this is easier to read on a plot.

**Examples**

```
## Not run:
# Requires the user to have run MGDriVE, deterministic or stochastic, analyzed
# the data, and stored it in the directory shown below.
# See vignette for complete example

# Folder where single run is stored
fPath <- "path/to/data/containing/folder"

# plot output to see effect
plotMGDrivEsingle(readDir=fPath,totalPop = TRUE,lwd=3.5,alpha=1)

## End(Not run)
```

---

reset\_Network

*Reset Network*


---

**Description**

Reset a [Network](#) between runs, useful for Monte Carlo simulation. This calls [reset\\_Patch](#) on each patch and resets tNow = 2 and increments the runID.

**Usage**

```
reset_Network(verbose = TRUE)
```

**Arguments**

verbose	Chatty? Default is TRUE
---------	-------------------------

---

retrieveOutput	<i>Retrieve Output</i>
----------------	------------------------

---

**Description**

Read in output from directory. The resulting object will be a nested list; outermost nesting dimension indexes runID, within runID elements are split by sex and innermost nesting is over patches.

**Usage**

```
retrieveOutput(readDir, verbose = TRUE)
```

**Arguments**

readDir	Directory where output was written to; must not end in path separator
verbose	Chatty? Default is TRUE

**Value**

Nested List

**Examples**

```
## Not run:
# Example assumes user has run and analyzed MGDrive.
# See vignette for examples of how to do that.

# set read directory
fPath <- "path/to/split/aggregated/output"

# read in data as nested lists
dataList <- retrieveOutput(readDir = fPath)

## End(Not run)
```

---

setupMGDrive	<i>Setup MGDrive</i>
--------------	----------------------

---

**Description**

Initialize methods in [Patch](#) to run deterministic or stochastic simulations. This sets internal function definitions so that [oneRun\\_Network](#) and [multRun\\_Network](#) run either deterministic or stochastic functions.

**Usage**

```
setupMGDrive(stochasticityON = FALSE, verbose = TRUE)
```

**Arguments**

```
stochasticityON      Enable/disable stochastic simulation. Default is FALSE, implying deterministic
                     simulation
verbose              Chatty? Default is TRUE
```

**Examples**

```
# run deterministic MGDive
setupMGDrive(stochasticityON = FALSE)

# run stochastic MGDive
setupMGDrive(stochasticityON = TRUE)
```

---

```
splitOutput          Split Output by Patch
```

---

**Description**

Split output into multiple files by patches.

**Usage**

```
splitOutput(readDir, writeDir = NULL, remFile = TRUE, verbose = TRUE)
```

**Arguments**

```
readDir             Directory where output was written to
writeDir            Directory to write output to. Default is readDir
remFile             Remove original output? Default is TRUE
verbose            Chatty? Default is TRUE
```

**Examples**

```
## Not run:
# This example assumes user has already run MGDive and generated output.
# If that's untrue, see vignette for complete example
fPath <- "path/to/data/containing/folder"
oPath <- "path/to/write/output"

# split data by patch, keep original files
# no return value
```

```
splitOutput(readDir = fPath, writeDir = oPath, remFile = FALSE)

# Alternatively, remove the original files and write new ones in their place
fPath <- "path/to/data/containing/folder"

splitOutput(readDir = fPath, writeDir = NULL, remFile = TRUE)

## End(Not run)
```

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