**polysmooth: A Model Running Guide**

**Description**

polysmooth is a complex mathematical model for the evaluation of insecticide resistance management (IRM) strategies. The polysmooth model assumes that resistance is polygenic, and selection is probabilistic. polysmooth offers a diverse range of potential IRM strategies, deployment decision making, and insecticide switching rules; and how insecticides can be mixed. This complexity means that running a single simulation can potentially be confusing as not all input parameters are needed for all strategies, and different strategies may have different requirements as to the insecticide deployment rules. This document intends to explain how to run the model and highlight any known issues with input values.

The running of the polysmooth model is conducted using the wrapper **run\_simulation\_advanced** function. This is a function with a large number of parameter inputs which can be used to describe a variety of biological/ecological factors, operational/logistical factors, insecticidal factors. Alongside other specific model performance parameters. The full function inputs are listed below. While the number and variety of input parameters may look daunting, details on their use are given in this document.

**run\_simulation\_advanced(irm.deployment.strategy,**

**irm.switch.strategy,**

**number.of.insecticides,**

**sd.scaled,**

**exposure.scaling.factor,**

**female.fitness.cost,**

**male.fitness.cost,**

**female.exposure,**

**male.exposure,**

**heritability,**

**dispersal.rate,**

**coverage,**

**standard.deviation,**

**vector.length,**

**maximum.bioassay.survival.proportion,**

**michaelis.menten.slope,**

**regression.coefficient,**

**regression.intercept,**

**maximum.generations,**

**half.population.bioassay.survival.resistance,**

**withdrawal.threshold.value,**

**return.threshold.value,**

**deployment.frequency,**

**maximum.resistance.value,**

**starting.refugia.resistance.score,**

**starting.intervention.resistance.score,**

**applied.insecticide.dose,**

**recommended.insecticide.dose,**

**threshold.generations,**

**base.efficacy.decay.rate,**

**rapid.decay.rate,**

**deployment.interval.llin,**

**deployment.interval.irs,**

**probability.only.i.male,**

**probability.only.j.male,**

**probability.both.i.j.male,**

**probability.only.i.female,**

**probability.only.j.female,**

**probability.both.i.j.female,**

**n.cycles,**

**intervention.coverage.1,**

**intervention.coverage.2,**

**intervention.coverage.1.2,**

**z.sd.intercept,**

**z.sd.coefficient,**

**mixture.strategy**

**llin.insecticides,**

**irs.insecticides,**

**min.cross.selection,**

**max.cross.selection**

**)**

The **run\_simulation\_advanced** function returns:

1. A data frame of the simulation. Exact details of the layout will depend on the **irm.deployment.strategy** used. The data frame will contain the polygenic resistance score for each insecticide in the simulation for each generation in the intervention site and refugia. There will additionally be columns in the data frame detailing which insecticide(s) are in deployment and the efficacy of those insecticides.
2. A data frame of the cross selection between insecticides.

run\_simulation\_advanced inputs

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# irm.deployment.strategy

The most important starting point for the model is to decide what IRM strategy is to be evaluated. This is because this choice of IRM strategy will dictate the requirement (or not) of other parameter inputs.

The **irm.deployment.strategy** describes the broad way in which insecticides can be deployed.; and therefore describes the overarching strategy being evaluated. The options are **“singles”**, **“mixtures”**, **“micromosaics”** or **“combinations”**. The **irm.deployment.strategy** is fixed throughout the simulation.

* In **irm.deployment.strategy = “singles**” a single insecticide is deployed at a time.
* In **irm.deployment.strategy = “mixtures”**, two insecticides are deployed at a time but in a single insecticide formulation such that the mosquitoes encounter both simultaneously in the same gonotrophic cycle.
* In **irm.deployment.strategy = “micromosaics”** two insecticides are deployed at the same time but spatially apart such that only one insecticide would be encountered in each gonotrophic cycle.
* In **irm.deployment.strategy = “combinations”** two insecticides are deployed at a time, one as an IRS and one as an LLIN; therefore there is a possibility that a mosquito encounter both insecticides in the same gonotrophic cycle if they are both in the same house for example.

The choice of the **irm.deployment.strategy** will dictate which other parameter inputs are needed to be included in the model.

# number.of.insecticides

This is the total number of different insecticides (and by extension resistance traits) in the simulation. A single number should be put as the input, e.g., **number.of.insecticides = 3**.

# irm.switch.strategy

The **irm.switch.strategy** describes the way in which insecticide formulations can be switched in and out of deployment. Different **irm.deployment.strategy** inputs have different requirements for the switching strategies. This is because with increasingly complex deployment methods there become more potential ways to allow for insecticide switching to occur. The different switching strategies are designed to try and mimic some practical/operational constraints which may occur during an IRM strategy, such as the need to preferentially use a cheaper insecticide for example. Therefore extending the model to be able to explore scenarios of policy/operational usefulness.

## irm.deployment.strategy = “singles”

**irm.switch.strategy = “sequence”**

The insecticides are deployed in a strict sequence.

**irm.switch.strategy = “rotation”**

The insecticides are deployed in rotation a strict rotation. That is the same insecticide cannot be deployed in the immediate subsequent deployment interval.

**irm.switch.strategy = “adaptive.rotation”**

The insecticides are deployed in rotation unless only one insecticide is available then the simulation switches to a sequence.

For “singles” the deployment interval between insecticide deployments is specified using **deployment.frequency = X**; where X is the time (in mosquito generations) between insecticide treatments. By default **deployment.frequency = 30** would be for LLIN deployment every 3 years**. deployment.frequency = 10** would be for annual IRS.

For **irm.deployment.strategy = “singles”**, the simulations always start with insecticide 1 in deployment.

## irm.deployment.strategy= “mixtures”

Obviously if **irm.deployment.strategy= “mixtures”** then **number.of.insecticides > 1.** As a mixture requires a minimum of two insecticides. Prior to explaining the available ways in which mixtures can be switched, we need to explain how mixtures can be made. This is specified with the **mixture.strategy** input:

* **mixture.strategy = “mix.sequential.discrete”**

Mixes insecticides into discrete non-overlapping batches. For example, if the number.of.insecticides = 6, then three mixture formulations would be made, consisting of 1+2 ; 3+4 ; 5+6. Note, when **mixture.strategy = “mix.sequential.discrete”**, the **number.of.insecticides** must be an even number.

* **mixture.strategy = “mix.sequential.continuous”**

Mixes insecticides into continuous overlapping mixtures. For example, if the **number.of.insecticides = 4,** the mixtures would contain the insecticides: 1+2; 2+3 ; 3+4 ; 4+1. That is each insecticide is partnered with its neighbour in numerical sequence.

* **mixture.strategy = “random.mixtures”**

Makes all possible mixtures (pairing each insecticide with every other insecticide), then samples these such that the total number of available mixtures is the same as the **number.of.insecticides**.

* **mixture.strategy = “pyrethroid.plus”**

Perhaps the most realistic of the mixing strategies, this pairs insecticide 1 with all the other insecticides included in the simulation. For example if the **number.of.insecticides = 4,** the mixture formulations would be 1+2 ; 1+3, 1+4.

Each individual mixture formulation (i.e., 1+2) is then given a unique ID number.

* **irm.switch.strategy = “rotation”**

The mixture (based on mixture ID number) is rotated at each deployment opportunity. The same insecticide is able to be deployed in the next rotation providing it has a different mixture ID. For example, a mixture of 1+2 could be rotated to a mixture of 2+3.

* **irm.switch.strategy = “sequence”**

The mixture formulation (based on the unique ID number) is deployed in sequence. As with the rotation, the same insecticide can be deployed as the next sequence, providing it is in a different mixture formulation (e.g. 1+2 followed by 2+3 ; providing insecticide 2 has not reached the withdrawal criteria).

* **irm.switch.strategy = “novel.sequence”**

Insecticide deployment decisions are made on the novel insecticide (that is any insecticide which is not insecticide 1). It is recommended that the **irm.switch.strategy = “novel.sequence”**, be combined with the **mixture.strategy = “pyrethroid.plus”.** If the resistance to insecticide 1 is above the withdrawal threshold, the mixture can still be deployed as the withdrawal of a mixture formulation is dependent only on the novel insecticide (i.e., any insecticide which is not 1). This is to allow the simulations to run as though a novel insecticide is being deployed in mixture with a pyrethroid (where the pyrethroid is never withdrawn even when there is substantial resistance).

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For **irm.deployment.strategy = “mixtures”** the deployment interval between insecticide deployments is specified using **deployment.frequency = X**; where X is the time (in mosquito generations) between insecticide treatments. By default **deployment.frequency = 30** would be for LLIN deployment every ~3 years and **deployment.frequency** = 10 would be for annual IRS.

The **deployment.frequency** indicates the resolution to which the model can terminate run time.

By default, the simulation starts with the first mixture being deployed (that is the mixture with the ID of 1).

## irm.deployment.strategy = “micromosaics”

Micro-mosaics involve the deployment of two different insecticides at a spatial such that a single mosquito encounters only one of the insecticides in each gonotrophic cycle. For example, a proportion of houses are given one brand of LLIN and the other remaining proportion of houses are given a different brand of LLIN.

While micro-mosaics are perhaps idealised as being a 50:50 split, the model allows for manual input of the actual relative coverage of each insecticide, using **intervention.coverage.1** and **intervention.coverage.2**; which are both proportions which must sum to one. Note, **intervention.coverage.1** is the coverage by the first insecticide and **intervention.coverage.2** is the coverage by the second insecticide and are not the coverage of insecticide 1 and insecticide 2.

There are therefore a large number of ways in which insecticides can be switched.

* + **irm.switch.strategy =** “partial.rotation”

If insecticide 1 and 2 are currently deployed they would be switched with 2 and 3 at the next deployment interval. This further means that the coverages get updated too. Such that insecticide 2 goes from having **intervention.coverage.2** to having **intervention.coverage.1**; with the newly deployed insecticide 3 having the coverage of **intervention.coverage.2**. That is only the lowest numerically valued insecticide is rotated out

* + **irm.switch.strategy =** “full.rotation”

In this switch strategy, both the insecticides deployed in the micro-mosaic are rotated out. For example if insecticides 1&2 were deployed they would be switched with the next two available insecticides such as 3%4. For this switch strategy to work, there needs to be 4 or more insecticides in the simulation.

* + **irm.switch.strategy =** “sequence”

In this switch strategy each insecticide is deployed in sequence. Being withdrawn only when reaching the withdrawal threshold. This is done independently for each insecticide in the micro-mosaic.

* + **irm.switch.strategy =** “rotate.expensive”

In this switch strategy, we assume that one of the insecticides is cheaper (e.g. a pyrethroid) than the other insecticides (e.g. they are novel insecticides). And therefore, to reduce the cost of running the insecticide deployments, the cheap insecticide is always deployed.

For “micromosaics” the deployment interval between insecticide deployments is specified using **deployment.frequency = X;** where X is the time (in mosquito generations) between insecticide treatments. By default **deployment.frequency = 30** would be for LLIN deployment every 3 years. **deployment.frequency = 10** would be for annual IRS.

Two additional parameter inputs are needed for the micromosaics strategy. Which are the relative coverage levels of the two insecticides being deployed. This is specified using the **intervention.coverage.1** and **intervention.coverage.2** inputs. Here these two parameter inputs must sum to 1. Note, if either insecticide is set to have a relative coverage of 1, then this is a de-facto singles deployment.

## irm.deployment.strategy = “combinations”

* + “rotate.irs”
  + “sequence.irs”

llin.insecticides = The insecticides which are deployed as LLINs.

irs.insecticides =

intervention.coverage.1 =

intervention.coverage.2 =

intervention.coverage.1.2 =

deployment.interval.llin =

deployment.interval.irs =

probability.only.i.male =

probability.only.j.male =

probability.both.i.j.male =

probability.only.i.female =

probability.only.j.female =

probability.both.i.j.female =

It is useful to note that the **irm.deployment.strategy = “combinations”** can be used to run **“mixtures”** if:

* intervention.coverage.1.2 = 1
* probability.both.i.j.male = 1
* probability.both.i.j.female = 1

It is useful to note that the **irm.deployment.strategy = “combinations”** can be used to run **“micromosaics”** if:

* intervention.coverage.1 = 0.5
* intervention.coverage.2 = 0.5

# Insecticide Switching Criteria

The criteria for switching insecticides are based on strict withdrawal/return thresholds.

**withdrawal.threshold** is the threshold at which an insecticide cannot be deployed. The input should be a proportion. E.g. **withdrawal.threshold = 0.1** would set the withdrawal threshold at 10% bioassay survival.

**return.threshold** is the threshold for which a withdrawn insecticide must return to prior to being returned to the insecticide armoury. The input should be a proportion, and generally less than the **withdrawal.threshold** (setting **return.threshold** > **withdrawal.threshold** prevents the return of withdrawn insecticides). E.g. **return.threshold = 0.05** would set the return threshold at 5% bioassay survival.

Note there are ways that this functionality is turned off, that is insecticides that should be withdrawn remain in deployment:

Mixtures:

Micromosaics:

Combinations:

# Biological/Chemical Parameters

## Giving the insecticide (and insecticide traits) unique properties:

* starting.refugia.resistance.score = 0,
* starting.intervention.resistance.score = 0,
* applied.insecticide.dose = 1,
* recommended.insecticide.dose = 1
* threshold.generations = 10,
* base.efficacy.decay.rate = 0,
* rapid.decay.rate = 0,
* female.fitness.cost = 0,
* male.fitness.cost = 0,
* heritability =0.3

## Cross selection

* **min.cross.selection**
* **max.cross.selection**

These are used to create a cross selection matrix, with resistance between insecticides sampled within a uniform distribution between the **min.cross.selection** and **max.cross.selection**. If cross selection is not wanted; then both the **min.cross.selection** and **max.cross.selection** should be set to zero.

Additional Notes:

vector.length = 1000,

maximum.bioassay.survival.proportion = 1,

michaelis.menten.slope = 1,

regression.coefficient = 0.48,

regression.intercept = 0.15,

half.population.bioassay.survival.resistance = 900,

maximum.resistance.value = 90000,

sd.scaled: TRUE / FALSE

standard.deviation

z.sd.intercept

z.sd.coefficient

Additional functions of technical use:::