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# simuPOP User's Guide

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## Abstract

simuPOP is a forward-time population genetics simulation environment. Unlike coalescent-based programs, simuPOP evolves populations forward in time, subject to arbitrary number of genetic and environmental forces such as mutation, recombination, migration and population/subpopulation size changes. Statistics of populations can be calculated and visualized dynamically which makes simuPOP an ideal tool to demonstrate population genetics models; generate datasets under various evolutionary settings, and more importantly, study complex evolutionary processes and evaluate gene mapping methods.

simuPOP is provided as a number of Python modules, which provide of a large number of Python objects and functions, including population, mating schemes, operators (objects that manipulate populations) and simulators to coordinate the evolutionary processes. It is the users' responsibility to write a Python script to glue these pieces together and form a simulation. At a more user-friendly level, simuPOP provides an increasing number of bundled scripts that perform simulations ranging from implementation of basic population genetics models to generating datasets under complex evolutionary scenarios. No knowledge about Python or simuPOP would be needed to run these simulations, if they happen to fit your need.

This user's guide shows you how to install and use simuPOP using a large number of examples. It describes all important concepts and features of simuPOP and shows you how to use them in a simuPOP script. For a complete and detailed description about all simuPOP functions and classes, please refer to the *simuPOP Reference Manual*. All resources, including a pdf version of this guide and a mailing list can be found at the simuPOP homepage <http://simupop.sourceforge.net>.

### How to cite simuPOP:

Bo Peng and Marek Kimmel (2005) simuPOP: a forward-time population genetics simulation environment. *bioinformatics*, **21** (18): 3686-3687

Bo Peng and Christopher Amos (2008) Forward-time simulations of nonrandom mating populations using simuPOP. *bioinformatics*, **24** (11) 1408-1409.



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# Chapter 1

## Introduction

### 1.1 What is simuPOP?

simuPOP is an individual-based forward-time population genetics simulation environment based on Python, a dynamic object-oriented programming language that has been widely used in biological studies. simuPOP provides a large number of Python objects and functions, and a mechanism to evolve populations forward in time. It is the users' responsibility to write a Python script to form a simulation. At a more user-friendly level, simuPOP provides an increasing number of built-in scripts so that users who are unfamiliar with Python and simuPOP can perform some pre-specified simulation processes. These scripts range from implementation of basic population genetics models to generating datasets under complex evolutionary scenarios. In addition, simuPOP modules and functions are provided to load and manipulate HapMap samples and to perform a number of popular gene-mapping methods.

Unlike other population genetics simulation applications that aim at specific evolutionary scenarios, simuPOP aims at providing a general purpose simulation program that can be used to write and study arbitrarily complex evolutionary scenarios. This makes simuPOP an ideal tool in a wide variety of applications ranging from demonstrating simple population genetics models to studying the evolution of complex human genetic diseases.

### 1.2 An overview of simuPOP concepts

A simuPOP **population** consists of individuals of the same **genotype structure**, which include properties such as number of homologous sets of chromosomes (ploidy), number of chromosomes, and names and locations of markers on each chromosome. Individuals can be divided into **subpopulations** that can be further divided into **virtual subpopulations** according to individual properties such as sex, affection status, or arbitrary auxiliary information such as age.

**Operators** are Python objects that act on a population. They can be applied to a population before or after mating during a life cycle of an evolutionary process (Figure 1.1), or to one or two parents during the production of each offspring. Arbitrary numbers of operators can be applied to an evolving population.

A simuPOP **mating scheme** is responsible for choosing parent or parents from a parental (virtual) subpopulation and for populating an offspring subpopulation. simuPOP provides a number of pre-defined mating schemes, such as random, consanguineous, monogamous, or polygamous mating, selfing, and haplodiploid mating in hymenoptera. More complicated nonrandom mating schemes such as mating in age-structured populations can be constructed using **heterogeneous mating schemes**.

simuPOP evolves a population generation by generation, following the evolutionary cycle depicted in Figure 1.1. Briefly speaking, a number of **pre-mating operators** such as a `mutator` are applied to a population before a mating scheme repeatedly chooses a parent or parents to produce offspring. **During-mating operators** such as *recombinator*

Figure 1.1: A life cycle of an evolutionary process

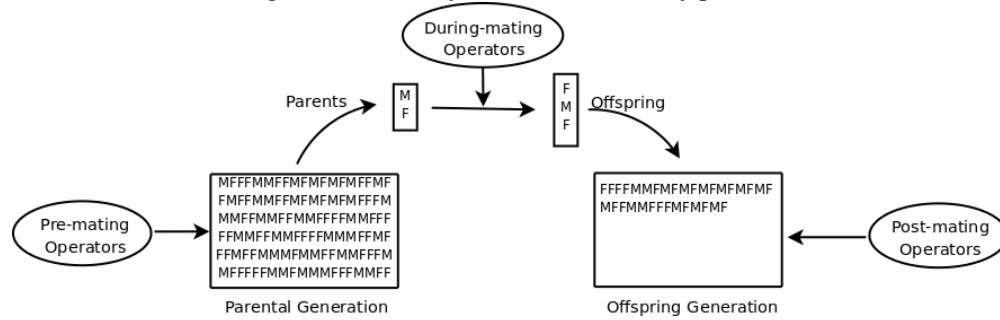


Illustration of the discrete-generation evolutionary model used by simuPOP.

can be used to adjust how offspring genotypes are formed from parental genotypes. After an offspring population is populated, **post-mating operators** can be applied, for example, to calculate population statistics. The offspring population will then become the parental population of the next evolutionary cycle.

Example 1.1: A simple example

```
>>> import simuPOP as sim
>>> pop = sim.population(size=1000, loci=2)
>>> simu = sim.simulator(pop, sim.randomMating(ops=sim.recombinator(rates=0.01)), rep=3)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([1, 2, 2, 1])
...     ],
...     postOps = [
...         sim.stat(LD=[0, 1]),
...         sim.pyEval(r"%0.2f\t\t % LD[0][1]", step=10),
...         sim.pyOutput('\n', reps=-1, step=10)
...     ],
...     gen=100
... )
0.24    0.25    0.24
0.21    0.23    0.22
0.17    0.21    0.20
0.13    0.17    0.18
0.10    0.15    0.18
0.11    0.14    0.16
0.12    0.10    0.16
0.11    0.11    0.15
0.09    0.10    0.14
0.07    0.10    0.11
(100, 100, 100)
```

These concepts are demonstrated in Example 1.1, where a standard diploid Wright-Fisher model with recombination is simulated. The first line imports the standard simuPOP module. The second line creates a diploid population with 1000 individuals, each having one chromosome with two loci. The third line creates a simulator with three replicates of this population. Random mating will be used to generate offspring but a `recombinator` is used to recombine parental chromosomes with the given recombination rate 0.01 during the generation of offspring. The last statement uses the `evolve()` function to evolve the populations for 100 generations, subject to five operators.

The first operator `initByValue` is applied to all populations before evolution. This operator initializes all individuals with the same genotype 12/21. The other operators can be applied at every generation. `stat` calculates linkage disequilibrium between the first and second loci. The results of this operator are stored in a local variable space of



each population. The last two operators `pyEval` and `pyOutput` are applied at the end of every 10 generations. `pyEval` is applied to all replicates to output calculated linkage disequilibrium values with a trailing tab, and the last operator outputs a newline after the last replicate. The result is a table of three columns, representing the decay of linkage disequilibrium of each replicate at 10 generation intervals. The return value of the `evolve` function, which is the number of evolved generations for each replicate, is also printed.

## 1.3 Features

simuPOP offers a long list of features, many of which are unique among all forward-time population genetics simulation programs. The most distinguished features include:

1. simuPOP provides three types of modules that use 1, 8 or 32 bits to store an allele. The binary module (1 bit) is suitable for simulating a large number of SNP markers and the long module (32 bits) is suitable for simulating some population genetics models such as the infinite allele mutation model. simuPOP supports different types of chromosomes such as autosome, sex chromosomes and mitochondrial, with arbitrary number of markers.
2. An arbitrary number of float numbers, called information fields, can be attached to individuals of a population. For example, information field `father_idx` and `mother_idx` are used to track an individual's parents, and `pack_year` can be used to simulate an environmental factor associated with smoking.
3. simuPOP does not impose any limit on number of homologous sets of chromosomes, the size of the genome, or the number of individuals in a population. During an evolutionary process, a population can hold more than one most-recent generations. Pedigrees can be sampled from such multi-generation populations.
4. An operator can be native (implemented in C++) or hybrid (Python assisted). A hybrid operator calls a user-provided Python function to implement arbitrary genetic effects. For example, a hybrid mutator passes to-be-mutated alleles to a user-provided function and mutates these alleles according to the returned values.
5. simuPOP provides more than 70 operators that cover all important aspects of genetic studies. These include mutation (*k*-allele, stepwise, generalized stepwise and hybrid), migration (arbitrary, can create new subpopulation), recombination and gene conversion (uniform or nonuniform, sex-specific), quantitative trait (single, multilocus or hybrid), selection (single-locus, additive, multiplicative or hybrid multi-locus models), penetrance (single, multi-locus or hybrid), ascertainment (case-control, affected sibpairs, random, nuclear and large pedigree), statistics calculation (including but not limited to allele, genotype, haplotype, heterozygote number and frequency; expected heterozygosity; bi-allelic and multi-allelic, and linkage disequilibrium measures), pedigree tracing, visualization (using R or other Python modules) and load/save in simuPOP's native format and many external formats such as Linkage.
6. Mating schemes and many operators can work on virtual subpopulations of a subpopulation. For example, positive assortative mating can be implemented by mating individuals with similar properties such as ancestry. The number of offspring per mating event can be fixed, or can follow a statistical distribution.

A number of forward-time simulation programs are available. If we exclude early forward-time simulation applications developed primarily for teaching purposes, notable forward-time simulation programs include *easyPOP*, *FPG*, *Nemo* and *quantiNemo*, *genoSIM* and *genomeSIMLA*, *FreGene*, *GenomePop*, *ForwSim*, and *ForSim*. These programs are designed with specific applications and specific evolutionary scenarios in mind, and excel in what they are designed for. For some applications, these programs may be easier to use than simuPOP. For example, using a special look-ahead algorithm, *ForwSim* is among the fastest programs to simulate a standard Wright-Fisher process, and should be used if such a simulation is needed. However, these programs are not flexible enough to be applied to problems outside of their designed application area. For example, none of these programs can be used to study the evolution of a disease predisposing mutant, a process that is of great importance in statistical genetics and genetic epidemiology. Compared to such programs, simuPOP has the following advantages:

- The scripting interface gives simuPOP the flexibility to create arbitrarily complex evolutionary scenarios. For example, it is easy to use simuPOP to explicitly introduce a disease predisposing mutant to an evolving population, trace the allele frequency of them, and restart the simulation if they got lost due to genetic drift.
- The Python interface allows users to define customized genetic effects in Python. In contrast, other programs either do not allow customized effects or force users to modify code at a lower (e.g. C++) level.
- simuPOP is the only application that embodies the concept of virtual subpopulation that allows evolutions at a finer scale. This is required for realistic simulations of complex evolutionary scenarios.
- simuPOP allows users to examine an evolutionary process very closely because all simuPOP objects are Python objects that can be assessed using their member functions. For example, users can keep track of genotype at particular loci during evolution. In contrast, other programs work more or less like a black box where only limited types of statistics can be outputted.

## 1.4 Installation

simuPOP is distributed under a GPL license and is hosted on <http://simupop.sourceforge.net>, the world's largest development and download repository of Open Source code and applications. simuPOP is available on any platform where Python is available, and is currently tested under both 32 and 64 bit versions of Windows (Windows 2000 and later), Linux (Redhat), MacOS X and Sun Solaris systems. Different C++ compilers such as Microsoft Visual C++, gcc and Intel icc are supported under different operating systems. Standard installation packages are provided for Windows, Linux, MacOS X, and Sun Solaris systems.

If a binary distribution is unavailable for a specific platform, it is usually easy to compile simuPOP from source, following the standard "python setup.py install" procedure. Besides a C++ compiler, several supporting tools and libraries are needed. Please refer to the INSTALL file for further information.

Thanks to the 'glue language' nature of Python, it is easy to inter-operate Python with other applications within a simuPOP script. For example, users can call any R function from Python/simuPOP for the purposes of visualization and statistical analysis, using R and a Python module RPY. This technique is widely used in simuPOP so it is highly recommended that you install R and rpy is your are familiar with R. In addition, although simuPOP uses the standard tkInter GUI toolkit when a graphical user interface is needed, it can make use of a wxPython toolkit if it is available.

## 1.5 Pythonic issues

### 1.5.1 `from simuPOP import *` v.s. `import simuPOP`

Generally speaking, it is recommended to use `import simuPOP` rather than `from simuPOP import *` to import a simuPOP module. That is to say, instead of using

```
from simuPOP import *
pop = population(size=100, loci=[5])
simu = simulator(pop, randomMating())
```

it is recommended that you use simuPOP like

```
import simuPOP
pop = simuPOP.population(size=100, loci=[5])
simu = simuPOP.simulator(pop, simuPOP.randomMating())
```

The major problem with `from simuPOP import *` is that it imports all simuPOP symbols to the global namespace and increases the chance of name clashes. For example, if you import a module `myModule` after `simuPOP`, which happens to have a variable named `MALE`, the following code might lead to a `TypeError` indicating your input for parameter `sex` is wrong.

```

from simuPOP import *
from myModule import *
pop = population(size=100, loci=[5])
InitSex(pop, sex=[MALE, FEMALE])

```

It can be even worse if the definition of MALE is changed to a different value of the same type (e.g. to FEMALE) and your simulation might produce erroranous result without a hint.

For the sake of brevity, all examples in this user's guide use `import simuPOP as sim` as an alternative form of the `import simuPOP` style. This saves some keystrokes by referring `simuPOP` functions as `sim.population()` instead of `simuPOP.population()`. Note that `simuPOP` has a number of submodules, which are not imported by default. The recommended syntax is:

```

# import and use submodule simuPOP.utils
from simuPOP import utils
utils.BackwardTrajectory(N=1000, endGen=100, endFreq=0.1)

```

## 1.5.2 References and the `clone()` member function

Assignment in Python only creates a new reference to an existing object. For example,

```

pop = population()
pop1 = pop

```

will create a reference `pop1` to population `pop`. Modifying `pop1` will modify `pop` as well and the removal of `pop` will invalidate `pop1`. For example, a reference to the first population in a simulator is returned from function `func()` in Example 1.2. The subsequent use of this `pop` object may crash `simuPOP` because the simulator `simu` is destroyed, along with all its internal populations, after `func()` is finished, leaving `pop` referring to an invalid object.

Example 1.2: Reference to a population in a simulator

```

def func():
    simu = simulator(population(10), randomMating(), rep=5)
    # return a reference to the first population in the simulator
    return simu.population(0)

pop = func()
# simuPOP will crash because pop refers to an invalid population.
pop.popSize()

```

If you would like to have an independent copy of a population, you can use the `clone()` member function. Example 1.2 would behave properly if the `return` statement is replaced by

```

return simu.population(0).clone()

```

although in this specific case, extracting the first population from the simulator using the `extract` function

```

return simu.extract(0)

```

would be more efficient because we do not need to copy the first population from `simu` if it will be destroyed soon.

The `clone()` function exists for all `simuPOP` classes (objects) such as *simulator*, *mating schemes* and *operators*. `simuPOP` also supports the standard Python shallow and deep copy operations so you can also make a cloned copy of `pop` using the `deepcopy` function defined in the Python `copy` module

```

import copy
pop1 = copy.deepcopy(pop)

```

### 1.5.3 Zero-based indexes, absolute and relative indexes

All arrays in **simuPOP** start at index 0. This conforms to Python and C++ indexes. To avoid confusion, I will refer the first locus as locus zero, the second locus as locus one; the first individual in a population as individual zero, and so on.

Another two important concepts are the *absolute index* and the *relative index* of a locus. The former index ignores chromosome structure. For example, if there are 5 and 7 loci on the first two chromosomes, the absolute indexes of the two chromosomes are (0, 1, 2, 3, 4), (5, 6, 7, 8, 9, 10, 11) and the relative indexes are (0, 1, 2, 3, 4), (0, 1, 2, 3, 4, 5, 6). Absolute indexes are more frequently used because they avoid the trouble of having to use two numbers (chrom, index) to refer to a locus. Two functions `chromLocusPair(idx)` and `absLocusIndex(chrom, index)` are provided to convert between these two kinds of indexes. An individual can also be referred by its *absolute index* and *relative index* where *relative index* is the index in its subpopulation. Related member functions are `subPopIndPair(idx)` and `absIndIndex(idx, subPop)`.

Example 1.3: Conversion between absolute and relative indexes

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[10, 20], loci=[5, 7])
>>> print pop.chromLocusPair(7)
(1, 2)
>>> print pop.absLocusIndex(1, 1)
6
>>> print pop.absIndIndex(2, 1)
12
>>> print pop.subPopIndPair(25)
(1, 15)
```

### 1.5.4 Ranges and iterators

Ranges in **simuPOP** also conform to Python ranges. That is to say, a range has the form of `[a,b)` where `a` belongs to the range, and `b` does not. For example, `pop.chromBegin(1)` refers to the index of the first locus on chromosome 1 (actually exists), and `pop.chromEnd(1)` refers to the index of the last locus on chromosome 1 **plus 1**, which might or might not be a valid index.

A number of **simuPOP** functions return Python iterators that can be used to iterate through an internal array of objects. For example, `population.individuals([subPop])` returns an iterator that can be used to iterate through all individuals, or all individuals in a (virtual) subpopulation. `simulator.populations()` can be used to iterate through all populations in a simulator. Example 2.10 demonstrates the use of ranges and iterators in **simuPOP**.

Example 1.4: Ranges and iterators

```
>>> import simuPOP as sim
>>> pop = sim.population(size=2, loci=[5, 6])
>>> sim.InitByFreq(pop, [0.2, 0.3, 0.5])
>>> for ind in pop.individuals():
...     for loc in range(pop.chromBegin(1), pop.chromEnd(1)):
...         print ind.allele(loc),
...     print
```

### 1.5.5 carray datatype

**simuPOP** uses mostly standard Python types such as tuples, lists and dictionaries. However, for efficiency considerations, **simuPOP** defines and uses a new `carray` datatype to refer to an internal array of genotypes. Such an object can only be returned from `individual.genotype` and `population.genotype` functions. Instead of copying all genotypes to a Python tuple or list, these functions return a `carray` object that directly reflect the underlying

genotype. This object behaves like a regular Python list except that the underlying genotype will be changed if elements of this object are changed. In addition, elements in this array will be changed if the underlying genotype is changed using another method.

Example 2.10 demonstrates the use of this datatype. It also shows how to get an independent list of alleles using the `list()` built-in function. Compare to `allele()`, `setAllele()` and `setGenotype()` functions, it is usually more efficient and more convenient to read and write genotypes using carray objects, although this usage is usually less readable.

Example 1.5: The carray datatype

```
>>> import simuPOP as sim
>>> pop = sim.population(size=2, loci=[3, 4])
>>> sim.InitByFreq(pop, [0.3, 0.5, 0.2])
>>> ind = pop.individual(0)
>>> arr = ind.genotype()      # a carray to the underlying genotype
>>> geno = list(arr)          # a list of alleles
>>> print arr
[1, 1, 0, 0, 1, 1, 1, 1, 0, 0, 2, 1, 1, 1]
>>> print geno
[1, 1, 0, 0, 1, 1, 1, 1, 0, 0, 2, 1, 1, 1]
>>> arr.count(1)              # count
9
>>> arr.index(2)              # index
10
>>> ind.setAllele(5, 3)      # change underlying genotype using setAllele
>>> print arr                # arr is change
[1, 1, 0, 5, 1, 1, 1, 1, 0, 0, 2, 1, 1, 1]
>>> print geno               # but not geno
[1, 1, 0, 0, 1, 1, 1, 1, 0, 0, 2, 1, 1, 1]
>>> arr[2:5] = 4              # can use regular Python slice operation
>>> print ind.genotype()
[1, 1, 4, 4, 4, 1, 1, 1, 0, 0, 2, 1, 1, 1]
```

## 1.5.6 defdict datatype

simuPOP uses dictionaries to save statistics such as allele frequencies. For example, `alleleFreq[5]` can be `{0:0.2, 3:0.8}` meaning there are 20% allele 0 and 80% allele 3 at locus 5 in a population. However, because it is sometimes unclear whether or not a particular allele exists in a population, `alleleFreq[5][allele]` can fail with a `KeyError` exception if `alleleFreq[5]` does not have key `allele`.

To address this problem, a special default dictionary type `defdict` is used for dictionaries with keys determined from a population. This derived dictionary type works just like a regular dictionary, but it returns 0, instead of raising a `KeyError` exception, when an invalid key is used. For example, subpopulations in Example 1.6 have different alleles. Although `pop.dvars(sp).alleleFreq[0]` have only two keys for `sp=0` or `1`, `pop.dvars(sp).alleleFreq[0][x]` are used to print frequencies of alleles 0, 1 and 2.

Example 1.6: The defdict datatype

```
>>> import simuPOP as sim
>>> pop = sim.population([100]*2, loci=1)
>>> sim.InitByFreq(pop, [0, 0.2, 0.8], subPops=0)
>>> sim.InitByFreq(pop, [0.2, 0.8], subPops=1)
>>> sim.Stat(pop, alleleFreq=0, vars=['alleleFreq_sp'])
>>> for sp in range(2):
...     print 'Subpop %d (with %d alleles): ' % (sp, len(pop.dvars(sp).alleleFreq[0])),
...     for a in range(3):
...         print '%.2f ' % pop.dvars(sp).alleleFreq[0][a],
...     print
```

**Note:** The standard `collections` module of Python has a `defaultdict` type that accepts a default factory function that will be used when an invalid key is encountered. The `defdict` type is similar to `defaultdict(int)` but with an important difference: when an invalid key is encountered, `d[key]` with a default value will be inserted to a `defaultdict(int)`, but will not be inserted to a `defdict`. That is to say, it is safe to use `alleleFreq[loc].keys()` to get available alleles after non-assignment `alleleFreq[loc][allele]` operations.

## 1.5.7 Parameter names and single and list input of parameters

simuPOP follows (at least tries to follow) the following naming convention:

- If a parameter only accept a single input, singular names such as `field`, `locus`, `value`, and `name` are used.
- If a parameter accepts a list of values, plural names such as `fields`, `loci`, `values` and `names` are used.
- **Plural form parameters usually accept single inputs.** For example, `loci=1` can be used as a shortcut for `loci=[1]` and `infoFields='x'` can be used as a shortcut for `infoFields=['x']`.

The same rules also hold for function names. For example, `population.addInfoFields()` accept a list of information fields but `pop.addInfoFields('field')` is also acceptable.

## 1.5.8 Value ALL\_AVAIL for parameters loci, reps and subPops

Parameters `loci`, `reps` and `subPops` are widely used in simuPOP to specify which loci, replicates or (virtual) subpopulations a function or operator is applied to. These parameter accepts a list of values such as `[1, 2]` and take single form inputs (e.g. `loci=1` is equivalent to `loci=[1]`). For example,

- `recombinator(loci=[])` recombine at no locus, and
- `recombinator(loci=1)` recombine at locus 1
- `recombinator(loci=[1, 2, 4])` recombine at loci 1, 2, and 4

However, in the majority of the cases, these parameters take a default value `ALL_AVAIL` which applies the function or operator to all available loci, replicates or subpopulations. That is to say, `recombinator()` or `recombinator(loci=ALL_AVAIL)` will recombine at all applicable loci, which will vary from population to population.

## 1.6 Getting help

### 1.6.1 Online help system

Most of the help information contained in this document and *the simuPOP reference manual* is available from command line. For example, after you install and import the simuPOP module, you can use `help(population.addInfoField)` to view the help information of member function `addInfoField` of class `population`.

Example 1.7: Getting help using the `help()` function

```
>>> import simuPOP as sim
>>> help(sim.population.addInfoFields)
Help on method population_addInfoFields in module _simuPOP_la:
```

```

population_addInfoFields(...) unbound simuPOP.simuPOP_la.population method
Usage:

    x.addInfoFields(fields, init=0)

Details:

    Add a list of information fields fields to a population and
    initialize their values to init. If an information field already
    exists, it will be re-initialized.

```

It is important that you understand that

- The constructor of a class is named `__init__` in Python. That is to say, you should use the following command to display the help information of the constructor of class `population`:

```
>>> help(population.__init__)
```

- Some classes are derived from other classes and have access to member functions of their base classes. For example, class `population` and `individual` are both derived from class `GenoStruTrait`. Therefore, you can use all `GenoStruTrait` member functions from these classes.

In addition, the constructor of a derived class also calls the constructor of its base class so you may have to refer to the base class for some parameter definitions. For example, parameters `begin`, `end`, `step`, `at` etc are shared by all operators, and are explained in details only in class `baseOperator`.

## 1.6.2 Debug-related operators/functions

If your `simuPOP` session or script does not behave as expected, it might be helpful to let `simuPOP` print out some debug information. For example, the following code will crash `simuPOP`:

```
>>> population(1, loci=[100]).individual(0).genotype()
```

It is unclear why this simple command causes us trouble, instead of outputting the genotype of the only individual of this population. However, the reason is clear if you turn on debug information:

Example 1.8: Turn on/off debug information

```

>>> TurnOnDebug('DBG_POPULATION')
>>> population(1, loci=[100]).individual(0).genotype()
Constructor of population is called
Destructor of population is called
Segmentation fault (core dumped)

```

`population(1, loci=[100])` creates a temporary object that is destroyed right after the execution of the command. When Python tries to display the genotype, it will refer to an invalid location. The right way to do this is to create a persistent population object:

```

>>> pop = population(1, loci=[100])
>>> pop.individual(0).genotype()

```

You can use `TurnOnDebug(code)` and `TurnOffDebug(code)` to turn on and off debug information where `code` can be any debug code listed in `ListDebugCode()`. If you would like to turn on debugging during an evolutionary process, you can use operators `turnOnDebug` and `turnOffDebug`. **Note:** All debug information is written to Python `sys.stderr`. It is possible to redirect it to a file so that debug information is not mixed with regular output.



### 1.6.3 Other help sources

If you are new to Python, it is recommended that you borrow a Python book, or at least go through the following online Python tutorials:

1. The Python tutorial (<http://docs.python.org/tut/tut.html>)
2. Other online tutorials listed at <http://www.python.org/doc/>

If you are new to simuPOP, please read this guide before you dive into *the simuPOP reference manual*, which describes all the details of simuPOP but does not show you how to use it. The PDF versions of both documents are distributed with simuPOP. You can also get the latest version of the documents online, from the simuPOP subversion repository (<http://simupop.sourceforge.net>, click SF.net summary > Code > SVN Browse > trunk > doc). However, because simuPOP is under active development, there may be discrepancies between your local simuPOP installation and these latest documents.

A number of bundled scripts are distributed with simuPOP. They range from simple demonstration of population genetics models to observing the evolution of complex human genetic diseases. These scripts can be a good source to learn how to write a simuPOP script. Of course, if any of these scripts happens to fit your need, you may be able to use them directly, with writing a line of code.

A *simuPOP cookbook* is under development. The goal of this book is to provide recipes of commonly used simulation scenarios. A number of recipes are currently available under the `doc/cookbook` directory of a simuPOP distribution. This book might be made available online so that users can submit their own recipes.

If you cannot find the answer you need, or if you believe that you have located a bug, or if you would like to request a feature, please subscribe to the simuPOP mailinglist and send your questions there.

## 1.7 How to read this user's guide

This user's guide describes all simuPOP features using a lot of examples. Chapter 2 describes all classes in the simuPOP core. Chapter 3 describes almost all simuPOP operators, divided largely by genetic models. Features listed in these two chapters are generally implemented at the C++ level and are provided through the `simuPOP` module. Chapter 4 describes features that are provided by various simuPOP utility modules. These modules provide extensions to the simuPOP core that greatly improves the usability and userfriendliness of simuPOP. The next chapter (Chapter 5) demonstrates how to write a script to solve a real-world simulation problem. Because some sections describe advanced features that are only used in the construction of highly complex simulations, or implementation details that concern only advanced users, new simuPOP users can safely skip these sections. **Sections that describe advanced topics are marked by one or two asterisks (\*) after the section heads.**

simuPOP is a comprehensive forward-time population genetics simulation environment with many unique features. If you are new to simuPOP, you can go through Chapter 2 and 3 quickly and understand what simuPOP is and what features it provide. Then, you can read Chapter 5 and learn how to apply simuPOP in real-world problems. After you play with simuPOP for a while and start to write simple scripts, you can study relevant sections in details. The *simuPOP reference manual* will become more and more useful when the complexity of your scripts grow.

Before we dive into the details of simuPOP, it is helpful to know a few name conventions that simuPOP tries to follow. Generally speaking,

- All classes (e.g. `population()`), member functions (e.g. `population.vars()`) and parameter names start with small character and use capital character for the first character of each word afterward (e.g. `population.subPopSize()`, `individual.setInfo()`).
- Standalone functions start with capital character. This is how you can differ an operator from its function version. For example, `TurnOnDebug(DBG_POPULATION)` is the function to turn on debug mode for population



related functions and `turnOnDebug(DBG_POPULATION)` will do nothing apparently, because it creates an operator.

- Constants are written in all capital characters with underscores separating words (e.g. `CHROMOSOME_X`, `UNIFORM_DISTRIBUTION`). Their names instead of their actual values should be used because those values can change without notice.
- `simuPOP` uses the abbreviated form of the following words in function and parameter names:

`pos` (position), `info` (information), `migr` (migration), `subPop` (subpopulation and virtual subpopulation), `subPops` (subpopulations and virtual subpopulations), `rep` (replicate), `reps` (replicates), `gen` (generation), `ops` (operators), `expr` (expression), `stmts` (statements).

It is usually possible to guess whether or not a parameter accepts a single or a list of objects by its name. For example, `subPop` accepts single subpopulation and `subPops` accepts a list of subpopulations.



## Chapter 2

# Core simuPOP components

### 2.1 Loading a simuPOP module

simuPOP consists of a number of Python modules, documents, tests and examples. Using Linux as an example, simuPOP installs the following files to your operating system:

- Core simuPOP modules (`simuPOP_XXX.py`, `_simuPOP_XXX.so`) and a number of utility modules (`simuUtil.py`, `simuOpt.py` etc) under `/usr/lib/python2X/site-packages`.
- `/usr/share/simuPOP/doc`: This directory contains the pdf version of this user's guide and the *simuPOP reference manual*.
- `/usr/share/simuPOP/test`: This directory contains all unit test cases. It is recommended that you test your simuPOP installation using these scripts if you compile simuPOP from source.
- `/usr/share/simuPOP/scripts`: This directory contains all the bundled scripts. It is worth noting that although these scripts are distributed with simuPOP, they are not tested as rigorously and as frequently as the simuPOP core. Please send an email to the simuPOP mailinglist if you notice any problem with them.

#### 2.1.1 Short, long and binary modules and their optimized versions

There are six flavors of the core simuPOP module: short, long and binary allele modules, and their optimized versions. The short allele modules use 8 bits to store each allele which limits the possible allele states to 256. This is enough most of the times but not so if you need to simulate models such as the infinite allele model. In those cases, you should use the long allele version of the modules, which use 32 bits for each allele and can have  $2^{32}$  possible allele states. On the other hand, if you would like to simulate a large number of binary (SNP) markers, binary libraries can save you a lot of RAM because they use 1 bit for each allele. Despite of differences in internal memory layout, all these modules have the same interface.

Standard libraries have detailed debug and run-time validation mechanism to make sure a simulation executes correctly. Whenever something unusual is detected, simuPOP would terminate with detailed error messages. The cost of such run-time validation varies from case to case but can be high under some extreme circumstances. Because of this, optimized versions for all modules are provided. They bypass all parameter checking and run-time validations and will simply crash if things go wrong. It is recommended that you use standard libraries whenever possible and only use the optimized version when performance is needed and you are confident that your simulation is running as expected.

Example 2.1 and 2.2 demonstrate the differences between standard and optimized modules, by executing two invalid commands. A standard module returns proper error messages, while an optimized module returns erroneous results and or simply crashes.

### Example 2.1: Use of standard simuPOP modules

```
>>> import simuPOP as sim
>>> pop = sim.population(10, loci=2)
>>> pop.locusPos(10)
Traceback (most recent call last):
  File "/var/folders/70/70zyfGRoH+i7iQCDzTkba+++TQ/-Tmp-/tmp0kf5j0", line 1, in <module>
    #begin_file log/standard.py
IndexError: src/genoStru.h:532 absolute locus index (10) out of range of 0 ~ 1
>>> pop.individual(20).setAllele(1, 0)
Traceback (most recent call last):
  File "/var/folders/70/70zyfGRoH+i7iQCDzTkba+++TQ/-Tmp-/tmp0kf5j0", line 1, in <module>
    #begin_file log/standard.py
IndexError: src/population.h:538 individual index (20) out of range of 0 ~ 9
```

### Example 2.2: Use of optimized simuPOP modules

```
% python
>>> from simuOpt import setOptions
>>> setOptions(optimized=True, alleleType='long', quiet=True)
>>> from simuPOP import *
>>> pop = population(10, loci=[2])
>>> pop.locusPos(10)
1.2731974748756028e-313
>>> pop.individual(20).setAllele(1, 0)
Segmentation fault
```

Example 2.2 also demonstrates how to use the `setOptions` function in the `simuOpt` module to control the choice of one of the six `simuPOP` modules. By specifying one of `short`, `long` or `binary` for option `alleleType`, and setting `optimized` to `True` or `False`, the right flavor of module will be chosen when `simuPOP` is loaded. In addition, option `quiet` can be used suppress initial output. An alternative method is to set environmental variable `SIMUALLELETYPE` to `short`, `long` or `binary` to use the standard short, long or binary module, and variable `SIMUOPTIMIZED` to use the optimized modules. Command line options `--optimized` can also be used. **Note:** Please do not make use of exceptions raised by `simuPOP` functions to direct the logic of your script (e.g. use a `try ... except ...` statement around function `infoIdx` to find a valid information field). Because the optimized modules do not raise these exceptions, such a script may crash or yield invalid results when the optimized module is used.

## 2.1.2 Random number generator \*

When `simuPOP` is loaded, it creates a default random number generator (RNG) of type `mt19937` using a random seed from a system random number generator that guarantees random seeds for all instances of `simuPOP` even if they are initialized at the same time. After `simuPOP` is loaded, you can reset this system RNG with a different random number generator (c.f. `AvailableRNGs()`, `SetRNG(name, seed)`). It is also possible to save the random seed of a `simuPOP` session (c.f. `GetRNG().seed()`) and use it to replay the session later. **Note:** `GetRNG().seed()` returns the seed of the `simuPOP` random number generator. It can be used to replay your simulation if `GetRNG()` is your only source of random number generator. If you also use the Python `random` module, it is a good practise to set its seed using `random.seed(GetRNG().seed())`.

## 2.1.3 Graphical user interface

There is no graphical user interface to `simuPOP` but various dialogs can be used for simple tasks. For example, a parameter input dialog can be constructed automatically from a parameter specification list, and be used to accept user input if class `simuOpt.simuOpt` is used to handle parameters. Other examples include class `simuUtil.simuProgress` that makes use of a progress dialog, and function `simuUtil.ViewVars` that uses

a dialog to display a large number of variables. Note that the **use of GUI in simuPOP is optional in the sense that all functionalities can be achieved without a GUI**. For examples, `simuOpt.getParam()` will use a terminal to accept user input and `simuUtil.simuProgress` turns to a text-based progress bar in the non-GUI mode.

The use of GUI can be controlled either globally or individually. More specifically,

- By default, a GUI is used whenever possible. All GUI-capable functions support `wxPython` so a `wxPython` dialog will be used if `wxPython` is available. Otherwise, `tkInter` based dialogs or text-mode will be used.
- If environmental variable `SIMUGUI` is set to `False`, no GUI will be used. If it is set to `Tkinter`, `Tkinter`-based dialogs will be used even if `wxPython` is available.
- The same parameters `True/False/wxPython/Tkinter` at the script level using command line option `--gui`. Note that `--gui=False` is commonly used to run scripts in batch mode.
- For each involved function or class, parameter `gui` is usually provided. The same set of options apply.

## 2.2 Genotypic structure

Genotypic structure refers to structural information shared by all individuals in a population, including number of homologous copies of chromosomes (c.f. `ploidy()`, `ploidyName()`), chromosome types and names (c.f. `numChrom()`, `chromType()`, `chromName()`), position and name of each locus (c.f. `numLoci(ch)`, `locusPos(loc)`, `locusName(loc)`), and axillary information attached to each individual (c.f. `infoField(idx)`, `infoFields()`). In addition to property access functions, a number of utility functions are provided to, for example, look up the index of a locus by its name (c.f. `locusByName()`, `chromBegin()`, `chromLocusPair()`).

In `simuPOP`, locus is a (named) position and alleles are just different numbers at that position. **A locus can be a gene, a nucleotide, or even a deletion, depending on how you define alleles and mutations.** For example,

- A codon can be simulated as a locus with 64 allelic states, or three locus each with 4 allelic states. Alleles in the first case would be codons such as AAC and a mutation event would mutate one codon to another (e.g. AAC -> ACC). Alleles in the second case would be A, C, T or G, and a mutation event would mutate one nucleotide to another (e.g. A -> G).
- You can use 0 and 1 (and the binary module of `simuPOP`) to simulate SNP (single-nucleotide polymorphism) markers and ignore the exact meaning of 0 and 1, or use 0, 1, 2, 3 to simulate different nucleotide (A, C, T, or G) in these markers. The mutation model in the second case would be more complex.
- For microsatellite markers, alleles are usually interpreted as the number of tandem repeats. It would be difficult (though doable) to simulate the expansion and contraction of genome caused by the mutation of microsatellite markers.
- The infinite site and infinite allele mutation models could be simulated using either a continuous sequence of nucleotides with a simple 2-allele mutation model, or a locus with a large number of possible allelic states. It is also possible to simulate an empty region (without any locus) with loci introduced by mutation events.
- If you consider deletion as a special allelic state, you can simulate gene deletions without shrinking a chromosome. For example, a deletion mutation event can set the allelic state of one or more loci to 0, which can no longer be mutated.
- In an implementation of an infinite-sites model, **individual loci are used to store mutation events**. In this example (Example 3.36), 100 loci are allocated for each individual and they are used to store mutation events (location of a mutation) that happens in a 10Mb region. Whenever a mutation event happens, its location is stored as an allele of an individual. At the end of the evolution, each individual has a list of mutation events which can be readily translated to real alleles. Similar ideas could be used to simulate the accumulation of recombination events.

In summary, the exact meaning of loci and their alleles are user defined. With appropriate mutation model and mating scheme, it is even possible to simulate phenotypic traits using this mechanism, although it is more natural to use information fields for quantitative traits.

A genotypic structure can be retrieved from *individual* and *population* objects. Because a population consists of individuals of the same type, genotypic information can only be changed for all individuals at the population level. Populations in a simulator usually have the same genotypic structure because they are created by as replicates, but their structure may change during evolution. Example 2.10 demonstrates how to access genotypic structure functions at the population and individual levels. Note that `lociPos` determines the order at which loci are arranged on a chromosome. Loci positions and names will be rearranged if given `lociPos` is unordered.

Example 2.3: Genotypic structure functions

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[2, 3], ploidy=2, loci=[5, 10],
...     lociPos=range(0, 5) + range(0, 20, 2), chromNames=['Chr1', 'Chr2'],
...     alleleNames=['A', 'C', 'T', 'G'])
>>> # access genotypic information from the sim.population
>>> pop.ploidy()
2
>>> pop.ploidyName()
'diploid'
>>> pop.numChrom()
2
>>> pop.locusPos(2)
2.0
>>> pop.alleleName(1)
'C'
>>> # access from an individual
>>> ind = pop.individual(2)
>>> ind.numLoci(1)
10
>>> ind.chromName(0)
'Chr1'
>>> ind.locusName(1)
''
>>> # utility functions
>>> ind.chromBegin(1)
5
>>> ind.chromByName('Chr2')
1
>>> # loci pos can be unordered within each chromosome
>>> pop = sim.population(loci=[2, 3], lociPos=[3, 1, 1, 3, 2],
...     lociNames=['loc%d' % x for x in range(5)])
>>> pop.lociPos()
(1.0, 3.0, 1.0, 2.0, 3.0)
>>> pop.lociNames()
('loc1', 'loc0', 'loc2', 'loc4', 'loc3')
```

**Note:** `simuPOP` does not assume any unit for loci positions. Depending on your application, it can be basepair (bp), kilo-basepair (kb), mega base pair (mb) or even using genetic-map distance such as centiMorgan. It is your responsibility to interpret and use loci positions properly. For example, recombination rate between two adjacent markers can be specified as the product between their physical distance and a recombination intensity. The scale of this intensity will vary by the unit assumed.

**Note:** Names of loci, alleles and subpopulations are optional. Empty names will be used if they are not specified. Whereas `locusName`, `subPopName` and `alleleName` always return a value (empty string or specified value) for any locus, subpopulation or allele, respectively, `lociNames`, `subPopNames` and `alleleNames` only return specified values, which can be empty lists.

## 2.2.1 Haploid, diploid and haplodiploid populations

simuPOP is most widely used to study human (diploid) populations. A large number of mating schemes, operators and population statistics are designed around the evolution of such a population. simuPOP also supports haploid and haplodiploid populations although there are fewer choices of mating schemes and operators. simuPOP can also support other types of populations such as triploid and tetraploid populations, but these features are largely untested due to their limited usage. It is expected that supports for these populations would be enhanced over time.

For efficiency considerations, simuPOP saves the same numbers of homologous sets of chromosomes even if some individuals have different numbers of homologous sets in a population. For example, in a haplodiploid population, because male individuals have only one set of chromosomes, their second homologous set of chromosomes are *unused*, which are labeled as ' \_ ', as shown in Example 2.10.

Example 2.4: An example of haplodiploid population

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[2,5], ploidy=sim.HAPLODIPLOID, loci=[3, 5])
>>> sim.InitByFreq(pop, [0.3, 0.7])
>>> sim.Dump(pop)
Ploidy: 2 (haplodiploid)
Chromosomes:
1: (AUTOSOME, 3 loci)
   (1), (2), (3)
2: (AUTOSOME, 5 loci)
   (1), (2), (3), (4), (5)
population size: 7 (2 subpopulations with 2, 5 individuals)
Number of ancestral populations: 0

Subpopulation 0 (), 2 individuals:
0: MU 110 01111 | ____
1: MU 111 10001 | ____
Subpopulation 1 (), 5 individuals:
2: MU 111 11111 | ____
3: MU 111 11001 | ____
4: MU 101 11011 | ____
5: MU 111 00011 | ____
6: MU 101 01110 | ____
```

## 2.2.2 Autosomes, sex chromosomes, and other types of chromosomes \*

The default chromosome type is autosome, which is the *normal* chromosomes in diploid, and in haploid populations. simuPOP supports three other types of chromosomes, namely *ChromosomeX*, *ChromosomeY* and *Customized*. Sex chromosomes are only valid in haploid populations where chromosomes X and Y are used to determine the sex of an offspring. Customized chromosomes rely on user defined functions and operators to be passed from parents to offspring.

Example 2.10 shows how to specify different chromosome types, and how genotypes of these special chromosomes are arranged.

Example 2.5: Different chromosome types

```
>>> import simuPOP as sim
>>> pop = sim.population(size=6, ploidy=2, loci=[3, 3, 6, 4, 4, 4],
...     chromTypes=[sim.AUTOSOME]*2 + [sim.CHROMOSOME_X, sim.CHROMOSOME_Y] + [sim.CUSTOMIZED]*2)
>>> sim.InitByFreq(pop, [0.3, 0.7])
>>> sim.Dump(pop, structure=False) # does not display genotypic structure information
Subpopulation 0 (), 6 individuals:
0: MU 110 011 111111 ____ 1111 1111 | 100 111 ____ 0111 1110 1111
```

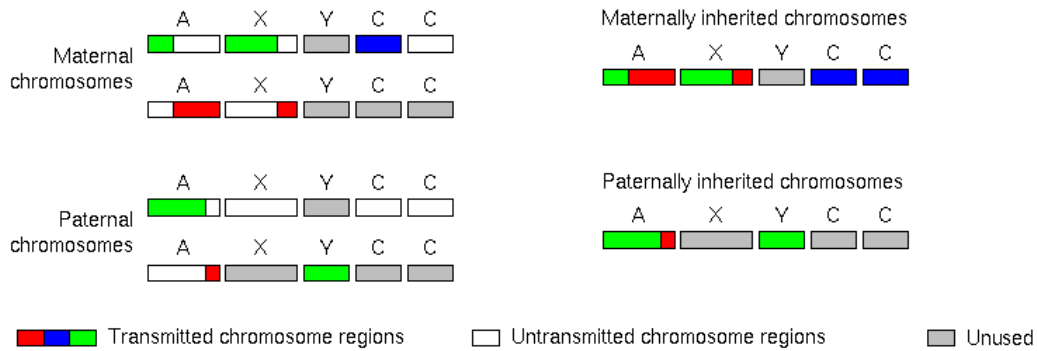
1: MU	111	110	011011	_____	1110	0011		011	111	_____	1110	0111	1111
2: MU	101	011	101111	_____	0111	1111		110	110	_____	0111	0111	1111
3: MU	111	001	111101	_____	1111	1101		110	111	_____	0001	0001	0010
4: MU	111	000	100111	_____	1101	1111		111	011	_____	1010	1111	1111
5: MU	110	111	100110	_____	0110	1110		111	101	_____	1100	1100	0101

The evolution of sex chromosomes follow the following rules

- There can be only one X chromosome and one Y chromosome. It is not allowed to have only one kind of sex chromosome.
- The Y chromosome of female individuals are ignored. The second homologous copy of the X chromosome and the first copy of the Y chromosome are ignored for male individuals.
- During mating, female parent pass one of her X chromosome to her offspring, male parent pass chromosome X or Y to his offspring. Recombination is allowed for the X chromosomes of females, but not allowed for males.
- The sex of offspring is determined by the types of sex chromosomes he/she inherits, XX for female, and XY for male.

As an advanced feature of simuPOP, chromosomes that do not follow the inheritance patterns of autosomes or sex chromosomes can be handled separately (see section 2.7.4 for an Example). Figure 2.1 depicts the possible chromosome structure of two diploid parents, and how offspring chromosomes are formed. It uses two customized chromosomes to model multiple copies of mitochondrial chromosomes that are passed randomly from mother to offspring. The second homologous copy of customized chromosomes are unused in this example.

Figure 2.1: Inheritance of different types of chromosomes in a diploid population



Individuals in this population have five chromosomes, one autosome (A), one X chromosome (X), one Y chromosome (Y) and two customized chromosomes (C). The customized chromosomes model multiple copies of mitochondrial chromosomes that are passed randomly from mother to offspring. Y chromosomes for the female parent, the second copy of chromosome X and the first copy of chromosome Y for the male parent, and the second copy of customized chromosomes are unused (gray chromosome regions). A male offspring inherits one copy of autosome from his mother (with recombination), one copy of autosome from his father (with recombination), an X chromosome from his mother (with recombination), a Y chromosome from his father (without recombination), and two copies of the first customized chromosome.

## 2.2.3 Information fields

Different kinds of simulations require different kinds of individuals. Individuals with only genotype information are sufficient to simulate the basic Wright-Fisher model. Sex is needed to simulate such a model in diploid populations



with sex. Individual fitness may be needed if selection is induced, and age may be needed if the population is age-structured. In addition, different types of quantitative traits or affection status may be needed to study the impact of genotype on individual phenotype. Because it is infeasible to provide all such information to an individual, simuPOP keeps genotype, sex (Male or Female) and affection status as *built-in properties* of an individual, and all others as optional *information fields* (float numbers) attached to each individual.

Information fields can be specified when a population is created, or added later using relevant function. They are essential for the function of many simuPOP operators. For example, all selection operators require information field `fitness` to store evaluated fitness values for each individual. Operator `migrator` uses information field `migrate_to` to store the ID of subpopulation an individual will migrate to. An error will be raised if these operators are applied to a population without needed information fields.

Example 2.6: Basic usage of information fields

```
>>> import simuPOP as sim
>>> pop = sim.population(10, loci=[20], ancGen=1,
...     infoFields=['father_idx', 'mother_idx'])
>>> simu = sim.simulator(pop, sim.randomMating(ops=sim.recombinator(rates=0.01)))
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([0]*20+[1]*20)
...     ],
...     duringOps = sim.parentsTagger(),
...     gen = 1
... )
(1,)
>>> pop = simu.extract(0)
>>> pop.indInfo('mother_idx') # mother of all offspring
(9.0, 9.0, 0.0, 9.0, 9.0, 1.0, 7.0, 7.0, 7.0, 0.0)
>>> ind = pop.individual(0)
>>> mom = pop.ancestor(ind.mother_idx, 1)
>>> print ind.genotype(0)
[0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0]
>>> print mom.genotype(0)
[0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 0]
>>> print mom.genotype(1)
[1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1, 1]
```

Example 2.6 demonstrates the basic usage of information fields. In this example, a population with two information fields `mother_idx` and `father_idx` are created. It can hold one ancestral generations (`ancGen=1`, see Section 2.4.7 for details) so the most recent parental generations will be kept in a population object. After initializing each individual with two chromosomes with all zero and all one alleles respectively, the population evolves one generation, subject to recombination at rate 0.01. Parents of each individual are recorded, by operator `parentsTagger`, to information fields `mother_idx` and `father_idx` of each offspring.

After evolution, the population is extracted from the simulator, and the values of information field `mother_idx` of all individuals are printed. The next several statements get the first individual from the population, and his mother from the parental generation using the index stored in this individual's information field. Genotypes at the first homologous copy of this individual's chromosome is printed, along with two parental chromosomes.

**Information fields can be accessed as attributes of individuals.** For example, `ind.info('father_idx')` is equivalent to `ind.father_idx` and `ind.setInfo(35, 'age')` is equivalent to `ind.age = 35`.

**Information fields can only be set or added at the population level** because all individuals need to have the same set of fields. Values of information fields could be accessed at individual or population levels, using functions such as `individual.info`, `individual.setInfo`, `population.indInfo`, `population.setIndInfo`. These functions will be introduced in their respective classes. **Note:** Information fields can be located both by names and by indexes, the former provides better readability at a slight cost of performance because these names have to be

translated into indexes each time. However, use of names are recommended in most cases for readability considerations.

## 2.3 Individual

Individuals are building blocks of populations. An individual object cannot be created independently, but references to individuals can be retrieved using member functions of a population object. In addition to structural information shared by all individuals in a population, the individual class provides member functions to get and set *genotype*, *sex*, *affection status* and *information fields* of an individual. Example 2.8 demonstrates how to access and modify individual sex, affection status and information fields.

Example 2.7: Access Individual properties

```
>>> import simuPOP as sim
>>> pop = sim.population([5, 4], loci=[2, 5], infoFields='x')
>>> # get an individual
>>> ind = pop.individual(3)
>>> ind.ploidy()           # access to genotypic structure
2
>>> ind.numChrom()
2
>>> ind.affected()
False
>>> ind.setAffected(True)  # access affection sim.status,
>>> ind.sex()              # sex,
1
>>> ind.setInfo(4, 'x')    # and information fields
>>> ind.x = 5              # the same as ind.setInfo(4, 'x')
>>> ind.info('x')          # get information field x
5.0
>>> ind.x                  # the same as ind.info('x')
5.0
```

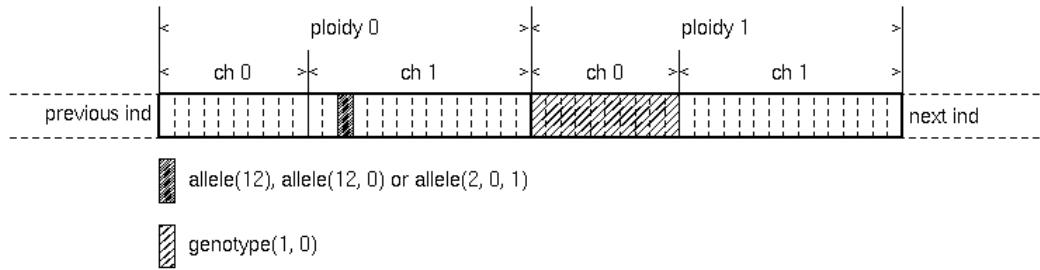
Genotypes of an individual are stored sequentially and can be accessed locus by locus, or in batch. The alleles are arranged by position, chromosome and ploidy. That is to say, the first allele on the first chromosome of the first homologous set is followed by alleles at other loci on the same chromosome, then markers on the second and later chromosomes, followed by alleles on the second homologous set of the chromosomes for a diploid individual. A consequence of this memory layout is that alleles at the same locus of a non-haploid individual are separated by `individual.totNumLoci()` loci. The memory layout of a diploid individual with two chromosomes is illustrated in Figure 2.2.

simuPOP provides several functions to read/write individual genotype. It is worth noting that, instead of copying genotypes of an individual to a Python tuple or list, the return value of function `genotype([p, [ch]])` is a special python carray object that reflects the underlying genotypes. Modifying elements of this array will change the genotype of an individual directly. Only `count` and `index` list functions can be used, but all comparison, assignment and slice operations are allowed. If you would like to copy the content of this carray to a Python list, use the `list()` function. Example 2.8 demonstrates the use of these functions.

Example 2.8: Access individual genotype

```
>>> import simuPOP as sim
>>> pop = sim.population([2, 1], loci=[2, 5])
>>> for ind in pop.individuals(1):
...     for marker in range(pop.totNumLoci()):
...         ind.setAllele(marker % 2, marker, 0)
...         ind.setAllele(marker % 2, marker, 1)
...         print '%d %d ' % (ind.allele(marker, 0), ind.allele(marker, 1))
```

Figure 2.2: Memory layout of individual genotype



Single-allele read: `allele(idx)`, `allele(idx, p)`, `allele(idx, p, ch)`

Single-allele write: `setAllele(allele, idx)`, `setAllele(allele, idx, p)`, `setAllele(allele, idx, p, ch)`

Batch read: `genotype()`, `genotype(p)`, `genotype(p, ch)`

Batch write: `setGenotype()`, `setGenotype(p)`, `setGenotype(p, ch)`

```
...
0 0
1 1
0 0
1 1
0 0
1 1
0 0
>>> ind = pop.individual(1)
>>> geno = ind.genotype(1)          # the second homologous copy
>>> geno
[0, 0, 0, 0, 0, 0, 0]
>>> geno[2] = 3
>>> ind.genotype(1)
[0, 0, 3, 0, 0, 0, 0]
>>> geno[2:4] = [3, 4]              # direct modification of the underlying genotype
>>> ind.genotype(1)
[0, 0, 3, 4, 0, 0, 0]
>>> # set genotype (genotype, ploidy, chrom)
>>> ind.setGenotype([2, 1], 1, 1)
>>> geno
[0, 0, 2, 1, 2, 1, 2]
```

## 2.4 Population

The `population` object is the most important object of `simuPOP`. It consists of one or more generations of individuals, grouped by subpopulations, and a local Python dictionary to hold arbitrary population information. This class provides a large number of functions to access and modify population structure, individuals and their genotypes and information fields. The following sections explain these features in detail.

### 2.4.1 Access and change individual genotype

From a user's point of view, genotypes of all individuals in a population are arranged sequentially. Similar to functions `individual.genotype()` and `individual.setGenotype()`, genotypes of a population can be accessed in batch using functions `population.genotype()` and `population.setGenotype()`. However, because it is error prone to locate an allele of a particular individual in this long array, these functions are usually used to perform population-level genotype operations such as clearing all alleles (e.g. `pop.setGenotype([0])`) or counting the number of a particular allele across all individuals (e.g. `pop.genotype().count(1)`).

Another way to change alleles across the whole population is to recode existing alleles to other numbers. This is sometimes needed if you need to change allele states to conform with a particular mutation model, assumptions of other software applications or genetic samples. For example, if the dataset you obtained uses 1, 2, 3, 4 for A, C, T, G alleles, and you would like to use alleles 0, 1, 2 and 3 for A, C, G, T (a convention for simuPOP when nucleotide mutation models are involved), you can use

```
pop.recodeAlleles([0, 0, 1, 3, 2], alleleNames=['A', 'C', 'G', 'T'])
```

to convert and rename the alleles (1 allele to 0, 2 allele to 1, etc). This operation will be applied to all subpopulations for all ancestral generations, but can be restricted to selected loci.

### 2.4.2 Subpopulations

A simuPOP population consists of one or more subpopulations. **If a population is not structured, it has one subpopulation that is the population itself.** Subpopulations serve as barriers of individuals in the sense that mating only happens between individuals in the same subpopulation. A number of functions are provided to merge, remove, resize subpopulations, and move individuals between subpopulations (migration). You will rarely get a chance to use them directly because such operations are usually handled by operators.

Example 2.10 demonstrates how to use subpopulation related functions. Of particular interest is the `setSubPopByIndInfo()` function. This function takes an information field as parameter and rearrange individuals according to their values at this information field. Individuals with invalid (negative) values at this information field are removed. This is essentially how migration is implemented in simuPOP.

Example 2.9: Manipulation of subpopulations

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[3, 4, 5], ploidy=1, loci=1, infoFields='x')
>>> # individual 0, 1, 2, ... will have an allele 0, 1, 2, ...
>>> pop.setGenotype(range(pop.popSize()))
>>> #
>>> pop.subPopSize(1)
4
>>> # merge subpopulations
>>> pop.mergeSubPops([1, 2])
1
>>> # split subpopulations
>>> pop.splitSubPop(1, [2, 7])
(1, 2)
>>> pop.subPopSizes()
(3, 2, 7)
>>> # set information field to each individual's new subpopulation ID
>>> pop.setIndInfo([0, 1, 2, -1, 0, 1, 2, -1, -1, 0, 1, 2], 'x')
>>> # this manually triggers an migration, individuals with negative values
>>> # at this information field are removed.
>>> pop.setSubPopByIndInfo('x')
>>> sim.Dump(pop, width=2, structure=False)
Subpopulation 0 (), 3 individuals:
    0: MU  0 |  0
```

```

1: MU 4 | 0
2: MU 9 | 0
Subpopulation 1 (), 3 individuals:
3: MU 1 | 1
4: MU 5 | 1
5: MU 10 | 1
Subpopulation 2 (), 3 individuals:
6: MU 2 | 2
7: MU 6 | 2
8: MU 11 | 2

```

Some population operations change the IDs of subpopulations. For example, if a population has three subpopulations 0, 1, and 2, and subpopulation 1 is split into two subpopulations, subpopulation 2 will become subpopulation 3. Tracking the ID of a subpopulation can be problematic, especially when conditional or random subpopulation operations are involved. In this case, you can specify names to subpopulations. These names will follow their associated subpopulations during population operations so you can identify the ID of a subpopulation by its name. Note that simuPOP allows duplicate subpopulation names.

Example 2.10: Use of subpopulation names

```

>>> import simuPOP as sim
>>> pop = sim.population(size=[3, 4, 5], subPopNames=['x', 'y', 'z'])
>>> pop.removeSubPops([1])
>>> pop.subPopNames()
('x', 'z')
>>> pop.subPopByName('z')
1
>>> pop.splitSubPop(1, [2, 3])
(1, 2)
>>> pop.subPopNames()
('x', 'z', 'z')
>>> pop.setSubPopName('z-1', 1)
>>> pop.subPopNames()
('x', 'z-1', 'z')
>>> pop.subPopByName('z')
2

```

### 2.4.3 Virtual subpopulations \*

simuPOP subpopulations can be further divided into virtual subpopulations (VSP), which are groups of individuals who share certain properties. For example, all male individuals, all unaffected individuals, all individuals with information field age > 20, all individuals with genotype 0, 0 at a given locus, can form VSPs. VSPs do not have to add up to the whole subpopulation, nor do they have to be non-overlapping. Unlike subpopulations that have strict boundaries, VSPs change easily with the changes of individual properties.

VSPs are defined by virtual splitters. A splitter defines the same number of VSPs in all subpopulations, although sizes of these VSPs vary across subpopulations due to subpopulation differences. For example, a `sexSplitter()` defines two VSPs, the first with all male individuals and the second with all female individuals, and a `infoSplitter(field='x', values=[1, 2, 4])` defines three VSPs whose members have values 1, 2 and 4 at information field x, respectively. This splitter also allows the use of cutoff values and ranges to define VSPs. If different types of VSPs are needed, a combined splitter can be used to combine VSPs defined by several splitters.

A VSP is represented by a [spID, vspID] pair. Its name and size can be obtained using functions `subPopName()` and `subPopSize()`. Example 2.11 demonstrates how to apply virtual splitters to a population, and how to check VSP names and sizes.

### Example 2.11: Define virtual subpopulations in a population

```
>>> import simuPOP as sim
>>> import random
>>> pop = sim.population(size=[200, 400], loci=[30], infoFields='x')
>>> # assign random information fields
>>> sim.InitSex(pop)
>>> sim.InitInfo(pop, lambda: random.randint(0, 3), infoFields='x')
>>> # define a virtual splitter by sex
>>> pop.setVirtualSplitter(sim.sexSplitter())
>>> pop.numVirtualSubPop()      # Number of defined VSPs
2
>>> pop.subPopName([0, 0])      # Each VSP has a name
'MALE'
>>> pop.subPopSize([0, 1])      # Size of VSP 0 in subpopulation 0
109
>>> # define a virtual splitter by information field 'x'
>>> pop.setVirtualSplitter(sim.infoSplitter(field='x', values=[0, 1, 2, 3]))
>>> pop.numVirtualSubPop()      # Number of defined VSPs
4
>>> pop.subPopName([0, 0])      # Each VSP has a name
'x = 0'
>>> pop.subPopSize([0, 0])      # Size of VSP 0 in subpopulation 0
45
>>> pop.subPopSize([1, 0])      # Size of VSP 0 in subpopulation 1
85
```

VSP provides an easy way to access groups of individuals in a subpopulation and allows finer control of an evolutionary process. For example, mating schemes can be applied to VSPs which makes it possible to apply different mating schemes to, for example, individuals with different ages. By applying migration, mutation etc to VSPs, it is easy to implement advanced features such as sex-biased migrations, different mutation rates for individuals at different stages of a disease. Example 2.12 demonstrates how to initialize genotype and information fields to individuals in male and female VSPs.

### Example 2.12: Applications of virtual subpopulations

```
>>> import simuPOP as sim
>>> import random
>>> pop = sim.population(10, loci=[2, 3], infoFields='Sex')
>>> sim.InitSex(pop)
>>> pop.setVirtualSplitter(sim.sexSplitter())
>>> # initialize male and females with different genotypes.
>>> sim.InitByValue(pop, [[0]*5, [1]*5], subPops=([0, 0], [0, 1]))
>>> # set Sex information field to 0 for all males, and 1 for all females
>>> pop.setIndInfo([sim.MALE], 'Sex', [0, 0])
>>> pop.setIndInfo([sim.FEMALE], 'Sex', [0, 1])
>>> # Print individual genotypes, followed by values at information field Sex
>>> sim.Dump(pop, structure=False)
Subpopulation 0 (), 10 individuals:
0: FU 11 111 | 11 111 | 2
1: FU 11 111 | 11 111 | 2
2: MU 00 000 | 00 000 | 1
3: MU 00 000 | 00 000 | 1
4: MU 00 000 | 00 000 | 1
5: MU 00 000 | 00 000 | 1
6: MU 00 000 | 00 000 | 1
7: FU 11 111 | 11 111 | 2
8: FU 11 111 | 11 111 | 2
9: FU 11 111 | 11 111 | 2
```

## 2.4.4 Advanced virtual subpopulation splitters \*\*

simuPOP provides a number of virtual splitters that can define VSPs using specified properties. For example, `infoSplitter(field='a', values=[1,2,3])` defines three VSPs whose individuals have values 1, 2, and 3 at information field a, respectively; `sexSplitter()` defines two VSPs of male and female individuals, respectively; and `rangeSplitter(ranges=[[0, 2000], [2000, 5000]])` defines two VSPs using two blocks of individuals.

A `combinedSplitter` can be used if your simulation needs more than one sets of VSPs. For example, you may want to split your subpopulations both by sex and by affection status. In this case, you can define a combined splitter using

```
combinedSplitter(splitters=[sexSplitter(), affectionSplitter()])
```

This splitter simply stacks VSPs defined in `affectionSplitter()` after `sexSplitter()` so that unaffected and affected VSPs are now VSPs 2 and 3 (0 and 1 are used for male and female VSPs).

There are also scenarios when you would like to define finer VSPs with individuals belonging to more than one VSPs. For example, you may want to have a look of frequencies of certain alleles in affected male vs affected females, or count the number of males and females with certain value at an information field. In this case, a `productSplitter` can be used to define VSPs using interactions of several VSPs. For example,

```
productSplitter(splitters=[sexSplitter(), affectionSplitter()])
```

defines 4 subpopulations by splitting VSPs defined by `sexSplitter()` with affection status. These four VSPs will then have unaffected male, affected male, unaffected female and affected female individuals, respectively.

If you consider `productSplitter` as an intersection splitter that defines new VSPs as intersections of existing VSPs, you may wonder how to define unions of VSPs. For example, you can make a case where you want to consider individuals with information field  $a < 0$  or  $a > 100$  together. A regular `infoSplitter(field='a', cutoff=[0, 100])` cannot do that because it defines three VSPs with  $a < 0$ ,  $0 \leq a < 100$  and  $a \geq 100$ , respectively. The trick here is to use parameter `vspMap` of a `combinedSplitter`. If this parameter is defined, multiple VSPs could be groups or reordered to define a new set of VSPs. For example,

```
combinedSplitter(splitters=[infoSplitter(field='a', cutoff=[0, 100])], vspMap=[[0,2], [1]])
```

defines two VSPs using VSPs 0 and 2, and VSP 1 defined by the `infoSplitter` so that the first VSP contains individuals with  $a < 0$  or  $a \geq 100$ .

Example 2.13 demonstrates some advanced usages of virtual splitters.

Example 2.13: Advanced virtual subpopulation usages.

```
>>> import simuPOP as sim
>>> import random
>>> pop = sim.population(size=[2000, 4000], loci=[30], infoFields='x')
>>> # assign random information fields
>>> sim.InitSex(pop)
>>> sim.InitInfo(pop, lambda: random.randint(0, 3), infoFields='x')
>>> #
>>> # 1, use a combined splitter
>>> pop.setVirtualSplitter(sim.combinedSplitter(splitters = [
...     sim.sexSplitter(),
...     sim.infoSplitter(field='x', values=[0, 1, 2, 3])
... ]))
>>> pop.numVirtualSubPop()      # Number of defined VSPs
6
>>> pop.subPopName([0, 0])      # Each VSP has a name
'MALE'
>>> pop.subPopSize([0, 0])      # sim.MALE
1011
```

```

>>> pop.subPopSize([1, 4])      # individuals in sp 1 with value 2 at field x
992
>>> #
>>> # use a product splitter that defines additional VSPs by sex and info
>>> pop.setVirtualSplitter(sim.productSplitter(splitters = [
...     sim.sexSplitter(names=['M', 'F']), # give a new set of names
...     sim.infoSplitter(field='x', values=[0, 1, 2, 3])
... ]))
>>> pop.numVirtualSubPop()      # Number of defined VSPs
8
>>> pop.subPopName([0, 0])      # Each VSP has a name
'M, x = 0'
>>> pop.subPopSize([0, 0])      # sim.MALE with value 1 in sp 0
267
>>> pop.subPopSize([1, 5])      # sim.FEMALE with value 1 in sp 1
493
>>> #
>>> # use a combined splitter to join VSPs defined by a
>>> # product splitter
>>> pop.setVirtualSplitter(sim.combinedSplitter([
...     sim.productSplitter([
...         sim.sexSplitter(),
...         sim.infoSplitter(field='x', values=[0, 1, 2, 3])]),
...     vspMap = [[0,1,2], [4,5,6], [7]],
...     names = ['Male x<=3', 'Female x<=3', 'Female x=4']))
>>> pop.numVirtualSubPop()      # Number of defined VSPs
3
>>> pop.subPopName([0, 0])      # Each VSP has a name
'Male x<=3'
>>> pop.subPopSize([0, 0])      # sim.MALE with value 0, 1, 2 at field x
762
>>> pop.subPopSize([1, 1])      # sim.FEMALE with value 0, 1 or 2 at field x
1507

```

## 2.4.5 Access individuals and their properties

There are many ways to access individuals of a population. For example, function `population.individual(idx)` returns a reference to the `idx`-th individual in a population. An optional parameter `subPop` can be specified to return the `idx`-th individual in the `subPop`-th subpopulation.

If you would like to access a group of individuals, either from a whole population, a subpopulation, or from a virtual subpopulation, `population.individuals([subPop])` is easier to use. This function returns a Python iterator that can be used to iterate through individuals. An advantage of this function is that `subPop` can be a virtual subpopulation which makes it easy to iterate through individuals with certain properties (such as all male individuals).

If more than one generations are stored in a population, function `ancestor(idx, [subPop], gen)` can be used to access individual from an ancestral generation (see Section 2.4.7 for details). Because there is no group access function for ancestors, it may be more convenient to use `useAncestralGen` to make an *ancestral* generation the *current* generation, and use `population.individuals`. Note that `ancestor()` function can always access individuals at a certain generation, regardless which generation the current generation is. Example 2.15 demonstrates how to use all these individual-access functions.

If an unique ID is assigned to all individuals in a population, you can look up individuals from their IDs using function `population.indByID()`. The information field to save individual ID is usually `ind_id` and you can use operator `idTagger` and its function form `TagID` to set this field. Note that this function can be used to look up individuals in the present and all ancestral generations, although a parameter (`ancGen`) can be used to limit the search to a specific generation if you know in advance which generation the individual locates.



### Example 2.14: Access individuals of a population

```
>>> import simuPOP as sim
>>> # create a sim.population with two generations. The current generation has values
>>> # 0-9 at information field x, the parental generation has values 10-19.
>>> pop = sim.population(size=[5, 5], loci=[2, 3], infoFields='x', ancGen=1)
>>> pop.setIndInfo(range(11, 20), 'x')
>>> pop1 = pop.clone()
>>> pop1.setIndInfo(range(10), 'x')
>>> pop.push(pop1)
>>> #
>>> ind = pop.individual(5)          # using absolute index
>>> ind.x
5.0
>>> ind.x          # the same as ind.x
5.0
>>> # use a for loop, and relative index
>>> for idx in range(pop.subPopSize(1)):
...     print pop.individual(idx, 1).x,
...
5.0 6.0 7.0 8.0 9.0
>>> # It is usually easier to use an iterator
>>> for ind in pop.individuals(1):
...     print ind.x,
...
5.0 6.0 7.0 8.0 9.0
>>> # Access individuals in VSPs
>>> pop.setVirtualSplitter(sim.infoSplitter(cutoff=[3, 7], field='x'))
>>> for ind in pop.individuals([1, 1]):
...     print ind.x,
...
5.0 6.0
>>> # Access individuals in ancestral generations
>>> pop.ancestor(5, 1).x          # absolute index
16.0
>>> pop.ancestor(0, 1, 1).x      # relative index
16.0
>>> # Or make ancestral generation the current generation and use 'individual'
>>> pop.useAncestralGen(1)
>>> pop.individual(5).x          # absolute index
16.0
>>> pop.individual(0, 1).x      # relative index
16.0
>>> # 'ancestor' can still access the 'present' (generation 0) generation
>>> pop.ancestor(5, 0).x
5.0
>>> # access individual by ID
>>> pop.addInfoFields('ind_id')
>>> sim.TagID(pop)
>>> [int(ind.ind_id) for ind in pop.individuals()]
[1, 2, 3, 4, 5, 6, 7, 8, 9, 10]
>>> # access individual by ID. Note that individual 12 is in the parental generation
>>> pop.indByID(12).x
1.0
```

Although it is easy to access individuals in a population, it is often more efficient to access genotypes and information fields in batch mode. For example, functions `genotype()` and `setGenotype()` can read/write genotype of all individuals in a population or (virtual) subpopulation, functions `indInfo()` and `setIndInfo()` can read/write certain information fields in a population or (virtual) subpopulation. The write functions work in a circular manner in

the sense that provided values are reused if they are not enough to fill all genotypes or information fields. Example 2.15 demonstrates the use of such functions.

Example 2.15: Access individual properties in batch mode

```
>>> import simuPOP as sim
>>> import random
>>> pop = sim.population(size=[4, 6], loci=2, infoFields='x')
>>> pop.setIndInfo([random.randint(0, 10) for x in range(10)], 'x')
>>> pop.indInfo('x')
(6.0, 0.0, 9.0, 5.0, 7.0, 6.0, 7.0, 10.0, 9.0, 10.0)
>>> pop.setGenotype([0, 1, 2, 3], 0)
>>> pop.genotype(0)
[0, 1, 2, 3, 0, 1, 2, 3, 0, 1, 2, 3]
>>> pop.setVirtualSplitter(sim.infoSplitter(cutoff=[3], field='x'))
>>> pop.setGenotype([0]) # clear all values
>>> pop.setGenotype([5, 6, 7], [1, 1])
>>> pop.indInfo('x', 1)
(7.0, 6.0, 7.0, 10.0, 9.0, 10.0)
>>> pop.genotype(1)
[5, 6, 7, 5, 6, 7, 5, 6, 7, 5, 6, 7, 5, 6, 7, 5, 6, 7, 5, 6, 7]
```

## 2.4.6 Information fields

Information fields are usually set during population creation, using the `infoFields` parameter of the population constructor. It can also be set or added using functions `setInfoFields`, `addInfoField` and `addInfoFields`. Example 2.16 demonstrates how to read and write information fields from an individual, or from a population in batch mode. Note that functions `population.indInfo` and `population.setIndInfo` can be applied to (virtual) subpopulation using an optional parameter `subPop`.

Example 2.16: Add and use of information fields in a population

```
>>> import simuPOP as sim
>>> pop = sim.population(10)
>>> pop.setInfoFields(['a', 'b'])
>>> pop.addInfoFields('c')
>>> pop.addInfoFields(['d', 'e'])
>>> pop.infoFields()
('a', 'b', 'c', 'd', 'e')
>>> #
>>> # information fields can be accessed in batch mode
>>> pop.setIndInfo([1], 'c')
>>> # as well as individually.
>>> for ind in pop.individuals():
...     ind.e = ind.c + 1
...
>>> print pop.indInfo('e')
(2.0, 2.0, 2.0, 2.0, 2.0, 2.0, 2.0, 2.0, 2.0, 2.0)
```

## 2.4.7 Ancestral populations

A `simuPOP` population usually holds individuals in one generation. During evolution, an offspring generation will replace the parental generation and become the present generation (population), after it is populated from a parental population. The parental generation is discarded.

This is usually enough when only the present generation is of interest. However, parental generations can provide useful information on how genotype and other information are passed from parental to offspring generations. `simuPOP`

provides a mechanism to store and access arbitrary number of ancestral generations in a population object. Applications of this feature include pedigree tracking, reconstruction, and pedigree ascertainment.

A parameter `ancGen` is used to specify how many generations a population object *can* store (which is usually called the *ancestral depth* of a population). This parameter is default to 0, meaning keeping no ancestral population. You can specify a positive number `n` to store `n` most recent generations; or -1 to store all generations. Of course, storing all generations during an evolutionary process is likely to exhaust the RAM of your computer quickly.

Several member functions can be used to manipulate ancestral generations:

- `ancestralGens()` returns the number of ancestral generations stored in a population.
- `setAncestralDepth(depth)` resets the number of generations a population can store.
- `push(pop)` will push population `pop` into the current population. `pop` will become the current generation, and the current generation will either be removed (if `ancGen == 0`), or become the parental generation of `pop`. The greatest ancestral generation may be removed. This function is rarely used because populations with ancestral generations are usually created during an evolutionary process.
- `useAncestralGen(idx)` set the present generation to `idx` generation. `idx = 1` for the parental generation, 2 for grand-parental, ..., and 0 for the present generation. This is useful because most population functions act on the *present* generation. You should always call `setAncestralPop(0)` after you examined the ancestral generations.

A typical use of ancestral generations is demonstrated in example 2.19. In this example, a population is created and is initialized with allele frequency 0.5. Its ancestral depth is set to 2 at the beginning of generation 18 so that it can hold parental generations at generation 18 and 19. The allele frequency at each generation is calculated and displayed, both during evolution using a `stat` operator, and after evolution using the function form this operator. Note that setting the ancestral depth at the end of an evolutionary process is a common practice because we are usually only interested in the last few generations.

Example 2.17: Ancestral populations

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(500, loci=1), sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5])
...     ],
...     # start recording ancestral generations at generation 18
...     preOps = sim.setAncestralDepth(2, at=[-2]),
...     postOps = [
...         sim.stat(alleleFreq=0, begin=-3),
...         sim.pyEval(r"'%.3f\n' % alleleFreq[0][0]", begin=-3)
...     ],
...     gen = 20
... )
0.495
0.510
0.506
(20,)
>>> pop = simu.population(0)
>>> # start from current generation
>>> for i in range(pop.ancestralGens(), -1, -1):
...     pop.useAncestralGen(i)
...     sim.Stat(pop, alleleFreq=0)
...     print '%d    %.3f' % (i, pop.dvars().alleleFreq[0][0])
... 
```

```

2  0.495
1  0.510
0  0.506
>>> # restore to the current generation
>>> pop.useAncestralGen(0)

```

## 2.4.8 Add and remove loci

Several functions are provided to remove, add empty loci or chromosomes, and to merge loci or chromosomes from another population. They can be used to trim unneeded loci, expand existing population or merge two populations. Example 2.19 demonstrates how to use these populations.

Example 2.18: Add and remove loci and chromosomes

```

>>> import simuPOP as sim
>>> pop = sim.population(10, loci=3, chromNames=['chr1'])
>>> # 1 1 1,
>>> pop.setGenotype([1])
>>> # 1 1 1, 0 0 0
>>> pop.addChrom(lociPos=[0.5, 1, 2], lociNames=['rs1', 'rs2', 'rs3'],
...             chromName='chr2')
>>> pop1 = sim.population(10, loci=3, chromNames=['chr3'],
...                      lociNames=['rs4', 'rs5', 'rs6'])
>>> # 2 2 2,
>>> pop1.setGenotype([2])
>>> # 1 1 1, 0 0 0, 2 2 2
>>> pop.addChromFrom(pop1)
>>> # 1 1 1, 0 0 0, 2 0 2 2 0
>>> pop.addLoci(chrom=[2, 2], pos=[1.5, 3.5], lociNames=['rs7', 'rs8'])
(7, 10)
>>> # 1 1 1, 0 0 0, 2 0 2 0
>>> pop.removeLoci([8])
>>> sim.Dump(pop)
Ploidy: 2 (diploid)
Chromosomes:
1: chr1 (AUTOSOME, 3 loci)
   (1), (2), (3)
2: chr2 (AUTOSOME, 3 loci)
   rs1 (0.5), rs2 (1), rs3 (2)
3: chr3 (AUTOSOME, 4 loci)
   rs4 (1), rs7 (1.5), rs6 (3), rs8 (3.5)
population size: 10 (1 subpopulations with 10 individuals)
Number of ancestral populations: 0

Subpopulation 0 (), 10 individuals:
0: MU 111 000 2020 | 111 000 2020
1: MU 111 000 2020 | 111 000 2020
2: MU 111 000 2020 | 111 000 2020
3: MU 111 000 2020 | 111 000 2020
4: MU 111 000 2020 | 111 000 2020
5: MU 111 000 2020 | 111 000 2020
6: MU 111 000 2020 | 111 000 2020
7: MU 111 000 2020 | 111 000 2020
8: MU 111 000 2020 | 111 000 2020
9: MU 111 000 2020 | 111 000 2020

```

## 2.4.9 Population extraction

Another import population member function is `population.extract(loci=ALL_AVAIL, info=ALL_AVAIL, subPops=ALL_AVAIL, ancGen=-1)`. It is a powerful function that can extract subset of individuals, loci, information fields and ancestral generations from an existing population. This function can be used to draw certain individuals from an existing population and form a sample. This function works as follows:

- If all default parameters are used, this function is equivalent to `population.clone()`.
- If a list of loci are given to parameter `loci`, only specified loci will be copied to the extracted population. Loci in parameter `loci` do not have to be in order but loci in the extracted population will keep their original positions, and thus in their original order.
- If a list of information fields are given to parameter `info`, only specified information fields will be copied to the extracted population.
- If a positive `ancGen` is given, only generations 0 - `ancGen` will be extracted.
- Subset of individuals is specified using a list of (virtual) subpopulations. For example, if you define virtual subpopulations by sex using a `sexSplitter`, you can draw all male individuals from a population using `subPops=[(0, 0)]`.

Example 2.19 demonstrates the use of this powerful function.

Example 2.19: Extract individuals, loci and information fields from an existing population

```
>>> import simuPOP as sim
>>> import random
>>> pop = sim.population(size=[20, 20], loci=[5, 5], infoFields=['x', 'y'])
>>> sim.InitByValue(pop, range(10))
>>> sim.InitInfo(pop, lambda: random.randint(0,5), infoFields='x')
>>> pop.setVirtualSplitter(sim.infoSplitter(field='x', values=[0, 1, 2, 3, 4, 5]))
>>> pop1 = pop.extractSubPops(subPops=[(0,1), (0,3)])
>>> sim.Dump(pop1, structure=False)
Subpopulation 0 (), 8 individuals:
0: MU 01234 56789 | 01234 56789 | 3 0
1: MU 01234 56789 | 01234 56789 | 1 0
2: MU 01234 56789 | 01234 56789 | 1 0
3: MU 01234 56789 | 01234 56789 | 1 0
4: MU 01234 56789 | 01234 56789 | 1 0
5: MU 01234 56789 | 01234 56789 | 3 0
6: MU 01234 56789 | 01234 56789 | 1 0
7: MU 01234 56789 | 01234 56789 | 1 0
```

## 2.4.10 Population Variables

Each `simuPOP` population has a Python dictionary that can be used to store arbitrary Python variables. These variables are usually used by various operators to share information between them. For example, the `stat` operator calculates population statistics and stores the results in this Python dictionary. Other operators such as the `pyEval` and `terminateIf` read from this dictionary and act upon its information.

`simuPOP` provides two functions, namely `population.vars()` and `population.dvars()` to access a population dictionary. These functions return the same dictionary object but `dvars()` returns a wrapper class so that you can access this dictionary as attributes. For example, `pop.vars()['alleleFreq'][0]` is equivalent to `pop.dvars().alleleFreq[0]`. Because dictionary `subPop[spID]` is frequently used by operators to store variables related to a particular (virtual) subpopulation, function `pop.vars(subPop)` is provided as a shortcut to `pop.vars()['subPop'][spID]`. Example 2.20 demonstrates how to set and access Population variables.

### Example 2.20: Population variables

```
>>> import simuPOP as sim
>>> from pprint import pprint
>>> pop = sim.population(100, loci=2)
>>> sim.InitByFreq(pop, [0.3, 0.7])
>>> print pop.vars()      # No variable now
{}
>>> pop.dvars().myVar = 21
>>> print pop.vars()
{'myVar': 21}
>>> sim.Stat(pop, popSize=1, alleleFreq=0)
>>> # pprint prints in a less messy format
>>> pprint(pop.vars())
{'alleleFreq': {0: {0: 0.27500000000000002, 1: 0.7249999999999998}},
 'alleleNum': {0: {0: 55.0, 1: 145.0}},
 'myVar': 21,
 'popSize': 100,
 'subPopSize': [100]}
>>> # print number of allele 1 at locus 0
>>> print pop.vars()['alleleNum'][0][1]
145.0
>>> # use the dvars() function to access dictionary keys as attributes
>>> print pop.dvars().alleleNum[0][1]
145.0
>>> print pop.dvars().alleleFreq[0]
defdict({0: 0.27500000000000002, 1: 0.7249999999999998})
```

It is important to understand that this dictionary forms a **local namespace** in which Python expressions can be evaluated. This is the basis of how expression-based operators work. For example, the `pyEval` operator in example 1.1 evaluates expression `''%.2f\t' % LD[0][1]''` in each population's local namespace when it is applied to that population. This yields different results for different population because their LD values are different. In addition to Python expressions, Python statements can also be executed in the local namespace of a population, using the `stmts` parameter of the `pyEval` or `pyExec` operator. Example 2.28 demonstrates the use of a `simuPOP` terminator, which terminates the evolution of a population when its expression is evaluated as `True`. Note that The `evolve()` function of this example does not specify how many generations to evolve so it will stop only after all replicates stop. The return value of this function indicates how many generations each replicate has evolved.

### Example 2.21: Expression evaluation in the local namespace of a population

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(100, loci=1),
...     sim.randomMating(), 5)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5])
...     ],
...     postOps = [
...         sim.stat(alleleFreq=0),
...         sim.terminateIf('len(alleleFreq[0]) == 1')
...     ]
... )
(129, 1540, 180, 247, 242)
```

## 2.4.11 Save and load a population

simuPOP populations can be saved to and loaded from disk files using `population.save(file)` member function and global function `LoadPopulation`. (Yes, it is `Load`.. not `load`.. because `LoadPopulation` is a global function.). **Virtual splitters are not saved** because they are considered as runtime definitions. Although files in any extension can be used, extension `.pop` is recommended.

The native simuPOP format is not human readable and is not recognized by other applications. Other formats such as the one used by the popular FSTAT software is supported. They are implemented in Python in a Python utility module `simuUtil.py`. simuPOP cannot use one of such formats because none of them can handle huge populations that simuPOP can handle, and unique features such as population variables. Example 2.28 demonstrates how to save and load a population in the native simuPOP format.

Example 2.22: Save and load a population

```
>>> import simuPOP as sim
>>> pop = sim.population(100, loci=5, chromNames=['chrom1'])
>>> pop.dvars().name = 'my sim.population'
>>> pop.save('sample.pop')
>>> pop1 = sim.LoadPopulation('sample.pop')
>>> pop1.chromName(0)
'chrom1'
>>> pop1.dvars().name
'my sim.population'
```

## 2.5 Operators

Operators are objects that act on populations. They can be used in the following ways:

- Operators are usually passed to the `ops`, `preOps` and `postOps` parameters of the `evolve` function of a simulator. The simulator will apply these operators before (`preOps`), after (`postOps`) or during (`ops`) an evolutionary process. Depending on parameters of an operator, it can be applied before, during, and/or after mating in a life cycle of a generation (parameter `stage`, see Figure 1.1), to a subset of generations (parameters `begin`, `end`, `step`, `at`), a subset of populations in a simulator (parameter `rep`), a subset of (virtual) subpopulations in each replicate (parameter `subPop`).
- During-mating operators are used by mating schemes to transmit parental genotype (and sometimes information fields) to offspring. Applicability parameters such as `begin`, `end`, `rep` are ignored.
- Most of the operators can be applied to a population directly, using their function forms. Applicability parameters are ignored.

The following sections will introduce common features of all operators. The next chapter will explain some of the operators in detail.

### 2.5.1 Applicable generations

A simuPOP life cycle (a *generation*) can be divided into *pre-mating*, *during-mating* and *post-mating*. In the pre-mating stage, the present generation is the parental generation. In the during-mating stage, an offspring generation is populated from the parental generation. In the post-mating stage, the offspring generation has become the present generation. Operators specified in the `preOps`, `duringOps` and `postOps` parameters of the `simulator.evolve` function are applied, respectively, at these stages.

Operators that are passed to the `simulator.evolve` function are, by default, applied to all generations during an evolutionary process. This can be changed using the `begin`, `end`, `step` and `at` parameters. As their names

indicate, these parameters control the starting generation (*begin*), ending generation (*end*), generations between two applicable generations (*step*), and an explicit list of applicable generations (*at*, a single generation number is also acceptable). Other parameters will be ignored if *at* is specified. It is worth noting that, if the simulator has an ending generation, negative generations numbers are allowed. They are counted backward from the ending generation.

For example, if a simulator starts at generation 0, and the `evolve` function has parameter `gen=10`, the simulator will stop at the *beginning* of generation 10. Generation -1 refers to generation 9, and generation -2 refers to generation 8, and so on. Example 2.23 demonstrates how to set applicable generations of an operator. In this example, a population is initialized before evolution using a `initByFreq` operator. allele frequency at locus 0 is calculated at generation 80, 90, but not 100 because the evolution stops at the beginning of generation 100. A `pyEval` operator outputs generation number and allele frequency at the end of generation 80 and 90. Another `pyEval` operator outputs similar information at generation 90 and 99, before and after mating. Note, however, because allele frequencies are only calculated twice, the pre-mating allele frequency at generation 90 is actually calculated at generation 80, and the allele frequencies display for generation 99 are calculated at generation 90. At the end of the evolution, the population is saved to a file using a `savePopulation` operator.

Example 2.23: Applicable generations of an operator.

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(1000, loci=[20]), sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.8, 0.2])
...     ],
...     preOps = [
...         sim.pyEval(r'''At the beginning of gen %d: allele Freq: %.2f\n' % (gen, alleleFreq[0][0])
...         at = [-10, -1])
...     ],
...     postOps = [
...         sim.stat(alleleFreq=0, begin=80, step=10),
...         sim.pyEval(r'''At the end of gen %d: allele freq: %.2f\n' % (gen, alleleFreq[0][0])",
...         begin=80, step=10),
...         sim.pyEval(r'''At the end of gen %d: allele Freq: %.2f\n' % (gen, alleleFreq[0][0])",
...         at = [-10, -1])
...     ],
...     finalOps = sim.savePopulation(output='sample.pop'),
...     gen=100
... )
At the end of gen 80: allele freq: 0.82
At the beginning of gen 90: allele Freq: 0.82
At the end of gen 90: allele freq: 0.82
At the end of gen 90: allele Freq: 0.82
At the beginning of gen 99: allele Freq: 0.82
At the end of gen 99: allele Freq: 0.82
(100,)
```

## 2.5.2 Applicable populations

A simulator can evolve multiple replicates of a population simultaneously. Different operators can be applied to different replicates of this population. This allows side by side comparison between simulations.

Parameter `reps` is used to control which replicate(s) an operator can be applied to. This parameter can be a list of replicate numbers or a single replicate number. Negative index is allowed where -1 refers to the last replicate. This technique has been widely used to produce table-like output where a `pyOutput` outputs a newline when it is applied to the last replicate of a simulator. Example 2.28 demonstrates how to use this `reps` parameter. It is worth noting that negative indexes are *dynamic* indexes relative to number of active populations. For example, `rep=-1` will refer



to a previous population if the last population has stopped evolving. Use a non-negative replicate number if this is not intended.

Example 2.24: Apply operators to a subset of populations

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(100, loci=[20]), sim.randomMating(), 5)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.2, 0.8])
...     ],
...     postOps = [
...         sim.stat(alleleFreq=0, step=10),
...         sim.pyEval('gen', step=10, reps=0),
...         sim.pyEval(r"\t%.2f" % alleleFreq[0][0]", step=10, reps=(0, 2, -1)),
...         sim.pyOutput('\n', step=10, reps=-1)
...     ],
...     gen=30,
... )
0      0.22    0.23    0.17
10     0.15    0.16    0.12
20     0.04    0.14    0.07
(30, 30, 30, 30, 30)
```

An operator can also be applied to specified (virtual) subpopulations. For example, an initializer can be applied to male individuals in the first subpopulation, and everyone in the second subpopulation using parameter `subPops=[(0, 0), 1]`, if a virtual subpopulation is defined by individual sex. Generally speaking,

- `subPops=[]` applies the operator to all subpopulation. This is usually the default value of an operator.
- `subPops=[vsp1, vsp2, ...]` applies the operator all specified (virtual) subpopulations. (e.g. `subPops=[(0, 0), 1]`).
- `subPops=sp` is an abbreviation for `subPops=[sp]`. If `sp` is virtual, it has to be written as `[sp]` because `subPops=(0, 1)` is interpreted as two non-virtual subpopulation.

However, not all operators support this parameter, and even if they do, their interpretations of parameter input may vary. Please refer to documentation for individual operators in *the simuPOP reference manual* for details.

### 2.5.3 Operator output \*

All operators we have seen, except for the `savePopulation` operator in Example 2.23, write their output to the standard output, namely your terminal window. However, it would be much easier for bookkeeping and further analysis if these output can be redirected to disk files. Parameter `output` is designed for this purpose.

Parameter `output` can take the following values:

- `"` (an empty string): No output.
- `'>'`: Write to standard output.
- `'filename'` or `'>filename'`: Write the output to a file named `filename`. If multiple operators write to the same file, or if the same operator writes to the file file several times, only the last write operation will succeed.
- `'>>filename'`: Append the output to a file named `filename`. The file will be opened at the beginning of `evolve` function and closed at the end. An existing file will be cleared.

- '`>>>filename`': This is similar to the '`>>>`' form but the file will not be cleared at the beginning of the `evolve` function.
- '`!expr`': `expr` is considered as a Python expression that will be evaluated at a population's local namespace whenever an output string is needed. For example, '`!"%d.txt" % gen`' would return `0.txt`, `1.txt` etc at generation 0, 1, ....
- A Python function that can accept a string as its only parameter (`func(msg)`). When an operator outputs a message, this function will be called with this message.

Because a table output such as the one in Example 2.28 is written by several operators, it is clear that all of them need to use the '`>>>`' output format.

The `savePopulation` operator in Example 2.23 write to file `sample.pop`. This works well if there is only one replicate but not so when the operator is applied to multiple populations. Only the last population will be saved successfully! In this case, the expression form of parameter `output` should be used.

The expression form of this parameter accepts a Python expression. Whenever a filename is needed, this expression is evaluated against the local namespace of the population it is applied to. Because the `evolve` function automatically sets variables `gen` and `rep` in a population's local namespace, such information can be used to produce an output string. Of course, any variable in this namespace can be used so you are not limited to these two variable.

Example 2.28 demonstrates the use of these two parameters. In this example, a table is written to file `LD.txt` using `output='>>>LD.txt'`. Similar operation to `output='R2.txt'` fails because only the last  $R^2$  value is written to this file. The last operator writes output for each replicate to their respective output file such as `LD_0.txt`, using an expression that involves variable `rep`.

Example 2.25: Use the output and outputExpr parameters

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(size=1000, loci=2),
...     sim.randomMating(ops=sim.recombinator(rates=0.01)), rep=3)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([1, 2, 2, 1])
...     ],
...     postOps = [
...         sim.stat(LD=[0, 1]),
...         sim.pyEval(r'"%.2f\t' % LD[0][1]", step=20, output='>>>LD.txt'),
...         sim.pyOutput('\n', reps=-1, step=20, output='>>>LD.txt'),
...         sim.pyEval(r'"%.2f\t' % R2[0][1]", output='R2.txt'),
...         sim.pyEval(r'"%.2f\t' % LD[0][1]", step=20, output="!'>>>LD_%d.txt' % rep"),
...     ],
...     gen=100
... )
(100, 100, 100)
>>> print open('LD.txt').read()
0.24    0.25    0.24
0.17    0.21    0.20
0.10    0.15    0.18
0.12    0.10    0.16
0.09    0.10    0.14

>>> print open('R2.txt').read()      # Only the last write operation succeed.
0.23
>>> print open('LD_2.txt').read()    # Each replicate writes to a different file.
0.24    0.20    0.18    0.16    0.14
```

Example 2.26 demonstrates an advanced usage of the output parameter. In this example, a logging object is created to write to a logfile as well as the standard output. The `info` and `debug` functions of this object are assigned to two operators so that their outputs can be sent to both a logfile and to the console window. One of the advantages of using a logging mechanism is that debugging output could be suppressed easily by adjusting the logging level of the logging object. Note that function `logging.info()` automatically adds a new line to its input messages before it writes them to an output.

Example 2.26: Output to a Python function

```
>>> import simuPOP as sim
>>> import logging
>>> # logging to a file simulation.log, with detailed debug information
>>> logging.basicConfig(
...     filename='simulation.log',
...     level=logging.DEBUG,
...     format='%(levelname)s: %(message)s',
...     filemode='w'
... )
>>> # logging to standard output with less information
>>> console = logging.StreamHandler()
>>> console.setLevel(logging.INFO)
>>> formatter = logging.Formatter('%(message)s')
>>> console.setFormatter(formatter)
>>> logger = logging.getLogger('')
>>> logger.addHandler(console)
>>> #
>>> simu = sim.simulator(sim.population(size=1000, loci=2),
...     sim.randomMating(ops=sim.recombinator(rates=0.01)))
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([1, 2, 2, 1])
...     ],
...     postOps = [
...         sim.stat(LD=[0, 1]),
...         sim.pyEval(r'''LD: %d, %.2f' % (gen, LD[0][1])'', step=20,
...             output=logger.info), # send LD to console and a logfile
...         sim.pyEval(r'''R2: %d, %.2f' % (gen, R2[0][1])'', step=20,
...             output=logger.debug), # send R2 only to a logfile
...     ],
...     gen=100
... )
LD: 0, 0.25
LD: 20, 0.20
LD: 40, 0.20
LD: 60, 0.18
LD: 80, 0.14
(100,)
>>> print open('simulation.log').read()
INFO: LD: 0, 0.25
DEBUG: R2: 0, 0.96
INFO: LD: 20, 0.20
DEBUG: R2: 20, 0.67
INFO: LD: 40, 0.20
DEBUG: R2: 40, 0.68
INFO: LD: 60, 0.18
DEBUG: R2: 60, 0.52
INFO: LD: 80, 0.14
DEBUG: R2: 80, 0.34
```

## 2.5.4 During-mating operators

All operators in Examples 2.23, 2.24 and 2.25 are applied before or after mating. There is, however, a hidden during-mating operator that is called by `randomMating()`. This operator is called `mendelianGenoTransmitter()` and is responsible for transmitting genotype from parents to offspring according to Mendel's laws. All pre-defined mating schemes (see Section 2.6) use a special kind of during-mating operator to transmit genotypes. They are called **genotype transmitters** just to show the kind of task they perform.

During mating operators could be used in two ways:

- In the `ops` parameter of a mating scheme (or an offspring generator if you are defining your own mating scheme). **Operators specified in this way will replace the default operator a mating scheme uses.**
- In the `ops` parameter of the `simulator.evolve` function. **These operators will be applied after an offspring is created using operators of a mating scheme.**

In another word,

- If you would like to change how genotypes are transmitted, replace the genotype transmitter of a mating scheme with your own ones. For example, `recombinator` should generally be used in a mating scheme.
- If you would like to modify individual property after his or her genotypes are transmitted, use them in the `simulator.evolve` function. A good example is operator `parentsTagger` that record the indexes of an offspring's parents in the parental generation.

There are some subtleties involved in the use of during-mating operators. For example,

- During-mating operators do not support parameter `subPops`. If you would like to apply different during-mating operators to different (virtual) subpopulations, you can use a heterogeneous mating scheme that applies different homogeneous mating schemes with different operators to different (virtual) subpopulations.
- Operators used in a mating scheme honor applicability parameters `begin`, `step`, `end`, `at` and `reps` although they do not support negative population and replicate indexes. It is therefore possible to apply different during-mating operators at different generations. For example, a `recombinator` is used in Example 2.27 to transmit parental genotypes to offspring after generation 30 while the `mendelianGenoTransmitter` is applied before that.
- Operators used in `simulator.evolve` are applied after an individual is created. If something needs to be done before the default genotype transmitter is used, you have to replace the default genotype transmitter with a list of operators which will be called by the mating scheme in the order at which operators are specified.

Example 2.27: Genotype transmitters

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(size=10000, loci=2),
...     sim.randomMating(ops=[
...         sim.mendelianGenoTransmitter(end=29),
...         sim.recombinator(rates=0.01, begin=30),
...     ])
... )
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([1, 2, 2, 1])
...     ],
...     postOps = [
...         sim.stat(LD=[0, 1]),
```

```

...         sim.pyEval(r"gen %d, LD: %.2f\n" % (gen, LD[0][1])), step=20)
...     ],
...     gen=100
... )
gen 0, LD: 0.25
gen 20, LD: 0.25
gen 40, LD: 0.22
gen 60, LD: 0.19
gen 80, LD: 0.16
(100,)

```

Section 2.7.4 and 3.4 list all genotype transmitters, Section 2.7.5 demonstrates how to define your own genotype transmitter.

### 2.5.5 Hybrid operators

Despite the large number of built-in operators, it is obviously not possible to implement every genetics models available. For example, although simuPOP provides several penetrance models, a user may want to try a customized one. In this case, one can use a *hybrid operator*.

A *hybrid operator* is an operator that calls a user-defined function when its applied to a population. The number and meaning of input parameters and return values vary from operator to operator. For example, a hybrid mutator sends a to-be-mutated allele to a user-defined function and use its return value as a mutant allele. A hybrid selector uses the return value of a user defined function as individual fitness. Such an operator handles the routine part of the work (e.g. scan through a chromosome and determine which allele needs to be mutated), and leave the creative part to users. Such a mutator can be used to implement complicated genetic models such as an asymmetric stepwise mutation model for microsatellite markers.

For example, Example 2.28 defines a three-locus heterogeneity penetrance model [Risch, 1990] that yields positive penetrance only when at least two disease susceptibility alleles are available. The underlying mechanism of this operator is that for each individual, simuPOP will collect genotype at specified loci (parameter `loci`) and send them to function `myPenetrance` and evaluate. The return values are used as the penetrance value of the individual, which is then interpreted as the probability that this individual will become affected.

Example 2.28: Use a hybrid operator

```

>>> import simuPOP as sim
>>> def myPenetrance(geno, gen):
...     'A three-locus heterogeneity penetrance model'
...     if sum(geno) < 2:
...         return 0
...     else:
...         return sum(geno)*0.1
...
>>> simu = sim.simulator(sim.population(1000, loci=[20]*3), sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.8, 0.2])
...     ],
...     postOps = [
...         sim.pyPenetrance(func=myPenetrance, loci=[10, 30, 50]),
...         sim.stat(numOfAffected=True),
...         sim.pyEval(r"%d: %d\n" % (gen, numOfAffected))
...     ],
...     gen = 5
... )
0: 82

```

```

1: 81
2: 83
3: 69
4: 106
(5,)

```

## 2.5.6 Python operators \*

If hybrid operators are still not flexible enough, you can always resort to a pure-Python operator `pyOperator`. This operator has full access to the evolving population (or parents and offspring when applied during-mating), and can therefore perform arbitrary operations.

A pre- or post-mating `pyOperator` expects a function in the form of

```
func(pop [, param])
```

where `param` is optional, depending on whether or not a parameter is passed to the `pyOperator()` constructor. Function `func` can perform arbitrary action to `pop` and must return `True` or `False`. **The evolution of pop will be stopped if this function returns False.** This is essentially how operator `terminateIf` works.

Example 2.29 defines such a function. It accepts a cutoff value and two mutation rates as parameters. It then calculate the frequency of allele 1 at each locus and apply a two-allele model at high mutation rate if the frequency is lower than the cutoff and a low mutation rate otherwise. The `KamMutate` function is the function form of a mutator `kamMutator` (see Section 2.5.8 for details).

Example 2.29: A frequency dependent mutation operator

```

import simuPOP as sim
def dynaMutator(pop, param):
    '''This mutator mutates common loci with low mutation rate and rare
    loci with high mutation rate, as an attempt to raise allele frequency
    of rare loci to an higher level.'''
    # unpack parameter
    (cutoff, mu1, mu2) = param;
    sim.Stat(pop, alleleFreq=range(pop.totNumLoci()))
    for i in range(pop.totNumLoci()):
        # Get the frequency of allele 1 (disease allele)
        if pop.dvars().alleleFreq[i][1] < cutoff:
            sim.KamMutate(pop, k=2, rates=mu1, loci=[i])
        else:
            sim.KamMutate(pop, k=2, rates=mu2, loci=[i])
    return True

```

Example 2.50 demonstrates how to use this operator. It first initializes the population using two `initByFreq` operators that initialize loci with different allele frequencies. It applies a `pyOperator` with function `dynaMutator` and a tuple of parameters. Allele frequencies at all loci are printed at generation 0, 10, 20, and 30. Note that this `pyOperator` is applied at to the parental generation so allele frequencies have to be recalculated to be used by post-mating operator `pyEval`.

Example 2.30: Use a `pyOperator` during evolution

```

>>> simu = sim.simulator(sim.population(size=10000, loci=[2, 3]),
...     sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([.99, .01], loci=[0, 2, 4]),
...         sim.initByFreq([.8, .2], loci=[1, 3])
...     ],

```

```

...     preOps = sim.pyOperator(func=dynaMutator, param=(.2, 1e-2, 1e-5)),
...     postOps = [
...         sim.stat(alleleFreq=range(5), step=10),
...         sim.pyEval(r"' '.join(['%.2f' % alleleFreq[x][1] for x in range(5)]) + '\n',
...             step=10),
...     ],
...     gen = 31
... )
0.02 0.20 0.02 0.20 0.02
0.12 0.21 0.10 0.21 0.10
0.18 0.20 0.18 0.20 0.17
0.20 0.21 0.20 0.21 0.21
(31,)

```

An `pyOperator` can also be applied during-mating. They can be used to filter out unwanted offspring (by returning `False` in a user-defined function), modify offspring, calculate statistics, or pass additional information from parents to offspring. Depending on parameter `param` and `offspringOnly`, such an operator accepts a function in the form of

```

func(pop, dad, mom, off [, param]) # if offspringOnly=False (default)
func(off [, param])                # if offspringOnly=True

```

Example 2.31 demonstrates the use of a during-mating Python operator. This operator rejects an offspring if it has allele 1 at the first locus of the first homologous chromosome, and results in an offspring population without such individuals.

Example 2.31: Use a during-mating `pyOperator`

```

>>> import simuPOP as sim
>>> def rejectInd(off):
...     'reject an individual if it off.allele(0) == 1'
...     return off.allele(0) == 0
...
>>> simu = sim.simulator(sim.population(size=100, loci=1),
...     sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5])
...     ],
...     duringOps = sim.pyOperator(func=rejectInd, offspringOnly=True),
...     gen = 1
... )
(1,)
>>> # You should see no individual with allele 1 at locus 0, ploidy 0.
>>> simu.population(0).genotype()[ :20]
[0, 0, 0, 0, 0, 0, 0, 0, 1, 0, 0, 0, 1, 0, 0, 0, 0, 0, 0, 0]

```

`pyOperator` is the most powerful operator in `simuPOP` and has been widely used, for example, to calculate statistics and is not supported by the `stat()` operator, to examine population property during evolution, or prepare populations for a special mating scheme. However, because `pyOperator` works in the Python interpreter, it is expected that it runs slower than operators that are implemented at the C/C++ level. If performance becomes an issue, you can re-implement part or all the operator in C++. Section 2.7.7 describes how to do this.

## 2.5.7 Define your own operators \*\*

`pyOperator` is a Python class so you can derive your own operator from this operator. The tricky part is that the constructor of the derived operator needs to call the `__init__` function of `pyOperator` will proper functions. This

technique has been used by simuPOP in a number of occasions. For example, the `varPlotter` operator defined in `plotter.py` is derived from `pyOperator`. This class encapsulates several different plot class that uses `rpy` to plot python expressions. One of the plotters is passed to the `func` parameter of `pyOperator.__init__` so that it can be called when this operator is applied.

Example 2.50 rewrites the `dynaMutator` defined in Example 2.29 into a derived operator. The parameters are now passed to the constructor of `dynaMutator` and are saved as member variables. A member function `mutate` is defined and is passed to the constructor of `pyOperator`. Other than making `dynaMutator` look like a real simuPOP operator, this example does not show a lot of advantage over defining a function. However, when the operator gets complicated (as in the case for `varPlotter`), the object oriented implementation will prevail.

Example 2.32: Define a new Python operator

```
>>> import simuPOP as sim
>>> class dynaMutator(sim.pyOperator):
...     '''This mutator mutates commom loci with low mutation rate and rare
...     loci with high mutation rate, as an attempt to raise allele frequency
...     of rare loci to an higher level.'''
...     def __init__(self, cutoff, mu1, mu2, *args, **kwargs):
...         self.cutoff = cutoff
...         self.mu1 = mu1
...         self.mu2 = mu2
...         sim.pyOperator.__init__(self, func=self.mutate, *args, **kwargs)
...     #
...     def mutate(self, pop):
...         sim.Stat(pop, alleleFreq=range(pop.totNumLoci()))
...         for i in range(pop.totNumLoci()):
...             # Get the frequency of allele 1 (disease allele)
...             if pop.dvars().alleleFreq[i][1] < self.cutoff:
...                 sim.KamMutate(pop, k=2, rates=self.mu1, loci=[i])
...             else:
...                 sim.KamMutate(pop, k=2, rates=self.mu2, loci=[i])
...         return True
...
>>> simu = sim.simulator(sim.population(size=10000, loci=[2, 3]),
...     sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([.99, .01], loci=[0, 2, 4]),
...         sim.initByFreq([.8, .2], loci=[1, 3])
...     ],
...     preOps = dynaMutator(cutoff=.2, mu1=1e-2, mu2=1e-5),
...     postOps = [
...         sim.stat(alleleFreq=range(5), step=10),
...         sim.pyEval(r"' '.join(['%.2f' % alleleFreq[x][1] for x in range(5)]) + '\n',
...             step=10),
...     ],
...     gen = 31
... )
0.02 0.20 0.02 0.20 0.02
0.12 0.21 0.10 0.21 0.10
0.18 0.20 0.18 0.20 0.17
0.20 0.21 0.20 0.21 0.21
(31,)
```

New during-mating operators can be defined similarly. They are usually used to define customized genotype transmitters. Section 2.7.5 will describe this feature in detail.



## 2.5.8 Function form of an operator

Operators are usually applied to populations through a simulator but they can also be applied to a population directly. For example, it is possible to create an `initByFreq` operator and apply to a population as follows:

```
initByFreq([.3, .2, .5]).apply(pop)
```

Similarly, you can apply the hybrid penetrance model defined in Example 2.28 to a population by

```
pyPenetrance(func=myPenetrance, loci=[10, 30, 50]).apply(pop)
```

This usage is used so often that it deserves some simplification. Equivalent functions are defined for most operators. For example, function `InitByFreq` is defined for operator `initByFreq` as follows

Example 2.33: The function form of operator `initByFreq`

```
>>> import simuPOP as sim
>>> def InitByFreq(pop, *args, **kwargs):
...     sim.initByFreq(*args, **kwargs).apply(pop)
...
>>> pop = sim.population(1000, loci=[2,3])
>>> sim.InitByFreq(pop, [.2, .3, .5])
```

These functions are called function form of operators. Using these functions, the above two example can be written as

```
InitByFreq(pop, [.3, .2, .5])
```

and

```
PyPenetrance(pop, func=myPenetrance, loci=[10, 30, 50])
```

respectively. Note that applicability parameters such as `begin` and `end` can still be passed, but they are ignored by these functions. **Note:** Whereas output files specified by `'>'` are closed immediately after they are written, those specified by `'>>'` and `'>>>'` are not closed after the operator is applied to a population. This is not a problem when operators are used in a simulator because `simulator.evolve` closes all files opened by operators, but can cause trouble when the operator is applied directly to a population. For example, multiple calls to `Dump(pop, output='>>file')` will dump `pop` to `file` repeatedly but `file` will not be closed afterward. In this case, `CloseOutput('file')` should be used to explicitly close the file.

## 2.6 Mating Schemes

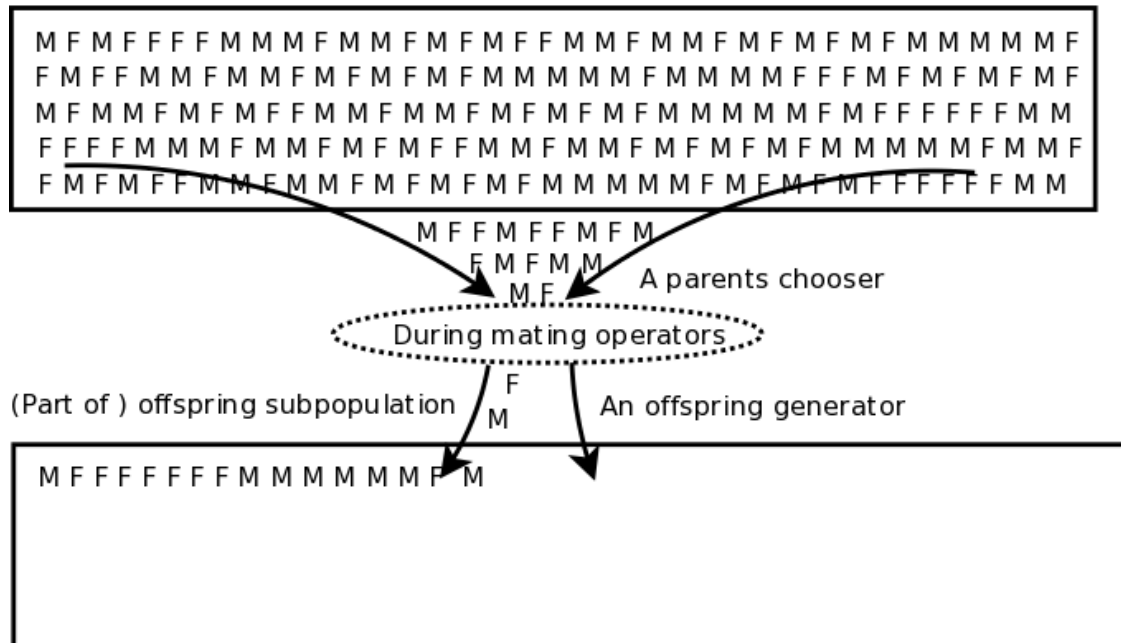
Mating schemes are responsible for populating an offspring generation from the parental generation. There are currently two types of mating schemes

- A **homogeneous mating scheme** is the most flexible and most frequently used mating scheme and is the center topic of this section. A homogeneous mating is composed of a *parent chooser* that is responsible for choosing parent(s) from a (virtual) subpopulation and an *offspring generator* that is used to populate all or part of the offspring generation. During-mating operators are used to transmit genotypes from parents to offspring. Figure 2.3 demonstrates this process.
- A **heterogeneous mating scheme** applies several homogeneous mating scheme to different (virtual) subpopulations. Because the division of virtual subpopulations can be arbitrary, this mating scheme can be used to simulate mating in heterogeneous populations such as populations with age structure.

This section describes some standard features of mating schemes and most pre-defined mating schemes. The next section will demonstrate how to build complex nonrandom mating schemes from scratch.

Figure 2.3: A homogeneous mating scheme

Parental (virtual) subpopulation



A homogeneous mating scheme is responsible to choose parent(s) from a subpopulation or a virtual subpopulation, and population part or all of the corresponding offspring subpopulation. A parent chooser is used to choose one or two parents from the parental generation, and pass it to an offspring generator, which produces one or more offspring. During mating operators such as taggers and recombinator can be applied when offspring is generated.

## 2.6.1 Control the size of the offspring generation

A mating scheme goes through each subpopulation and populates the subpopulations of an offspring generation sequentially. The number of offspring in each subpopulation is determined by the mating scheme, following the following rules:

- A simuPOP mating scheme, by default, produces an offspring generation that has the same subpopulation sizes as the parental generation. This does not guarantee a constant population size because some operators, such as a migrator, can change population or subpopulation sizes.
- If fixed subpopulation sizes are given to parameter `subPopSize`. A mating scheme will generation an offspring generation with specified sizes even if an operator has changed parental population sizes.
- A **demographic function** can be specified to parameter `subPopSize`. This function should take two parameters: the generation number and the current parental population, and return an array of new subpopulation sizes. A single number can be returned if there is only one subpopulation.

The following examples demonstrate these cases. Example 2.34 uses a default `randomMating()` scheme that keeps parental subpopulation sizes. Because migration between two subpopulations are asymmetric, the size of the first subpopulation increases at each generation, although the overall population size keeps constant.

Example 2.34: Free change of subpopulation sizes

```
>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(size=[500, 1000], infoFields='migrate_to'),
```

```

...     sim.randomMating())
>>>
>>> simu.evolve(
...     initOps = sim.initSex(),
...     preOps = sim.migrator(rate=[[0.8, 0.2], [0.4, 0.6]]),
...     postOps = [
...         sim.stat(popSize=True),
...         sim.pyEval(r'"%s\n" % subPopSize')
...     ],
...     gen = 3
... )
[843, 657]
[948, 552]
[1010, 490]
(3,)

```

Example 2.35 uses the same migrator to move individuals between two subpopulations. Because a constant subpopulation size is specified, the offspring generation always has 500 and 1000 individuals in its two subpopulations. Note that operators `stat` and `pyEval` are applied both before and after mating. It is clear that subpopulation sizes changes before mating as a result of migration, although the pre-mating population sizes vary because of uncertainties of migration.

Example 2.35: Force constant subpopulation sizes

```

>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(size=[500, 1000], infoFields='migrate_to'),
...     sim.randomMating(subPopSize=[500, 1000]))
>>> simu.evolve(
...     initOps = sim.initSex(),
...     preOps = [
...         sim.migrator(rate=[[0.8, 0.2], [0.4, 0.6]]),
...         sim.stat(popSize=True),
...         sim.pyEval(r'"%s\n" % subPopSize')
...     ],
...     postOps = [
...         sim.stat(popSize=True),
...         sim.pyEval(r'"%s\n" % subPopSize')
...     ],
...     gen = 3
... )
[843, 657]
[500, 1000]
[795, 705]
[500, 1000]
[821, 679]
[500, 1000]
(3,)

```

Example 2.41 uses a demographic function to control the subpopulation size of the offspring generation. This example implements a linear population expansion model but arbitrarily complex demographic model can be implemented similarly.

Example 2.36: Use a demographic function to control population size

```

>>> import simuPOP as sim
>>> def demo(gen, pop=None):
...     return [500 + gen*10, 1000 + gen*10]
...
>>> simu = sim.simulator(

```

```

...     sim.population(size=[500, 1000], infoFields='migrate_to'),
...     sim.randomMating(subPopSize=demo))
>>> simu.evolve(
...     initOps = sim.initSex(),
...     preOps = sim.migrator(rate=[[0.8, 0.2], [0.4, 0.6]]),
...     postOps = [
...         sim.stat(popSize=True),
...         sim.pyEval(r'"%s\n" % subPopSize')
...     ],
...     gen = 3
... )
[500, 1000]
[510, 1010]
[520, 1020]
(3,)

```

## 2.6.2 Advanced use of demographic functions \*

The parental population passed to a demographic function is usually used to determine offspring population size from parental population size. However, because this function is called immediately before mating happens, it provides a good opportunity for you to prepare the parental generation for mating. Such activities could generally be done by operators, but operations related to demographic changes could be done here. For example, Example 2.37 uses a demographic function to split populations at certain generation. The advantage of this method over the use of a `splitSubPops` operator (for example as in Example 3.16) is that all demographic information presents in the same function so you do not have to worry about changing an operator when your demographic model changes.

Example 2.37: Use a demographic function to split parental population

```

>>> import simuPOP as sim
>>> def demo(gen, pop):
...     if gen < 2:
...         return 1000 + 100 * gen
...     if gen == 2:
...         # this happens right before mating at generation 2
...         size = pop.popSize()
...         pop.splitSubPop(0, [size/2, size - size/2])
...         # for generation two and later
...         return [x + 50 * gen for x in pop.subPopSizes()]
...
>>> simu = sim.simulator(sim.population(1000),
...     sim.randomSelection(subPopSize=demo))
>>> simu.evolve(
...     preOps = [
...         sim.stat(popSize=True),
...         sim.pyEval(r'"Gen %d:\t%s (before mating)\t" % (gen, subPopSize)')
...     ],
...     postOps = [
...         sim.stat(popSize=True),
...         sim.pyEval(r'"%s (after mating)\n" % subPopSize')
...     ],
...     gen = 5
... )
Gen 0: [1000] (before mating) [1000] (after mating)
Gen 1: [1000] (before mating) [1100] (after mating)
Gen 2: [1100] (before mating) [650, 650] (after mating)
Gen 3: [650, 650] (before mating) [800, 800] (after mating)
Gen 4: [800, 800] (before mating) [1000, 1000] (after mating)
(5,)

```

### 2.6.3 Determine the number of offspring during mating

simuPOP by default produces only one offspring per mating event. Because more parents are involved in the production of offspring, this setting leads to larger effective population sizes than mating schemes that produce more offspring at each mating event. However, various situations require a larger family size or even varying family sizes. In these cases, parameter `numOffspring` can be used to control the number of offspring that are produced at each mating event. This parameter takes the following types of inputs

- If a single number is given, `numOffspring` offspring are produced at each mating event.
- If a Python function is given, this function will be called each time when a mating event happens. Generation number will be passed to this function, which allows different numbers of offspring at different generations.
- If a tuple (or list) with more than one numbers is given, the first number must be one of `GEOMETRIC_DISTRIBUTION`, `POISSON_DISTRIBUTION`, `BINOMIAL_DISTRIBUTION` and `UNIFORM_DISTRIBUTION`, with one or two additional parameters. The number of offspring will then follow a specific statistical distribution. Note that all these distributions are adjusted so that the minimal number of offspring is 1.

More specifically,

- `numOffspring=(GEOMETRIC_DISTRIBUTION, p)`: The number of offspring for each mating event follows a geometric distribution with mean  $1/p$  and variance  $(1-p)/p^2$ :

$$\Pr(k) = p(1-p)^{k-1} \text{ for } k \geq 1$$

- `numOffspring=(POISSON_DISTRIBUTION, p)`: The number of offspring for each mating event follows a shifted Poisson distribution with mean  $p+1$  (you need to specify, for example, 2, if you want a mean family size of 3) and variance  $p$ . The distribution is

$$\Pr(k) = p^{k-1} \frac{e^{-p}}{(k-1)!} \text{ for } k \geq 1$$

- `numOffspring=(BINOMIAL_DISTRIBUTION, p, n)`: The number of offspring for each mating event follows a shifted Binomial distribution with mean  $(n-1)p+1$  and variance  $(n-1)p(1-p)$ .

$$\Pr(k) = \frac{(n-1)!}{(k-1)!(n-k)!} p^{k-1} (1-p)^{n-k} + 1 \text{ for } n \geq k \geq 1$$

- `numOffspring=(UNIFORM_DISTRIBUTION, a, b)`: The number of offspring for each mating event follows a discrete uniform distribution with lower bound  $a$  and upper bound  $b$ .

$$\Pr(k) = \frac{1}{b-a+1} \text{ for } b \geq k \geq a$$

Example 2.38 demonstrates how to use parameter `numOffspring`. In this example, a function `checkNumOffspring` is defined. It takes a mating scheme as its input parameter and use it to evolve a population with 30 individuals. After evolving a population for one generation, parental indexes are used to identify siblings, and then the number of offspring per mating event.

Example 2.38: Control the number of offspring per mating event.

```
>>> import simuPOP as sim
>>> def checkNumOffspring(ms):
...     '''Check the number of offspring for each family using
...     information field father_idx
...     '''
```

```

...     simu = sim.simulator(
...         sim.population(size=[30], infoFields=['father_idx', 'mother_idx']),
...         matingScheme=ms)
...     simu.evolve(
...         initOps = sim.initSex(),
...         duringOps = sim.parentsTagger(),
...         gen=1)
...     # get the parents of each offspring
...     parents = [(x, y) for x, y in zip(simu.population(0).indInfo('mother_idx'),
...         simu.population(0).indInfo('father_idx'))]
...     # Individuals with identical parents are considered as siblings.
...     famSize = []
...     lastParent = (-1, -1)
...     for parent in parents:
...         if parent == lastParent:
...             famSize[-1] += 1
...         else:
...             lastParent = parent
...             famSize.append(1)
...     return famSize
...
>>> # Case 1: produce the given number of offspring
>>> checkNumOffspring(sim.randomMating(numOffspring=2))
[2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2, 2]
>>> # Case 2: Use a Python function
>>> import random
>>> def func(gen):
...     return random.randint(5, 8)
...
>>> checkNumOffspring(sim.randomMating(numOffspring=func))
[8, 5, 5, 5, 6, 1]
>>> # Case 3: A geometric distribution
>>> checkNumOffspring(sim.randomMating(numOffspring=(sim.GEOMETRIC_DISTRIBUTION, 0.3)))
[2, 3, 1, 2, 1, 1, 3, 1, 3, 1, 9, 3]
>>> # Case 4: A Poisson distribution
>>> checkNumOffspring(sim.randomMating(numOffspring=(sim.POISSON_DISTRIBUTION, 3)))
[2, 4, 4, 3, 1, 12, 4]
>>> # Case 5: A Binomial distribution
>>> checkNumOffspring(sim.randomMating(numOffspring=(sim.BINOMIAL_DISTRIBUTION, 0.1, 10)))
[1, 1, 3, 2, 2, 4, 2, 3, 3, 1, 2, 1, 2, 3]
>>> # Case 6: A uniform distribution
>>> checkNumOffspring(sim.randomMating(numOffspring=(sim.UNIFORM_DISTRIBUTION, 2, 6)))
[3, 4, 2, 3, 2, 2, 4, 2, 5, 3]

```

## 2.6.4 Determine offspring sex

Because sex can influence how genotypes are transmitted (e.g. sex chromosomes, haplodiploid population), simuPOP determines offspring sex before it passes an offspring to a *genotype transmitter* (during-mating operator) to transmit genotype from parents to offspring. The default `sexMode` in almost all mating schemes is `RandomSex`, in which case simuPOP assign Male or Female to offspring with equal probability.

Other sex determination methods are also available:

- `sexMode=NO_SEX`: Sex is not simulated so everyone is MALE. This is the default mode where offspring can be MALE or FEMALE with equal probability.
- `sexMode=(PROB_OF_MALES, prob)`: Produce males with given probability.

- `sexMode=(NUM_OF_MALES, n)`: The first `n` offspring in each family will be Male. If the number of offspring at a mating event is less than or equal to `n`, all offspring will be male.
- `sexMode=(NUM_OF_FEMALES, n)`: The first `n` offspring in each family will be Female.

`NumOfMales` and `NumOfFemales` are useful in theoretical studies where the sex ratio of a population needs to be controlled strictly, or in special mating schemes, usually for animal populations, where only a certain number of male or female individuals are allowed in a family. It worth noting that a genotype transmitter can override specified offspring sex. This is the case for `cloneGenoTransmitter` where an offspring inherits both genotype and sex from his/her parent.

Example 2.39 demonstrates how to use parameter `sexMode`. In this example, a function `checkSexMode` is defined. It takes a mating scheme as its input parameter and use it to evolve a population with 40 individuals. After evolving a population for one generation, sexes of all offspring are returned as a string.

Example 2.39: Determine the sex of offspring

```
>>> import simuPOP as sim
>>> def checkSexMode(ms):
...     '''Check the assignment of sex to offspring'''
...     simu = sim.simulator(
...         sim.population(size=[40]),
...         matingScheme=ms)
...     simu.evolve(initOps = sim.initSex(), gen=1)
...     # return individual sex as a string
...     return ''.join([ind.sexChar() for ind in simu.population(0).individuals()])
...
>>> # Case 1: sim.NO_SEX (all male, sim.randomMating will not continue)
>>> checkSexMode(sim.randomMating(sexMode=sim.NO_SEX))
'MMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMMM'
>>> # Case 2: sim.RANDOM_SEX (sim.Male/Female with probability 0.5)
>>> checkSexMode(sim.randomMating(sexMode=sim.RANDOM_SEX))
'MFFFFFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFF'
>>> # Case 3: sim.PROB_OF_MALES (Specify probability of male)
>>> checkSexMode(sim.randomMating(sexMode=(sim.PROB_OF_MALES, 0.8)))
'MMFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFF'
>>> # Case 4: sim.NUM_OF_MALES (Specify number of male in each family)
>>> checkSexMode(sim.randomMating(numOffspring=3, sexMode=(sim.NUM_OF_MALES, 1)))
'MFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFF'
>>> # Case 5: sim.NUM_OF_FEMALES (Specify number of female in each family)
>>> checkSexMode(sim.randomMating(
...     numOffspring=(sim.UNIFORM_DISTRIBUTION, 4, 6),
...     sexMode=(sim.NUM_OF_FEMALES, 2))
... )
'FFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFFMFF'
```

## 2.6.5 Monogamous mating

Monogamous mating (monogamy) in `simuPOP` refers to mating schemes in which each parent mates only once. In an asexual setting, this implies parents are chosen without replacement. In sexual mating schemes, this means that parents are chosen without replacement, they have only one spouse during their life time so that all siblings have the same parents (no half-sibling).

`simuPOP` provides a diploid sexual monogamous mating scheme `monogamousMating`. However, without careful planning, this mating scheme can easily stop working due to the lack of parents. For example, if a population has 40 males and 55 females, only 40 successful mating events can happen and result in 40 offspring in the offspring generation. `monogamousMating` will exit if the offspring generation is larger than 40.

Example 2.40 demonstrates one scenario of using a monogamous mating scheme where sex of parents and offspring are strictly specified so that parents will not be exhausted. The sex initializer `initSex` assigns exactly 10 males and 10 females to the initial population. Because of the use of `numOffspring=2`, `sexMode=(NUM_OF_MALES, 1)`, each mating event will produce exactly one male and one female. Unlike a random mating scheme that only about 80% of parents are involved in the production of an offspring population with the same size, this mating scheme makes use of all parents.

Example 2.40: Sexual monogamous mating

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(20, infoFields=['father_idx', 'mother_idx']),
...     sim.monogamousMating(numOffspring=2, sexMode=(sim.NUM_OF_MALES, 1)))
>>> simu.evolve(
...     initOps = sim.initSex(sex=(sim.MALE, sim.FEMALE)),
...     duringOps = sim.parentsTagger(),
...     gen = 5
... )
(5,)
>>> pop = simu.extract(0)
>>> [ind.sex() for ind in pop.individuals()]
[1, 2, 1, 2, 1, 2, 1, 2, 1, 2, 1, 2, 1, 2, 1, 2, 1, 2]
>>> [int(ind.father_idx) for ind in pop.individuals()]
[6, 6, 18, 18, 12, 12, 10, 10, 14, 14, 0, 0, 8, 8, 4, 4, 2, 2, 16, 16]
>>> [int(ind.mother_idx) for ind in pop.individuals()]
[11, 11, 7, 7, 5, 5, 3, 3, 9, 9, 19, 19, 15, 15, 1, 1, 17, 17, 13, 13]
>>> # count the number of distinct parents
>>> len(set(pop.indInfo('father_idx')))
10
>>> len(set(pop.indInfo('mother_idx')))
10
```

## 2.6.6 Polygamous mating

In comparison to monogamous mating, parents in a polygamous mate with more than one spouse during their life-cycle. Both *polygamy* (one man has more than one wife) and *polyandry* (one woman has more than one husband) are supported.

Other than regular parameters such as `numOffspring`, mating scheme `polygamousMating` accepts parameters `polySex` (default to Male) and `polyNum` (default to 1). During mating, an individual with `polySex` is selected and then mate with `polyNum` randomly selected spouse. Example 2.41 demonstrates the use of this mating schemes. Note that this mating scheme support natural selection, but does not yet handle varying `polyNum` and selection of parents without replacement.

Example 2.41: Sexual polygamous mating

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(100, infoFields=['father_idx', 'mother_idx']),
...     sim.polygamousMating(polySex=sim.MALE, polyNum=2))
>>> simu.evolve(
...     initOps = sim.initSex(),
...     duringOps = sim.parentsTagger(),
...     gen = 5
... )
(5,)
>>> pop = simu.extract(0)
>>> [int(ind.father_idx) for ind in pop.individuals()][:20]
[67, 67, 42, 42, 91, 91, 25, 25, 65, 65, 47, 47, 18, 18, 16, 16, 96, 96, 57, 57]
>>> [int(ind.mother_idx) for ind in pop.individuals()][:20]
[58, 58, 58, 0, 68, 32, 37, 89, 6, 85, 12, 58, 36, 12, 66, 44, 51, 85, 60, 29]
```



### 2.6.7 Asexual random mating

Mating scheme `randomSelection` implements an asexual random mating scheme. It randomly select parents from a parental population (with replacement) and copy them to an offspring generation. Both genotypes and sex of the parents are copied because genotype and sex are sometimes related. This mating scheme can be used to simulate the evolution of haploid sequences in a standard haploid Wright-Fisher model.

Example 2.42 applies a `randomSelection` mating scheme to a haploid population with 100 sequences. A `parentTagger` is used to track the parent of each individual. Although sex information is not used in this mating scheme, individual sexes are initialized and passed to offspring.

Example 2.42: Asexual random mating

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(100, ploidy=1, loci=[5, 5], ancGen=1,
...     infoFields='parent_idx'),
...     sim.randomSelection())
>>> simu.evolve(
...     initOps = sim.initByFreq([0.3, 0.7]),
...     duringOps = sim.parentsTagger(infoFields='parent_idx'),
...     gen = 5
... )
(5,)
>>> pop = simu.extract(0)
>>> ind = pop.individual(0)
>>> par = pop.ancestor(ind.parent_idx, 1)
>>> print ind.sex(), ind.genotype()
1 [1, 1, 0, 1, 1, 0, 1, 0, 0, 0]
>>> print par.sex(), par.genotype()
1 [1, 1, 0, 1, 1, 0, 1, 0, 0, 0]
```

### 2.6.8 Mating with alpha individuals \*

The `alphaMating` mating scheme is intended to simulate animal populations in which only individuals with alpha status have the power to mate. In this mating scheme, a number of alpha individuals with specified sex (`alphaSex`) are determined, either randomly (`alphaNum`) or according to values at an information field (`alphaField`). During mating, only individuals from this alpha group can be selected to mate.

Example 2.43 gives a simple evolutionary scenario where two alpha males are chosen according to individual fitness values at each generation. The fitness value of each individual is determined by his/her genotype at the first locus, 0.8, 0.8, and 1 for genotype AA, Aa, and aa respectively. Because individuals having mutant a have a high probability to be selected, and become the alpha male in this population, the frequency of this mutant tend to increase in this population.

Example 2.43: Random mating with alpha individuals

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(1000, loci=5,
...     infoFields=['father_idx', 'mother_idx', 'fitness']),
...     sim.alphaMating(alphaSex=sim.MALE, alphaNum=2))
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5])
...     ],
...     preOps = sim.maSelector(loci=0, fitness=[0.8, 0.8, 1]),
...     duringOps = sim.parentsTagger(),
...     postOps = [
```

```

...     sim.stat(alleleFreq=0),
...     sim.pyEval(r'("%.2f\n" % alleleFreq[0][1]', step=5)
... ],
...     gen = 20,
... )
0.74
0.98
1.00
1.00
(20,)
>>> pop = simu.extract(0)
>>> [int(ind.father_idx) for ind in pop.individuals()][:10]
[999, 815, 999, 999, 999, 815, 999, 815, 999, 815]
>>> [int(ind.mother_idx) for ind in pop.individuals()][:10]
[135, 937, 780, 67, 397, 380, 907, 757, 881, 731]

```

## 2.6.9 Mating in haplodiploid populations

Male individuals in a haplodiploid population are derived from unfertilized eggs and thus have only one set of chromosomes. Mating in such a population is handled by a special mating scheme called `haplodiploidMating`. This mating scheme chooses a pair of parents randomly and produces some offspring. It transmit maternal chromosomes and paternal chromosomes (the only copy) to female offspring, and only maternal chromosomes to male offspring. Example 2.44 demonstrates how to use this mating scheme. It uses three initializers because sex has to be initialized before two other initializers can initialize genotype by sex.

Example 2.44: Random mating in haplodiploid populations

```

>>> import simuPOP as sim
>>> pop = sim.population(10, ploidy=sim.HAPLODIPLOID, loci=[5, 5],
...     infoFields=['father_idx', 'mother_idx'])
>>> pop.setVirtualSplitter(sim.sexSplitter())
>>> simu = sim.simulator(pop, sim.haplodiploidMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([0]*10, subPops=[(0, 0)]),
...         sim.initByValue([1]*10+[2]*10, subPops=[(0, 1)])
...     ],
...     preOps = sim.dumper(structure=False),
...     duringOps = sim.parentsTagger(),
...     postOps = sim.dumper(structure=False),
...     gen = 1
... )
Subpopulation 0 (), 10 individuals:
  0: FU 11111 11111 | 22222 22222 | 0 0
  1: FU 11111 11111 | 22222 22222 | 0 0
  2: MU 00000 00000 | _____ | 0 0
  3: MU 00000 00000 | _____ | 0 0
  4: MU 00000 00000 | _____ | 0 0
  5: MU 00000 00000 | _____ | 0 0
  6: MU 00000 00000 | _____ | 0 0
  7: FU 11111 11111 | 22222 22222 | 0 0
  8: FU 11111 11111 | 22222 22222 | 0 0
  9: FU 11111 11111 | 22222 22222 | 0 0
Subpopulation 0 (), 10 individuals:
  0: MU 11111 11111 | _____ | 4 9
  1: MU 11111 22222 | _____ | 4 8
  2: MU 22222 11111 | _____ | 6 8

```

```

3: MU 22222 11111 | _____ | 3 8
4: MU 22222 22222 | _____ | 2 8
5: MU 22222 22222 | _____ | 6 9
6: FU 22222 22222 | 00000 00000 | 2 1
7: FU 22222 22222 | 00000 00000 | 2 1
8: FU 22222 22222 | 00000 00000 | 3 9
9: FU 11111 11111 | 00000 00000 | 5 8
(1,)

```

Note that this mating scheme does not support recombination and the standard recombinator does not work with haplodiploid populations. Please refer to the next Chapter for how to define a customized genotype transmitter to handle such a situation.

## 2.6.10 Self-fertilization

Some plant populations evolve through self-fertilization. That is to say, a parent fertilizes with itself during the production of offspring (seeds). In a `selfMating` mating scheme, parents are chosen randomly (one at a time), and are used twice to produce two homologous sets of offspring chromosomes. The standard recombinator can be used with this mating scheme. Example 2.45 initializes each chromosome with different alleles to demonstrate how these alleles are transmitted in this population.

Example 2.45: Selfing mating scheme

```

>>> import simuPOP as sim
>>> pop = sim.population(20, loci=8)
>>> # every chromosomes are different. :-)
>>> for idx, ind in enumerate(pop.individuals()):
...     ind.setGenotype([idx*2], 0)
...     ind.setGenotype([idx*2+1], 1)
...
>>> simu = sim.simulator(pop, sim.selfMating(ops=sim.recombinator(rates=0.01)))
>>> simu.evolve( gen = 1)
(1,)
>>> sim.Dump(simu.population(0), width=3, structure=False, max=10)
Subpopulation 0 (), 20 individuals:
0: FU 36 36 36 36 36 36 36 36 | 37 37 37 37 37 37 37 37
1: FU 38 38 38 38 38 38 38 38 | 39 39 39 39 39 39 39 39
2: FU 18 18 18 18 18 18 18 18 | 18 18 18 18 18 18 18 18
3: FU 26 26 26 26 26 26 26 26 | 27 27 27 27 27 27 27 27
4: FU 37 37 37 37 37 37 37 37 | 37 37 37 37 37 37 37 37
5: MU 29 29 29 29 29 29 29 29 | 28 28 28 28 28 28 28 28
6: MU 14 14 14 14 14 14 14 14 | 15 15 15 15 15 15 15 15
7: MU 27 27 27 27 27 27 27 27 | 26 26 26 26 26 26 26 26
8: MU 6 6 6 6 6 6 6 6 | 6 6 6 6 6 6 6 6
9: MU 28 28 28 28 28 28 29 29 | 28 28 28 28 28 28 28 28

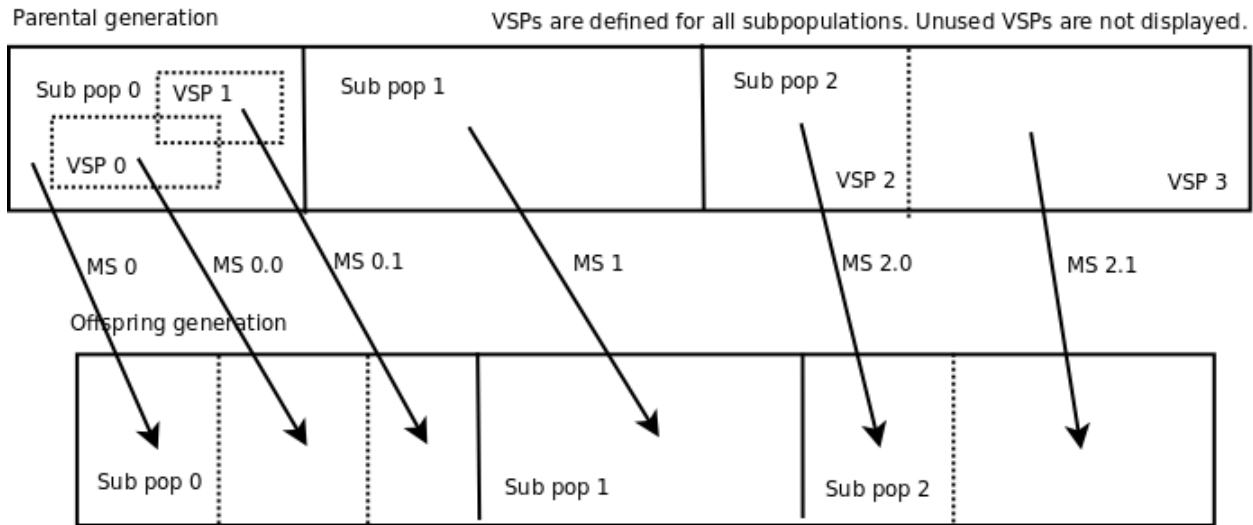
```

## 2.6.11 Heterogeneous mating schemes \*

Different groups of individuals in a population may have different mating patterns. For example, individuals with different properties can have varying fecundity, represented by different numbers of offspring generated per mating event. This can be extended to aged populations in which only adults (may be defined by age > 20 and age < 40) can produce offspring, where other individuals will either be copied to the offspring generation or die.

A heterogeneous mating scheme (`heteroMating`) accepts a list of mating schemes that are applied to different subpopulation or virtual subpopulations. If multiple mating schemes are applied to the same subpopulation, each of them only population part of the offspring subpopulation. This is illustrated in Figure 2.4.

Figure 2.4: Illustration of a heterogeneous mating scheme



A heterogeneous mating scheme that applies homogeneous mating schemes MS0, MS0.0, MS0.1, MS1, MS2.0 and MS2.1 to subpopulation 0, the first and second virtual subpopulation in subpopulation 0, subpopulation 1, the first and second virtual subpopulation in subpopulation 2, respectively. Note that VSP 0 and 1 in subpopulation 0 overlap, and do not add up to subpopulation 0.

For example, Example 2.46 applies two random mating schemes to two subpopulations. The first mating scheme produces two offspring per mating event, and the second mating scheme produces four.

Example 2.46: Applying different mating schemes to different subpopulations

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[1000, 1000], loci=2,
... infoFields=['father_idx', 'mother_idx'])
>>> simu = sim.simulator(pop, sim.heteroMating(
... [sim.randomMating(numOffspring=2, subPops=0),
...  sim.randomMating(numOffspring=4, subPops=1)
... ])
... )
>>> simu.evolve(
...  initOps = sim.initSex(),
...  duringOps = sim.parentsTagger(),
...  gen=10
... )
(10,)
>>> pop = simu.extract(0)
>>> [int(ind.father_idx) for ind in pop.individuals(0)][:10]
[134, 134, 451, 451, 780, 780, 443, 443, 457, 457]
>>> [int(ind.father_idx) for ind in pop.individuals(1)][:10]
[1978, 1978, 1978, 1978, 1582, 1582, 1582, 1582, 1322, 1322]
```

The real power of heterogeneous mating schemes lies on their ability to apply different mating schemes to different virtual subpopulations. For example, due to different micro-environmental factors, plants in the same population may exercise both self and cross-fertilization. Because of the randomness of such environmental factors, it is difficult to divide a population into self and cross-mating subpopulations. Applying different mating schemes to groups of individuals in the same subpopulation is more appropriate.

Example 2.47 applies two mating schemes to two VSPs defined by proportions of individuals. In this mating scheme, 20% of individuals go through self-mating and 80% of individuals go through random mating. This can be seen from

the parental indexes of individuals in the offspring generation: individuals whose `mother_idx` are -1 are genetically only derived from their fathers.

It might be surprising that offspring resulted from two mating schemes mix with each other so the same VSPs in the next generation include both selfed and cross-fertilized offspring. If this not desired, you can set parameter `shuffleOffspring=False` in `heteroMating()`. Because the number of offspring that are produced by each mating scheme is proportional to the size of parental (virtual) subpopulation, the first 20% of individuals that are produced by self-fertilization will continue to self-fertilize.

Example 2.47: Applying different mating schemes to different virtual subpopulations

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[1000], loci=2,
...     infoFields=['father_idx', 'mother_idx'])
>>> pop.setVirtualSplitter(sim.proportionSplitter([0.2, 0.8]))
>>> simu = sim.simulator(pop, sim.heteroMating(
...     matingSchemes = [
...         sim.selfMating(subPops=[(0, 0)]),
...         sim.randomMating(subPops=[(0, 1)])
...     ])
>>> simu.evolve(
...     initOps = sim.initSex(),
...     duringOps = sim.parentsTagger(),
...     gen = 10
... )
(10,)
>>> pop = simu.extract(0)
>>> [int(ind.father_idx) for ind in pop.individuals(0)][:15]
[789, 666, 726, 125, 681, 183, 727, 308, 392, 11, 917, 223, 208, 146, 309]
>>> [int(ind.mother_idx) for ind in pop.individuals(0)][:15]
[370, 272, -1, 520, 121, 91, 220, 519, 101, 271, -1, 263, 663, -1, 286]
```

Because there is no restriction on the choice of VSPs, mating schemes can be applied to overlapped (virtual) subpopulations. For example,

```
heteroMating(
    matingSchemes = [
        selfMating(subPops=[(0, 0)]),
        randomMating(subPops=0)
    ]
)
```

will apply `selfMating` to the first 20% individuals, and `randomMating` will be applied to all individuals. Similarly,

```
heteroMating(
    matingSchemes = [
        selfMating(subPops=0),
        randomMating(subPops=0)
    ]
)
```

will allow all individuals to be involved in both `selfMating` and `randomMating`.

This raises the question of how many offspring each mating scheme will produce. By default, the number of offspring produced will be proportional to the size of parental (virtual) subpopulations. In the last example, because both mating schemes are applied to the same subpopulation, half of all offspring will be produced by selfing and the other half will be produced by random mating.

This behavior can be changed by a weighting scheme controlled by parameter `weight` of each homogeneous mating scheme. Briefly speaking, a positive weight will be compared against other mating schemes. a negative weight is

considered proportional to the existing (virtual) subpopulation size. Negative weights are considered before position or zero weights.

This weighting scheme is best explained by an example. Assuming that there are three mating schemes working on the same parental subpopulation

- Mating scheme A works on the whole subpopulation of size 1000
- Mating scheme B works on a virtual subpopulation of size 500
- Mating scheme C works on another virtual subpopulation of size 800

Assuming the corresponding offspring subpopulation has  $N$  individuals,

- If all weights are 0, the offspring subpopulation is divided in proportion to parental (virtual) subpopulation sizes. In this example, the mating schemes will produce  $\frac{10}{23}N$ ,  $\frac{5}{23}N$ ,  $\frac{8}{23}N$  individuals respectively.
- If all weights are negative, they are multiplied to their parental (virtual) subpopulation sizes. For example, weight (-1, -2, -0.5) will lead to sizes (1000, 1000, 400) in the offspring subpopulation. If  $N \neq 2400$  in this case, an error will be raised.
- If all weights are positive, the number of offspring produced from each mating scheme is proportional to these weights. For example, weights (1, 2, 3) will lead to  $\frac{1}{6}N$ ,  $\frac{2}{6}N$ ,  $\frac{3}{6}N$  individuals respectively. In this case, 0 weights will produce no offspring.
- If there are mixed positive and negative weights, the negative weights are processed first, and the rest of the individuals are divided using non-negative weights. For example, three mating schemes with weights (-0.5, 2, 3) will produce 500,  $\frac{2}{5}(N - 500)$ ,  $\frac{3}{5}(N - 500)$  individuals respectively.

The last case is demonstrated in Example 2.48 where three random mating schemes are applied to subpopulation 0, virtual subpopulation (0, 0) and virtual subpopulation (0, 1), with weights -0.5, 2, and 3 respectively. This example uses an advanced features that will be described in the next section. Namely, three during-mating Python operators are passed to each mating scheme to mark their offspring with different numbers.

Example 2.48: A weighting scheme used by heterogeneous mating schemes.

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[1000], loci=2,
...     infoFields='mark')
>>> pop.setVirtualSplitter(sim.rangeSplitter([[0, 500], [200, 1000]]))
>>> def markOff(param):
...     '''define a Python during mating operator that marks
...         individual information field 'mark'
...     '''
...     def func(off, param):
...         off.mark = param
...         return True
...     return sim.pyOperator(func=func, param=param, offspringOnly=True)
>>> simu = sim.simulator(pop, sim.heteroMating(
...     matingSchemes = [
...         sim.randomMating(subPops=0, weight=-0.5, ops=[markOff(0), sim.mendelianGenoTransmitter],
...         sim.randomMating(subPops=[(0, 0)], weight=2, ops=[markOff(1), sim.mendelianGenoTransmitter],
...         sim.randomMating(subPops=[(0, 1)], weight=3, ops=[markOff(2), sim.mendelianGenoTransmitter],
...     ])
... )
>>> simu.evolve(
...     initOps = sim.initSex(),
...     gen = 10
```

```

... )
(10,)
>>> marks = list(simu.extract(0).indInfo('mark'))
>>> marks.count(0.)
500
>>> marks.count(1.)
200
>>> marks.count(2.)
300

```

## 2.7 Non-random and customized mating schemes \*

### 2.7.1 The structure of a homogeneous mating scheme \*

A *homogeneous mating scheme* populates an offspring generation as follows:

1. Create an empty offspring population (generation) with appropriate size. Parental and offspring generation can differ in size but they must have the same number of subpopulations.
2. For each subpopulation, repeatedly choose a parent or a pair of parents from the parental generation. This is done by a simuPOP object called a **parent chooser**.
3. One or more offspring are produced from the chosen parent(s) and are placed in the offspring population. This is done by a simuPOP **offspring generator**.
4. A offspring generator uses one or more during-mating operators to transmit parental genotype to offspring. These operators are call **genotype transmitters**.
5. After the offspring generation is populated, it will replace the parental generation and becomes the present generation of a population.

A simuPOP mating scheme uses a particular set of parent chooser, offspring generator, and genotype transmitters. For example, a `selfingMating` mating scheme uses a `randomParentChooser` to choose a parent randomly from a population, possibly according to individual fitness, it uses a standard `offspringGenerator` that uses a `selfingOffspringGenerator` to transmit genotype.

Example 2.49 demonstrates how the most commonly used mating scheme, the diploid sexual `randomMating` mating scheme is defined in `simuPOP.py`. The following sections basically explain how you can construct your own mating scheme from scratch, using stocked or customized parent chooser, offspring generator and genotype transmitters.

Example 2.49: Define a random mating scheme

```

def randomMating(numOffspring = 1., sexMode = sim.RANDOM_SEX,
    preOps = sim.mendelianGenoTransmitter(), subPopSize = [],
    subPops = ALL_AVAIL, weight = 0, selectionField = 'fitness'):
    'A basic diploid sexual random mating scheme.'
    return sim.homoMating(
        chooser = sim.randomParentsChooser(True, selectionField),
        generator = sim.offspringGenerator(ops, numOffspring, sexMode),
        subPopSize = subPopSize,
        subPops = subPops,
        weight = weight)

```

## 2.7.2 homoMating mating scheme \*

`homoMating` is used to define all pre-defined homogeneous mating schemes. It takes five parameters: `chooser` (a *parent chooser* that is responsible for choosing one or two parents from the parental generation), `generator` (an *offspring generator* that is responsible for generating a number of offspring from the chosen parents), `subPopSize` (parameter to control offspring subpopulation sizes), `subPops` (applicable subpopulation or virtual subpopulations), and `weight` (weighting parameter when used in a heterogeneous mating scheme). When this mating scheme is applied to the whole population, `subPopSize` is used to determine the subpopulation sizes of the offspring generation (see Section 2.6.1 for details), parameters `subPops` and `weight` are ignored. Otherwise, the number of offspring this mating scheme will produce is determined by the heterogeneous mating scheme.

Parameters `subPopSize`, `subPops` and `weight` are more or less standard but different parent choosers and offspring generators can be combined to define a large number of homogeneous mating schemes. For example, the standard `selfMating` mating scheme uses a `randomParentChooser` but you can easily use a `sequentialParentChooser` to choose parents sequentially and self-fertilize parents one by one. This is demonstrated in Example 2.50.

Example 2.50: Define a sequential selfing mating scheme

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(100, loci=5*3, infoFields='parent_idx'),
...     sim.homoMating(sim.sequentialParentChooser(),
...     sim.offspringGenerator(ops=sim.selfingGenoTransmitter()))
>>> simu.evolve(
...     initOps = [sim.initByFreq([0.2]*5)],
...     preOps = sim.dumper(structure=False, max=5),
...     duringOps = sim.parentsTagger(infoFields='parent_idx'),
...     postOps = sim.dumper(structure=False, max=5),
...     gen = 1
... )
Subpopulation 0 (), 100 individuals:
  0: MU 410122433334001 | 400424241040114 | 0
  1: MU 344433321234330 | 342404413041321 | 0
  2: MU 044022204342401 | 334444434011322 | 0
  3: MU 122302034302144 | 332340411023120 | 0
  4: MU 112003324342132 | 113403434421310 | 0
Subpopulation 0 (), 100 individuals:
  0: MU 410122433334001 | 400424241040114 | 0
  1: FU 344433321234330 | 342404413041321 | 1
  2: MU 334444434011322 | 044022204342401 | 2
  3: FU 332340411023120 | 122302034302144 | 3
  4: FU 113403434421310 | 112003324342132 | 4
(1,)
```

The `simuPOP` reference manual lists all pre-defined parent choosers and offspring generators. They may or may not work together depending on the number of parents a parent chooser produces, and the number of parents an offspring generator can handle. You can also define your own parent choosers and offspring generators, as shown below.

## 2.7.3 Offspring generators \*

An `offspringGenerator` accepts a parameters `ops` (a list of during-mating operators), `numOffspring` (control number of offspring per mating event) and `sexMode` (control offspring sex). We have examined the last two parameters in detail in sections 2.6.3 and 2.6.4.

The most tricky parameter is the `ops` parameter. It accepts a list of during mating operators that are used to transmit genotypes from parent(s) to offspring and/or set individual information fields. The standard `offspringGenerator` does not have any default operator so no genotype will be transmitted by default. All stock mating schemes use



a default genotype transmitter. (e.g, a `mendelianGenoTransmitter` in Example 2.49 is passed to the offspring generator used in `randomMating`). Note that you need to specify all needed operators if you use parameter `ops` to change the operators used in a mating scheme (see Example 2.48). That is to say, you can use `ops=recombinator()` to replace a default `mendelianGenoTransmitter()`, but you have to use `ops=[idTagger(), mendelianGenoTransmitter()]` if you would like to add a during-mating operator to the default one.

Another offspring generator is provided in `simuPOP`. This `controlledOffspringGenerator` is used to control an evolutionary process so that the allele frequencies at certain loci follows some pre-simulated *frequency trajectories*. Please refer to Peng et al. [2007] for rationals behind such an offspring generator and its applications in the simulation of complex human diseases.

Example 2.51 demonstrates the use of such a controlled offspring generator. Instead of using a realistic frequency trajectory function, it forces allele frequency at locus 5 to increase linearly. In contrast, the allele frequency at locus 15 on the second chromosome oscillates as a result of genetic drift. Note that the random mating version of this mating scheme is defined in `simuPOP` as `controlledRandomMating`.

Example 2.51: A controlled random mating scheme

```
>>> import simuPOP as sim
>>> def traj(gen):
...     return [0.5 + gen * 0.01]
...
>>> simu = sim.simulator(sim.population(1000, loci=[10]*2),
...     sim.homoMating(sim.randomParentChooser(),
...     sim.controlledOffspringGenerator(loci=5,
...     alleles=[0], freqFunc=traj,
...     ops = sim.selfingGenoTransmitter()))
... )
>>> # evolve the sim.population while keeping allele frequency 0.5
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5])
...     ],
...     postOps = [
...         sim.stat(alleleFreq=[5, 15]),
...         sim.pyEval(r'%.2f\t%.2f\n' % (alleleFreq[5][0], alleleFreq[15][0]))
...     ],
...     gen = 5
... )
0.50    0.47
0.51    0.47
0.52    0.49
0.53    0.50
0.54    0.52
(5,)
```

## 2.7.4 Pre-defined genotype transmitters \*

Although any during mating operators can be used in parameter `ops` of an offspring generator, those that transmit genotype from parents to offspring are customarily called **genotype transmitters**. `simuPOP` provides a number of genotype transmitters including `clone`, `Mendelian`, `selfing`, `haplodiploid`, `genotype transmitter`, and a `recombinator`. They are usually used implicitly in a mating scheme, but they can also be used explicitly.

All genotype transmitters only handle known chromosome types such as `AUTOSOME`, `CHROMOSOME_X` and `CHROMOSOME_Y`. Customized chromosomes are left untouched because `simuPOP` does not know how they should

be transmitted from parents to offspring. In case that Customized chromosomes are treated as mitochondrial chromosomes, a `mitochondrialGenoTransmitter` can be used to transmit customized chromosomes randomly from mother to offspring. Example 2.52 demonstrates the use of a `recombinator` to recombine an autosome and two sex chromosomes, and a `mitochondrialGenoTransmitter` to transmit mitochondrial chromosomes. Note that the default `mendelianGenoTransmitter` is replaced by these two operators. It will be (wastefully) applied if the new during-mating operators are used in the `simulator.evolve` function.

Example 2.52: Transmission of mitochondrial chromosomes

```
>>> import simuPOP as sim
>>> pop = sim.population(10, loci=[5]*5,
... # one autosome, two sex chromosomes, and two mitochondrial chromosomes
... chromTypes=[sim.AUTOSOME, sim.CHROMOSOME_X, sim.CHROMOSOME_Y] + [sim.CUSTOMIZED]*2,
... infoFields=['father_idx', 'mother_idx'])
>>> simu = sim.simulator(pop, sim.randomMating(ops= [
... sim.recombinator(rates=0.1),
... sim.mitochondrialGenoTransmitter()])))
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.4] + [0.2]*3)
...     ],
...     duringOps = sim.parentsTagger(),
...     postOps = sim.dumper(structure=False),
...     gen = 2
... )
Subpopulation 0 (), 10 individuals:
 0: MU 10000 00023 _____ 00331 00331 | 21120 _____ 02011 00000 00000 | 3 9
 1: MU 11000 20023 _____ 00331 32313 | 03220 _____ 03030 00000 00000 | 5 9
 2: MU 00310 00113 _____ 00230 00230 | 03220 _____ 03030 00000 00000 | 5 0
 3: FU 03300 22030 _____ 10000 10000 | 00010 01310 _____ 00000 00000 | 4 1
 4: MU 02001 30220 _____ 10031 02122 | 00133 _____ 00003 00000 00000 | 2 8
 5: MU 11000 20231 _____ 00331 32313 | 00010 _____ 31310 00000 00000 | 4 9
 6: FU 01000 13000 _____ 01002 31131 | 03220 10330 _____ 00000 00000 | 5 7
 7: MU 00310 30113 _____ 00230 00230 | 10133 _____ 00003 00000 00000 | 2 0
 8: FU 01000 30000 _____ 01002 01002 | 00220 10330 _____ 00000 00000 | 5 7
 9: MU 20200 30113 _____ 20011 20011 | 03321 _____ 01201 00000 00000 | 6 0
Subpopulation 0 (), 10 individuals:
 0: MU 01000 30330 _____ 01002 01002 | 00010 _____ 31310 00000 00000 | 5 8
 1: MU 00200 30000 _____ 01002 01002 | 00133 _____ 00003 00000 00000 | 4 8
 2: MU 03300 22030 _____ 10000 10000 | 00010 _____ 31310 00000 00000 | 5 3
 3: MU 00000 22030 _____ 10000 10000 | 11000 _____ 03030 00000 00000 | 1 3
 4: MU 01000 13330 _____ 31131 01002 | 03220 _____ 03030 00000 00000 | 2 6
 5: FU 01000 10300 _____ 01002 01002 | 03220 20023 _____ 00000 00000 | 1 8
 6: MU 00220 30000 _____ 01002 01002 | 00101 _____ 00003 00000 00000 | 4 8
 7: FU 01000 10330 _____ 31131 01002 | 11000 20023 _____ 00000 00000 | 1 6
 8: MU 03300 01310 _____ 10000 10000 | 03220 _____ 03030 00000 00000 | 2 3
 9: FU 01000 10330 _____ 31131 01002 | 03220 20023 _____ 00000 00000 | 1 6
(2,)
```

## 2.7.5 Customized genotype transmitter \*\*

Although `simuPOP` provides a number of genotype transmitters, they may still be cases where customized genotype transmitter is needed. For example, a `recombinator` can be used to recombine parental chromosomes but it is well known that male and female individuals differ in recombination rates. How can you apply two different recombinators to male and female individuals separately?

An immediate thought can be the use of virtual subpopulations. If you apply two random mating schemes to two

virtual subpopulations defined by sex, `randomParentsChooser` will not work because no opposite sex can be found in each virtual subpopulation. In this case, a customized genotype transmitter can be used.

A customized genotype transmitter is only a Python during-mating operator. Although it is possible to define a function and use a `pyOperator` directly (Example 2.29), it is much better to derive an operator from `pyOperator`, as the case in Example 2.32.

Example 2.53 defines a `sexSpecificRecombinator` that uses, internally, two different recombinators to recombine male and female parents. The key statement is the `pyOperator.__init__` line which initializes a Python operator with given function `self.transmitGenotype`.

The actual function to transmit parental genotype is `self.transmitGenotype`. This function initializes two recombinators if they have not been initialized and uses them to transmit parental genotypes. Example 2.53 outputs the population in two generations. You should notice that paternal chromosome are not recombined when they are transmitted to offspring.

Example 2.53: A customized genotype transmitter for sex-specific recombination

```
>>> import simuPOP as sim
>>> class sexSpecificRecombinator(sim.pyOperator):
...     def __init__(self, intensity=0, rates=0, loci=[], convMode=sim.NO_CONVERSION,
...                 maleIntensity=0, maleRates=0, maleLoci=[], maleConvMode=sim.NO_CONVERSION,
...                 *args, **kwargs):
...         # This operator is used to recombine maternal chromosomes
...         self.recombinator = sim.recombinator(rates, intensity, loci, convMode)
...         # This operator is used to recombine paternal chromosomes
...         self.maleRecombinator = sim.recombinator(maleRates, maleIntensity,
...         maleLoci, maleConvMode)
...         #
...         self.initialized = False
...         #
...         sim.pyOperator.__init__(self, func=self.transmitGenotype, *args, **kwargs)
...     #
...     def transmitGenotype(self, pop, off, dad, mom):
...         # Recombinators need to be initialized. Basically, they cache some
...         # sim.population properties to speed up genotype transmission.
...         if not self.initialized:
...             self.recombinator.initialize(pop)
...             self.maleRecombinator.initialize(pop)
...             self.initialized = True
...         # Form the first homologous copy of offspring.
...         self.recombinator.transmitGenotype(mom, off, 0)
...         self.maleRecombinator.transmitGenotype(dad, off, 1)
...         return True
...
>>> pop = sim.population(10, loci=[15]*2, infoFields=['father_idx', 'mother_idx'])
>>> simu = sim.simulator(pop, sim.randomMating(
...     ops = sexSpecificRecombinator(rates=0.1, maleRates=0)))
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.4] + [0.2]*3)
...     ],
...     duringOps = sim.parentsTagger(),
...     postOps = sim.dumper(structure=False),
...     gen = 2
... )
Subpopulation 0 (), 10 individuals:
0: FU 300322010100110 110002023130102 | 300003300301002 331000200103000 | 6 7
1: FU 003103011323230 200110023003300 | 313300120022322 302203131033111 | 3 0
```

```

2: MU 220303230010000 203320013311200 | 011303111300010 013100222032022 | 3 1
3: MU 323130033110110 203130001330001 | 232023010200303 211200030002011 | 2 8
4: FU 001210201010003 211020020013121 | 330020011223313 310301330001000 | 5 9
5: MU 003103011323230 331203102132333 | 130000302310200 311310200130220 | 6 0
6: MU 202020000123300 200110023003300 | 232023010200303 321010012133330 | 2 0
7: FU 200101003102122 110002023130102 | 000031131033013 321010012133330 | 2 7
8: FU 130303223301102 211020020013121 | 032120322002100 121003120132100 | 4 9
9: FU 202020000123300 200110023003300 | 330020011223313 310301330001000 | 5 0
Subpopulation 0 (), 10 individuals:
0: MU 003103011323230 302203131033111 | 003103011323230 311310200130220 | 5 1
1: MU 003103011323230 302203131033111 | 202020000123300 321010012133330 | 6 1
2: FU 200101003102122 321010012133330 | 232023010200303 211200030002011 | 3 7
3: FU 313300120022322 200110023003300 | 130000302310200 331203102132333 | 5 1
4: MU 130303223301102 211020020013121 | 323130033110110 211200030002011 | 3 8
5: FU 313300120022322 200110023003300 | 130000302310200 311310200130220 | 5 1
6: FU 130303223301102 211020020013121 | 323130033110110 211200030002011 | 3 8
7: MU 202020000123300 310301330001000 | 232023010200303 211200030002011 | 3 9
8: FU 130303223301102 211020020013121 | 232023010200303 211200030002011 | 3 8
9: FU 003103011323230 200110023003300 | 323130033110110 211200030002011 | 3 1
(2,)

```

## 2.7.6 A Python parent chooser \*

Parent choosers are responsible for choosing one or two parents from a parental (virtual) subpopulation. `simuPOP` defines a few parent choosers that choose parent(s) sequentially, randomly (with or without replacement), or with additional conditions. Some of these parent choosers support natural selection. We have seen sequential and random parent choosers in Examples 2.50 and 2.51. Please refer to the `simuPOP` reference manual for details about these objects.

A parent choosing scheme can be quite complicated in reality. For example, salamanders along a river may mate with their neighbors and form several subspecies. This behavior cannot be readily simulated using any pre-define parent choosers so a hybrid parent chooser `pyParentsChooser()` should be used.

A `pyParentsChooser` accepts a user-defined Python generator function, instead of a normal python function, that returns a parent, or a pair of parents repeatedly. Briefly speaking, when a generator function is called, it returns a *generator* object that provides an iterator interface. Each time when this iterator iterates, this function resumes where it was stopped last time, executes and returns what the next *yield* statement returns. For example, example 2.54 defines a function that calculate  $f(k) = \sum_{i=1}^k \frac{1}{i}$  for  $k = 1, \dots, 5$ . It does not calculate each  $f(k)$  repeatedly but returns  $f(1)$ ,  $f(2)$ , ... sequentially.

Example 2.54: A sample generator function

```

>>> import simuPOP as sim
>>> def func():
...     i = 1
...     all = 0
...     while i <= 5:
...         all += 1./i
...         i += 1
...         yield all
...
>>> for i in func():
...     print '%.3f' % i,

```

A `pyParentsChooser` accepts a parent generator function, which takes a population and a subpopulation index as parameters. When this parent chooser is applied to a subpopulation, it will call this generator function and ask the generated generator object repeated for either a parent, or a pair of parents (*references to individual objects or indexes*

relative to a subpopulation). Note that `pyParentsChooser` does not support virtual subpopulation but you can mimic the effect by returning only parents from certain virtual subpopulations.

Example 2.55 implements a hybrid parent chooser that chooses parents with equal social status (`rank`). In this parent chooser, all males and females are categorized by their sex and social status. A parent is chosen randomly, and then his/her spouse is chosen from females/males with the same social status. The rank of their offspring can increase or decrease randomly. It becomes obvious now that whereas a python function can return random male/female pair, the generator interface is much more efficient because the identification of sex/status groups is done only once.

Example 2.55: A hybrid parent chooser that chooses parents by their social status

```
>>> import simuPOP as sim
>>> from random import randint
>>> def randomChooser(pop, sp):
...     males = []
...     females = []
...     # identify males and females in each social rank
...     for rank in range(3):
...         males.append([x for x in pop.individuals(sp) \
...             if x.sex() == sim.MALE and x.rank == rank])
...         females.append([x for x in pop.individuals(sp) \
...             if x.sex() == sim.FEMALE and x.rank == rank])
...     #
...     while True:
...         # choose a rank randomly
...         rank = int(pop.individual(randint(0, pop.subPopSize(sp) - 1), sp).rank)
...         yield males[rank][randint(0, len(males[rank]) - 1)], \
...             females[rank][randint(0, len(females[rank]) - 1)]
...
>>> def setRank(pop, dad, mom, off):
...     'The rank of offspring can increase or drop to zero randomly'
...     off.rank = (dad.rank + randint(-1, 1)) % 3
...
>>> pop = sim.population(size=[1000, 2000], loci=1, infoFields='rank')
>>> simu = sim.simulator(pop, sim.homoMating(
...     sim.pyParentsChooser(randomChooser),
...     sim.offspringGenerator(ops=sim.mendelianGenoTransmitter())))
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initInfo(lambda : randint(0, 2), infoFields='rank')
...     ],
...     gen = 5
... )
(5,)
```

## 2.7.7 Using C++ to implement a parent chooser \*\*

A user defined parent chooser can be fairly complex and computationally intensive. For example, if a parent tends to find a spouse in his/her vicinity, geometric distances between all qualified individuals and a chosen parent need to be calculated for each mating event. If the optimization of the parent chooser can speed up the simulation significantly, it may be worthwhile to write the parent chooser in C++.

Although it is feasible, and sometimes easier to derive a class from class `parentChooser` in `mating.h` (.cpp), modifying `simuPOP` source code is not recommended because you would have to modify a new version of `simuPOP` whenever you upgrade your `simuPOP` distribution. Implementing your parent choosing algorithm in another Python module is preferred.

The first step is to write your own parent chooser in C/C++. Basically, you will need to pass all necessary information to the C++ level and implement an algorithm to choose parents randomly. Although simple function based solutions are possible, a C++ level class such as the `myParentsChooser` class defined in Example 2.56 is recommended. This class is initialized with indexes of male and female individuals and use a function `chooseParents` to return a pair of parents randomly. This parent chooser is very simple but more complicated parent selection scenarios can be implemented similarly.

Example 2.56: Implement a parent chooser in C++

```
#include <stdlib.h>
#include <vector>
#include <utility>
using std::pair;
using std::vector;
class myParentsChooser
{
public:
    // A constructor takes all locations of male and female.
    myParentsChooser(const std::vector<int> & m, const std::vector<int> & f)
        : male_idx(m), female_idx(f)
    {
        srand(time(0));
    }

    pair<unsigned long, unsigned long> chooseParents()
    {
        unsigned long male = rand() % male_idx.size();
        unsigned long female = rand() % male_idx.size();
        return std::make_pair(male, female);
    }
private:
    vector<int> male_idx;
    vector<int> female_idx;
};
```

The second step is to wrap your C++ functions and classes to a Python module. There are many tools available but SWIG ([www.swig.org](http://www.swig.org)) is arguably the most convenient and powerful one. To use SWIG, you will need to prepare an interface file, which basically tells SWIG which functions and classes you would like to expose and how to pass parameters between Python and C++. Example 2.57 lists an interface file for the C++ class defined in Example 2.56. Please refer to the SWIG reference manual for details.

Example 2.57: An interface file for the `myParentsChooser` class

```
%module myParentsChooser
%{
#include "myParentsChooser.h"
%}
// std_vector.i for std::vector
#include "std_vector.i"
%template() std::vector<int>;
// stl.i for std::pair
#include "stl.i"
%template() std::pair<unsigned long, unsigned long>;
#include "myParentsChooser.h"
```

The exact procedure to generate and compile a wrapper file varies from system to system, and from compiler to compiler. Fortunately, the standard Python module setup process supports SWIG. All you need to do is to write a Python `setup.py` file and let the `distutil` module of Python handle all the details for you. A typical `setup.py` file is demonstrated in Example 2.58.

### Example 2.58: Building and installing the myParentsChooser module

```
from distutils.core import setup, Extension
import sys
# Under linux/gcc, lib stdc++ is needed for C++ based extension.
if sys.platform == 'linux2':
    libs = ['stdc++']
else:
    libs = []
setup(name = "myParentsChooser",
      description = "A sample parent chooser",
      py_modules = ['myParentsChooser'], # will be generated by SWIG
      ext_modules = [
          Extension('_myParentsChooser',
                  sources = ['myParentsChooser.i'],
                  swig_opts = ['-O', '-templatereduce', '-shadow',
                              '-python', '-c++', '-keyword', '-nodefaultctor'],
                  include_dirs = ["."],
                  )
      ]
)
```

You parent chooser can now be compiled and installed using the standard Python `setup.py` commands such as

```
python setup.py install
```

Please refer to the Python reference manual for other building and installation options. Note that Python 2.4 and earlier do not support option `swig_opts` well so you might have to pass these options using command

```
python setup.py build_ext --swig-opts=-O -templatereduce \
    -shadow -c++ -keyword -nodefaultctor install
```

Example 2.56 demonstrates how to use such a C++ parents chooser in your `simuPOP` script. It uses the same Python parent chooser interface as in 2.55, but leaves all the (potentially) computationally intensive parts to the C++ level `myParentsChooser` object.

### Example 2.59: Implement a parent chooser in C++

```
import simuPOP as sim

# The class myParentsChooser is defined in module myParentsChooser
try:
    from myParentsChooser import myParentsChooser
except ImportError:
    # if failed to import the C++ version, use a Python version
    import random
    class myParentsChooser:
        def __init__(self, maleIndexes, femaleIndexes):
            self.maleIndexes = maleIndexes
            self.femaleIndexes = femaleIndexes
        def chooseParents(self):
            return self.maleIndexes[random.randint(0, len(self.maleIndexes)-1)], \
                   self.femaleIndexes[random.randint(0, len(self.femaleIndexes)-1)]

def parentsChooser(pop, sp):
    'How to call a C++ level parents chooser.'
    # create an object with needed information (such as x, y) ...
    pc = myParentsChooser(
        [x for x in range(pop.popSize()) if pop.individual(x).sex() == sim.MALE],
        [x for x in range(pop.popSize()) if pop.individual(x).sex() == sim.FEMALE])
```

```

    while True:
        # return indexes of parents repeatedly
        yield pc.chooseParents()

pop = sim.population(100, loci=1)
simu = sim.simulator(pop,
    sim.homoMating(sim.pyParentsChooser(parentsChooser),
    sim.offspringGenerator(ops=sim.mendelianGenoTransmitter()))
)
simu.evolve(
    initOps = [
        sim.initSex(),
        sim.initByFreq([0.5, 0.5])
    ],
    gen = 100
)

```

## 2.8 Simulator

A `simuPOP` simulator evolves one or more copies of a population forward in time, subject to various operators. Although simulators have been used extensively in the previous chapters, it is worthwhile to have a detailed look at this object.

### 2.8.1 Number of generations to evolve

A simulator usually evolves a specific number of generations according to parameter `gen` of the `evolve` function. A generation number is used to track the number of generations a simulator has evolved. Because a new simulator has generation number 0, a simulator would be at the beginning of generation  $n$  after it evolves  $n$  generations. The generation number would increase if the simulator continues to evolve. During evolving, variables `rep` (replicate number) and `gen` (current generation number) are set to each population's local namespace.

It is not always possible to know in advance the number of generations to evolve. For example, you may want to evolve a population until a specific allele gets fixed or lost in the population. In this case, you can let the simulator run indefinitely (do not set the `gen` parameter) and depend on a *terminator* to terminate the evolution of a population. The easiest method to do this is to use population variables to track the status of a population, and use a `terminateIf` operator to terminate the evolution according to the value of an expression. Example 2.60 demonstrates the use of such a terminator, which terminates the evolution of a population if allele 0 at locus 5 is fixed or lost. It also shows the application of an interesting operator `ifElse`, which applies an operator, in this case `pyEval`, only when an expression returns `True`. Note that this example calls the `evolve` function twice so the second part starts at generation 5. You can also use `simu.setGen(0)` to reset the generation number if you would like to have a fresh start for the second `evolve()` call.

Example 2.60: Generation number of a simulator

```

>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(50, loci=[10], ploidy=1),
...     sim.randomSelection(), rep=3)
>>> simu.evolve(gen = 5)
(5, 5, 5)
>>> simu.gen()
5
>>> simu.evolve(
...     initOps = [sim.initByFreq([0.5, 0.5])],
...     postOps = [
...         sim.stat(alleleFreq=5),

```



```

...     sim.ifElse('alleleNum[5][0] == 0',
...         sim.pyEval(r"Allele 0 is lost in rep %d at gen %d\n" % (rep, gen))),
...     sim.ifElse('alleleNum[5][0] == 50',
...         sim.pyEval(r"Allele 0 is fixed in rep %d at gen %d\n" % (rep, gen))),
...     sim.terminateIf('len(alleleNum[5]) == 1'),
...     ],
... )
Allele 0 is lost in rep 2 at gen 17
Allele 0 is lost in rep 1 at gen 25
Allele 0 is lost in rep 0 at gen 44
(40, 21, 13)
>>> simu.gen()
45

```

## 2.8.2 Population access and other simulator operations

Function `population()` and `populations()` are provided to access populations within a simulator. Similar to functions `individual()` and `individuals()` for a population, `population(rep)` returns a reference to the `repth` population in a simulator and `populations()` returns an Python iterator that can be used to iterate through all populations. Modifying these references will change the corresponding populations within the simulator. An independent copy of a population can be made using the `clone()` function of a population (e.g. `simu.population(0).clone()`).

Populations in a simulator can be added or removed using functions `add()` and `extract()`. The **newly added populations do not have to have the same genotypic structure as existing populations**. However, because the same operators will be applied to all populations, it is your responsibility to make sure that the operators can be applied to these populations.

Just like populations, a simulator can be cloned, saved and loaded. This makes it easy to stop a simulator, take a snapshot and resume evolution. It is even easy to save a simulator, transfer it to another machine and resume the evolution over there. Because **virtual splitters are not saved with populations**, you will have to re-assign splitters to populations if they are needed for subsequent simulations.

Example 2.61: Clone, save and load a simulator

```

>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(100, loci=[5, 10], infoFields='x'),
...     sim.randomMating(), rep=5)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.4, 0.6])
...     ],
...     gen=10
... )
(10, 10, 10, 10, 10)
>>> # clone
>>> cloned = simu.clone()
>>> # save and load, using a different mating scheme
>>> simu.save("sample.sim")
>>> loaded = sim.LoadSimulator("sample.sim", sim.randomMating(numOffspring=2))
>>> #
>>> simu.numRep()
5
>>> loaded.numRep()
5
>>> for pop1, pop2 in zip(cloned.populations(), loaded.populations()):
...     assert pop1 == pop2

```

```

...
>>> # continue to evolve
>>> simu.evolve(gen=10)
(10, 10, 10, 10, 10)
>>> simu.gen()
20

```

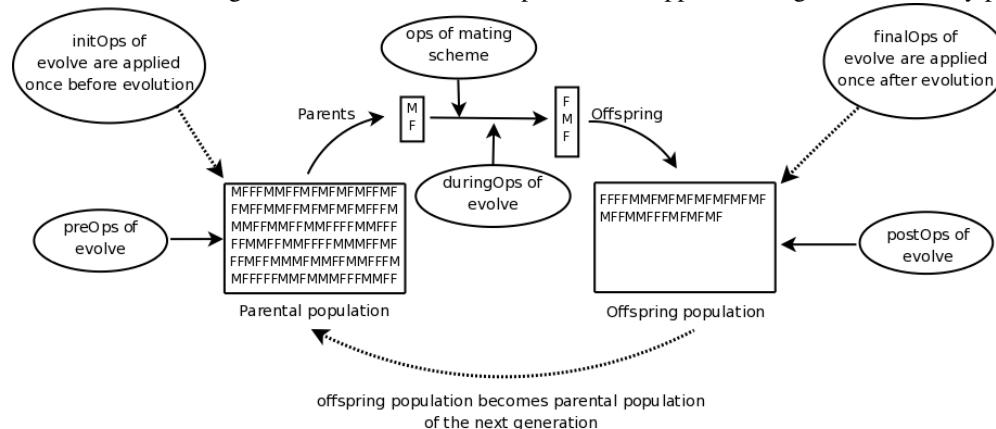
### 2.8.3 Evolve populations in a simulator

There are a number of rules about when and how operators are applied during the evolution of a population. In summary, in the order at which operators are processed and applied,

- Operators specified in parameter `initOps` of function `simulator.evolve` will be applied to the initial population before evolution, subject to replicate applicability restraint specified by parameter `reps`.
- Operators specified in parameter `preOps` of function `simulator.evolve` will be applied to the parental population at each generation, subject to replicate and generation applicability restraint specified by parameters `begin`, `end`, `step`, `at`, and `reps`.
- During-mating operators specified in the `ops` parameter of a mating scheme will be called during mating to transmit genotype (and possibly information fields etc) from parental to offspring, subject to replicate and generation applicability restraint specified by parameters `begin`, `end`, `step`, `at`, and `reps`.
- During-mating operators specified in the `duringOps` of function `simulator.evolve` parameter of `simulator.evolve` will be applied after an offspring is produced, subject to replicate and generation applicability restraint specified by parameters `begin`, `end`, `step`, `at`, and `reps`.
- Operators specified in parameter `postOps` of function `simulator.evolve` will be applied to the offspring population at each generation, subject to replicate and generation applicability restraint specified by parameters `begin`, `end`, `step`, `at`, and `reps`.
- Operators specified in parameter `finalOps` of function `simulator.evolve` will be applied to the final population after evolution, subject to replicate applicability restraint specified by parameter `reps`.

Figure 2.5 illustrated how operators are applied to an evolutionary process. It worth noting that a default during-mating operator is defined for each mating scheme. User-specified operators will **replace** the default operator so you need to explicitly specify the default operator if you intent to add another one.

Figure 2.5: Orders at which operators are applied during an evolutionary process



If you suspect that your simulation is not running as expected, you can have a close look at your evolutionary process using function `simulator.describe()`. This function takes the same set of parameters as `simulator.evolve()` and returns a description of the evolution process, which can help you identify misuse of operators that cause, for example, duplicated (if you use a recombinator in parameter `duringOps` of `simulator.evolve()`), or missing (if you replace `medelianGenoTransmitter` of `randomMating` using `ops=idTagger()`) genotype transmission to offspring.

Example 2.62: Describe an evolutionary process

```
>>> import simuPOP as sim
>>> pop = sim.population(10000, loci=100, infoFields=['ind_id', 'age'])
>>> pop.setVirtualSplitter(sim.infoSplitter(field='age', cutoff=[20, 50, 75]))
>>>
>>> def outputStat(pop):
...     'Calculate and output statistics, ignored'
...     return True
...
>>> simu = sim.simulator(pop,
...     sim.heteroMating([
...         sim.cloneMating(subPops=[(0,0), (0,1), (0,2)], weight=-1),
...         sim.randomMating(ops=[
...             sim.idTagger(),
...             sim.recombinator(intensity=1e-4)
...         ], subPops=[(0,1)]),
...     ])
... )
>>> # describe this evolutionary process
>>> print simu.describe(
...     initOps = [
...         sim.initSex(),
...         sim.initInfo(lambda: random.randint(0, 75), infoFields='age'),
...         sim.initByFreq([0.5, 0.5]),
...         sim.idTagger(),
...         sim.pyOutput('Prevalence of disease in each age group:\n'),
...     ],
...     preOps = sim.infoExec('age += 1'),
...     duringOps = sim.pedigreeTagger(),
...     postOps = [
...         sim.maPenetrance(loci=0, penetrance=[0.01, 0.1, 0.3]),
...         sim.pyOperator(func=outputStat)
...     ],
...     gen = 100
... )
```

Replicate 0:

Apply pre-evolution operators to the initial population (`initOps`).

- \* `<simuPOP.initSex>` initialize sex randomly
- \* `<simuPOP.initInfo>` initialize information field `age` using a Python function `<lambda>`
- \* `<simuPOP.initByFreq>` initialize individual genotype using a list of allele frequencies
- \* `<simuPOP.idTagger>` assign an unique ID to individuals
- \* `<simuPOP.pyOutput>` write `'Prevalence of disease in each age group:...' ' to output`

Evolve a population **for** 100 generations. (generations 0 - 99, stops at generation 100)

- \* Apply pre-mating operators to the parental generation (`preOps`)
  - # `<simuPOP.infoExec>` execute statement `age += 1` using information fields as variables.

```

* Populate an offspring population from the parental population using mating
  scheme <simuPOP.heteroMating> a heterogeneous mating scheme with 2
  homogeneous mating schemes:
  # <simuPOP.homoMating> a homogeneous mating scheme that uses
    - <simuPOP.sequentialParentChooser> chooses a parent sequentially
    - <simuPOP.offspringGenerator> produces offspring using operators
      . <simuPOP.cloneGenoTransmitter> clone genotype, sex and
        information fields of parent to offspring
    in subpopulations (0, 0), (0, 1), (0, 2).
  # <simuPOP.homoMating> a homogeneous mating scheme that uses
    - <simuPOP.randomParentsChooser> chooses two parents randomly
    - <simuPOP.offspringGenerator> produces offspring using operators
      . <simuPOP.idTagger> assign an unique ID to individuals
      . <simuPOP.recombinator> genetic recombination.
    in subpopulations (0, 1).

  With additional during mating operators
    - <simuPOP.pedigreeTagger> record parental IDs (father_id and
      mother_id) to field ind_id of each offspring.

* Apply post-mating operators to the offspring population (postOps).
  # <simuPOP.maPenetrance> multiple-alleles penetrance
  # <simuPOP.pyOperator> calling a Python function outputStat

```

No operator **is** applied to the final population (finalOps).

## 2.8.4 Modifying populations and mating scheme \*

Although a standard Wright-Fisher random mating scheme is usually preferred because it leads to a larger effective population size than other mating schemes, it is difficult to ascertain pedigrees from a random mating population because there will be very few siblings in such a population. In addition, because we usually only sample from the last few generations, it would be more efficient to keep track of pedigree information only for these generations. Such considerations lead to the popularity of a two stage evolutionary scenario where the standard random mating scheme is used in the first stage and another mating scheme that is more suitable for pedigree ascertainment is used in the second stage. Example 2.63 demonstrates the implementation of such a scenario.

Example 2.63: A two-stage evolutionary process

```

>>> import simuPOP as sim
>>> # First stage: use the standard random mating scheme, do not use any
>>> # information field for efficiency considerations.
>>> simu = sim.simulator(sim.population(500, loci=[10]), sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5])
...     ],
...     gen = 50
... )
(50,)
>>> # Second stage: track parents and produce more offspring per mating
>>> # event. In preparation for sim.pedigree ascertainment.
>>> for pop in simu.populations():
...     pop.addInfoFields(['ind_id', 'father_id', 'mother_id'])
...     pop.setAncestralDepth(1)
...

```

```

>>> simu.setMatingScheme(sim.randomMating(numOffspring=2))
>>> simu.evolve(
...     initOps = sim.idTagger(),
...     duringOps = [
...         sim.idTagger(),
...         sim.pedigreeTagger(),
...     ],
...     postOps = sim.maPenetrance(loci=0, penetrance=(0.2, 0.4, 0.5)),
...     gen = 5
... )
(5,)
>>> # Sample affected sibpairs
>>> pop = simu.extract(0)
>>> from simuPOP.sampling import DrawAffectedSibpairSample
>>> sample = DrawAffectedSibpairSample(pop, families=5)
>>> [int(ind.father_id) for ind in sample.individuals()]
[2252, 2252, 2385, 2385, 2178, 2178, 2232, 2232, 2309, 2309]

```

## 2.8.5 Change genotypic structure during evolution \*\*

Most operators do not change the genotypic structure of populations during evolution. However, it is possible to change the structure of a population, such as adding or removing information fields, loci or chromosomes during evolution. The only restriction is that all individual in a population needs to have the same genotypic structure. That is to say, if you are inserting a new locus to an individual, all individuals in this population should have it. This is why there is no individual-level structure-modification functions.

Example 2.64 gives an example of a dynamic mutator. This mutator is not a conventional mutator in that it does not mutate any existing loci. It assumes a chromosome region that originally has no polymorphic markers. When a mutation happens, a monomorphic marker that is not simulated becomes polymorphic and is inserted to the chromosome. If the region is long enough, this example effectively simulates an infinite allele mode.

Example 2.64: A Python mutator that adds new loci to populations.

```

>>> import simuPOP as sim
>>> import random
>>> def mutator(pop, param):
...     'Parameter has a length of region and a mutation rate at each basepair'
...     region, rate = param
...     # there are certainly more efficient algorithm, but this
...     # example just mutate each basepair one by one....
...     for i in range(region):
...         if random.random() < rate:
...             try:
...                 idx = pop.addLoci(chrom=0, pos=i)[0]
...             except:
...                 # position might duplicate
...                 continue
...             # choose someone to mutate
...             ind = pop.individual(random.randint(0, pop.popSize() - 1))
...             ind.setAllele(1, idx)
...     return True
>>> # The sim.populations start with no loci at all.
>>> simu = sim.simulator(sim.population(1000, loci=[]), sim.randomMating(), rep=3)
>>> simu.evolve(
...     initOps = sim.initSex(),
...     postOps = sim.pyOperator(func=mutator, param=(10000, 2e-6)),
...     gen = 200
... )

```

```

... )
(200, 200, 200)
>>> for pop in simu.populations():
...     print pop.totNumLoci(), pop.lociPos()
...
4 (1894.0, 3737.0, 8613.0, 8860.0)
4 (635.0, 7327.0, 8353.0, 9866.0)
4 (2404.0, 6443.0, 8285.0, 9576.0)

```

## 2.9 Pedigrees

A pedigree object is basically a static population object that is used to track relationship between individuals. It is currently used in the `simuPOP.sampling` module to identify eligible pedigrees but future development will allow a mating scheme to follow a complete pedigree constructed manually or saved from a previous evolutionary process. This will allow, for example, to repeat the same evolutionary process for different chromosomes when a large number of loci are simulated.

A pedigree is created from a population object with an ID field (default to `ind_id`), and two parental ID fields (default to `father_id` and `mother_id`). Genotype information and additional information fields can be copied to a pedigree object if needed. The ID field should have a unique ID for each individual and the parental ID fields should record the ID of his or her parents.

A pedigree object provides several functions for you to identify spouse, sibling and more distant relatives of each individual. The results are stored to additional information fields of each individual. For example, if you would like to know the offspring of all individuals, you can call function `pedigree.locateRelatives` as follows:

```

offFields = ['off1', 'off2', 'off3']
ped.addInfoFields(offFields)
ped.locateRelatives(OFFSPRING, resultFields=offFields)

```

This function will locate up to 3 (determined by the length of `resultFields`) offspring of each individual and put their IDs in specified informaton fields. This function allows you to identify spouses (it is common to have multiple spouses when random mating is used), outbred spouse (exclude spouses who share at least one of the parents), offspring (all offspring) and common offspring with a specified spouse, siblings (share at least one parent) and full siblings (share two parents). It also allows you to limit the result by sex and affection status (e.g. find only affected female offspring).

More distant relationship can be derived from these relationship using function `pedigree.traceRelatives`. This function accepts a path of information fields and follows the path to identify relatives. For example

```

sibFields = ['sib1', 'sib2']
offFields = ['off1', 'off2', 'off3']
cousinFields = ['cousin1', 'cousin2', 'cousin3']
ped.addInfoFields(sibFields + offFields + cousinFields)
ped.locateRelatives(FULLSIBLING, resultFields=sibFields)
ped.locateRelatives(OFFSPRING, resultFields=offFields)
ped.traceRelatives(['father_id', 'mother_id'], sibFields, offFields,
    sex=[ANY_SEX, MALE_ONLY, FEMALE_ONLY],
    resultField=cousinFields)

```

would first identify full siblings and offspring of all individuals and then locate father or mother's male sibling's daughters. As you can imagine, this function can be used to track very complicated relationships.

This function also provides a function for you to identify individuals with specified relatives. Example 2.65 gives an example how to locate a grandfather with at least five grandchildren. With such information, functions such as `population.extractIndividuals()` could be used to extract pedigrees from a population. This is basically how `simuPOP.sampling` module works.

### Example 2.65: Locate close and distant relatives of individuals

```
>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(1000, ancGen=2, infoFields=['ind_id', 'father_id', 'mother_id']),
...     sim.randomMating(numOffspring=(sim.UNIFORM_DISTRIBUTION, 2, 4)))
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.idTagger(),
...     ],
...     duringOps = [
...         sim.idTagger(),
...         sim.pedigreeTagger()
...     ],
...     gen = 5
... )
(5,)
>>> ped = sim.pedigree(simu.extract(0))
>>> offFields = ['off%d' % x for x in range(4)]
>>> grandOffFields = ['grandOff%d' % x for x in range(5)]
>>> ped.addInfoFields(['spouse'] + offFields + grandOffFields)
>>> # only look spouse for fathers...
>>> ped.locateRelatives(sim.OUTBRED_SPOUSE, ['spouse'], sex=sim.FEMALE_ONLY)
>>> ped.locateRelatives(sim.COMMON_OFFSPRING, ['spouse'] + offFields)
>>> # trace offspring of offspring
>>> ped.traceRelatives([offFields, offFields], resultFields=grandOffFields)
True
>>> #
>>> IDs = ped.individualsWithRelatives(grandOffFields)
>>> # check on ID.
>>> grandFather = IDs[0]
>>> grandMother = ped.indByID(grandFather).spouse
>>> # some ID might be invalid.
>>> children = [ped.indByID(grandFather).info(x) for x in offFields]
>>> childrenSpouse = [ped.indByID(x).spouse for x in children if x >= 1]
>>> childrenParents = [ped.indByID(x).father_id for x in children if x >= 1] \
...     + [ped.indByID(x).mother_id for x in children if x >= 1]
>>> grandChildren = [ped.indByID(grandFather).info(x) for x in grandOffFields]
>>> grandChildrenParents = [ped.indByID(x).father_id for x in grandChildren if x >= 1] \
...     + [ped.indByID(x).mother_id for x in grandChildren if x >= 1]
>>>
>>> def idString(IDs):
...     uniqueIDs = list(set(IDs))
...     uniqueIDs.sort()
...     return ', '.join(['%d' % x for x in uniqueIDs if x >= 1])
...
>>> print '''GrandParents: %d, %d
... Children: %s
... Children's spouses: %s
... Children's parents: %s
... GrandChildren: %s
... GrandChildren's parents: %s ''' % \
...     (grandFather, grandMother, idString(children), idString(childrenSpouse),
...     idString(childrenParents), idString(grandChildren), idString(grandChildrenParents))
GrandParents: 6060, 6867
Children: 7098, 7099, 7100
Children's spouses: 7466, 7817
Children's parents: 6060, 6867
GrandChildren: 8208, 8209, 8899, 8900, 8901
```

```
GrandChildren's parents: 7098, 7099, 7466, 7817  
>>>
```



## Chapter 3

# simuPOP Operators

simuPOP is large, consisting of more than 80 operators and various functions that covers all important aspects of genetic studies. These includes mutation ( $k$ -allele, stepwise, generalized stepwise), migration (arbitrary, can create new subpopulation), recombination (uniform or nonuniform), gene conversion, quantitative trait, selection, penetrance (single or multi-locus, hybrid), ascertainment (case-control, affected sibpairs, random), statistics calculation (allele, genotype, haplotype, heterozygote number and frequency; expected heterozygosity; bi-allelic and multi-allelic  $D$ ,  $D'$  and  $r^2$  linkage disequilibrium measures;  $F_{st}$ ,  $F_{it}$  and  $F_{is}$ ); pedigree tracing, visualization (using R or other Python modules). This chapter covers the basic and some not-so-basic usages of these operators, organized roughly by genetic factors.

### 3.1 Initialization

simuPOP provides three operators to initialize individual sex and genotype. A number of parameter are provided to cover most commonly used initialization scenarios. A Python operator can be used to initialize a population explicitly if none of the operators fits your need.

#### 3.1.1 Initialize individual sex (operator `initSex`)

Operator `initSex()` and function `InitSex()` initialize individual sex either randomly or using a given sequence. In the first case, individuals are assigned `Male` or `Female` with equal probability unless parameter *maleFreq* is used to specify the probability of having a male individual. Alternatively, parameter *maleProp* can be used to specify exact proportions of male individuals. In the second case, a sequence of sex (`Male` or `Female`) is assigned to individuals succesively. The list will be reused if needed. If a list of (virtual) subpopulations are given, this operator will only initialize individuals in these (virtual) subpopulations. Example 3.1 uses two `initSex` operators to initialize two subpopulations.

Example 3.1: Initialize individual sex

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[1000, 1000])
>>> sim.InitSex(pop, maleFreq=0.3, subPops=0)
>>> sim.InitSex(pop, sex=[sim.MALE, sim.FEMALE, sim.FEMALE], subPops=1)
>>> sim.Stat(pop, numOfMales=True, vars='numOfMales_sp')
>>> print pop.dvars(0).numOfMales
290
>>> print pop.dvars(1).numOfMales
334
```

### 3.1.2 Initialize by allele frequency (operator `initByFreq`)

Operator `initByFreq` (and its function form `InitByFreq`) initialize individual genotype by **allelic spectrum**, which is the number and frequency of alleles at a locus. For example, `alleleFreq=(0, 0.2, 0.4, 0.2)` will yield allele 0, 1, 2, and 3 with probability 0, 0.2, 0.4 and 0.2 respectively. Parameter `loci` and `ploidy` can be used to specify a subset of loci and homologous sets of chromosomes to initialize, and parameter `subPops` can be used to specify subsets of individuals to initialize. In the latter case, a list of allelic spectra can be given to assign different genotype with different allele frequency for each (virtual) subpopulation.

Example 3.2: Initialize by allele frequency

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[2, 3], loci=[5, 7])
>>> sim.InitByFreq(pop, alleleFreq=[[.2, .8], [.8, .2]])
>>> sim.Dump(pop, structure=False)
Subpopulation 0 (), 2 individuals:
  0: MU 11011 1111111 | 10011 1111010
  1: MU 00111 1111111 | 11111 1101111
Subpopulation 1 (), 3 individuals:
  2: MU 00010 0000001 | 00001 0010000
  3: MU 10000 1000000 | 01000 0100101
  4: MU 00100 0100000 | 10000 0000000
```

It is sometimes desired to create identical individuals with random genotype. Parameter `identicalInds` can be used for this purpose. When this parameter is set to true, a random individual will be created for each subpopulation (using different allele frequencies if a list of allelic spectra are given), and be copied to all other individuals in the subpopulation. Example 3.3 demonstrates this usage.

Example 3.3: Initialize by allele frequency with identical individuals in each subpopulation

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[2, 3], loci=[5, 7])
>>> sim.InitByFreq(pop, alleleFreq=[.2, .8], identicalInds=True)
>>> sim.Dump(pop, structure=False)
Subpopulation 0 (), 2 individuals:
  0: MU 11011 1111111 | 10011 1111010
  1: MU 11011 1111111 | 10011 1111010
Subpopulation 1 (), 3 individuals:
  2: MU 00111 1111111 | 11111 1101111
  3: MU 00111 1111111 | 11111 1101111
  4: MU 00111 1111111 | 11111 1101111
```

### 3.1.3 Initialize by haplotype (operator `initByValue`)

Operator `initByValue` (and its function form `InitByValue`) initializes individual genotypes using given haplotypes. The simplest form of this operator is to specify genotype on one or all homologous sets of chromosomes. For example, all individuals in Example 3.4 get the same genotype using such an operator.

Example 3.4: initialize by haplotype

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[2, 3], loci=[5, 7])
>>> sim.InitByValue(pop, [1]*5 + [2]*7 + [3]*5 + [4]*7)
>>> sim.Dump(pop, structure=False)
Subpopulation 0 (), 2 individuals:
  0: MU 11111 2222222 | 33333 4444444
  1: MU 11111 2222222 | 33333 4444444
Subpopulation 1 (), 3 individuals:
```

```

2: MU 11111 2222222 | 33333 4444444
3: MU 11111 2222222 | 33333 4444444
4: MU 11111 2222222 | 33333 4444444

```

A number of parameters are provided to initialize individual genotype at a finer scale. More specifically, you can apply the operator to specified loci (parameter *loci*), (virtual) subpopulations (parameter *subPops*), homologous sets of chromosomes (parameter *ploidy*). If multiple haplotypes are given, you can specify the proportions at which each haplotype will be used using parameter *proportions*, or by frequencies using parameter *frequencies*. Example 3.5 demonstrates the use of these parameters.

Example 3.5: initialize by haplotypes with given proportion

```

>>> import simuPOP as sim
>>> pop = sim.population(size=[6, 8], loci=[5, 7])
>>> pop.setVirtualSplitter(sim.sexSplitter())
>>> # initialize sex and the first two loci
>>> sim.InitSex(pop)
>>> sim.InitByValue(pop, loci=range(5), value=range(10))
>>> # initialize all males
>>> sim.InitByValue(pop, loci=range(5, 12), value=[2]*7,
...               subPops=[(0, 0), (1, 0)])
>>> # initialize females by proportion
>>> sim.InitByValue(pop, loci=range(5, 12), ploidy=1, value=[[3]*7, [4]*7],
...               subPops=[(0, 1), (1, 1)], proportions=[0.4, 0.6])
>>> sim.Dump(pop, structure=False)
Subpopulation 0 (), 6 individuals:
  0: FU 01234 0000000 | 56789 3333333
  1: FU 01234 0000000 | 56789 4444444
  2: MU 01234 2222222 | 56789 2222222
  3: MU 01234 2222222 | 56789 2222222
  4: MU 01234 2222222 | 56789 2222222
  5: MU 01234 2222222 | 56789 2222222
Subpopulation 1 (), 8 individuals:
  6: MU 01234 2222222 | 56789 2222222
  7: FU 01234 0000000 | 56789 4444444
  8: FU 01234 0000000 | 56789 4444444
  9: FU 01234 0000000 | 56789 4444444
 10: FU 01234 0000000 | 56789 4444444
 11: FU 01234 0000000 | 56789 3333333
 12: FU 01234 0000000 | 56789 3333333
 13: MU 01234 2222222 | 56789 2222222

```

### 3.1.4 Initialize information fields (operator `initInfo`)

Operator `initInfo` and its function form `InitInfo` initialize one or more information fields of all individuals or individuals in selected (virtual) subpopulations using either a list of values or a Python function. If a value or a list of value is given, it will be used repeatedly to assign values of specified information fields of all applicable individuals. For example, `InitInfo(pop, values=1, infoFields='x')` will assign value 1 to information field `x` of all individuals, and

```
InitInfo(pop, values=[1, 2, 3], infoFields='x', subPops=[(0,1)])
```

will assign values 1, 2, 3, 1, 2, 3... to information field `x` of individuals in the second virtual subpopulation of subpopulation 0.

The `values` parameter also accepts a Python function. This feature is usually used to assign random values to an information field. For example, `values=random.random` would assign a random value between 0 and 1. If a function takes parameters, a lambda function can be used. For example,

```
InitInfo(pop, lambda : random.randint(2, 5), infoFields=['x', 'y'])
```

assigns random integers between 2 and 5 to information fields *x* and *y* of all individuals in *pop*. Example 3.6 demonstrates these usages.

Example 3.6: initialize information fields

```
>>> import simuPOP as sim
>>> import random
>>> pop = sim.population(size=[5], loci=[2], infoFields=['sex', 'age'])
>>> pop.setVirtualSplitter(sim.sexSplitter())
>>> sim.InitSex(pop)
>>> sim.InitInfo(pop, 0, subPops=[(0,0)], infoFields='sex')
>>> sim.InitInfo(pop, 1, subPops=[(0,1)], infoFields='sex')
>>> sim.InitInfo(pop, lambda: random.randint(20, 70), infoFields='age')
>>> sim.Dump(pop, structure=False)
Subpopulation 0 (), 5 individuals:
0: FU 00 | 00 | 1 38
1: FU 00 | 00 | 1 42
2: MU 00 | 00 | 0 63
3: MU 00 | 00 | 0 48
4: MU 00 | 00 | 0 65
```

## 3.2 Expressions and statements

### 3.2.1 Output a Python string (operator `pyOutput`)

Operator `pyOutput` is a simple operator that prints a Python string when it is applied to a population. It is commonly used to print the progress of a simulation (e.g. `pyOutput('start migration\n', at=200)`) or output separators to beautify outputs from `pyEval` outputs (e.g. `pyOutput('\n', rep=-1)`).

### 3.2.2 Execute Python statements (operator `pyExec`)

Operator `pyExec` executes Python statements in a population's local namespace when it is applied to that population. This operator is designed to execute short Python statements but multiple statements separated by newline characters are allowed.

Example 3.7 uses two `pyExec` operators to create and use a variable `traj` in each population's local namespace. The first operator initialize this variable as an empty list. During evolution, the frequency of allele 1 at locus 0 is calculated (operator `stat`) and appended to this variable (operator `pyExec`). The result is a trajectory of allele frequencies during evolution.

Example 3.7: Execute Python statements during evolution

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(100, loci=1),
...     sim.randomMating(), rep=2)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.2, 0.8]),
...         sim.pyExec('traj=[]')
...     ],
...     postOps = [
...         sim.stat(alleleFreq=0),
...         sim.pyExec('traj.append(alleleFreq[0][1])'),
...     ]
... )
```

```

...     ],
...     gen=5
... )
(5, 5)
>>> # print trajectory
>>> print ', '.join(['%.3f' % x for x in simu.dvars(0).traj])
0.775, 0.790, 0.760, 0.750, 0.750

```

### 3.2.3 Evaluate and output Python expressions (operator `pyEval`)

Operator `pyEval` evaluate a given Python expression in a population's local namespace and output its return value. This operator has been widely used (e.g. Example 1.1, 2.17, 2.23 and 2.25) to output statistics of populations and report progress.

Two additional features of this operator may become handy from time to time. First, an optional Python statements (parameter *stmts*) can be specified which will be executed before the expression is evaluated. Second, the population being applied can be exposed in its own namespace as a variable (parameter *exposePop*). This makes it possible to access properties of a population other than its variables. Example 3.8 demonstrates both features. In this example, two statements are executed to count the number of unique parents in an offspring population and save them as variables `numFather` and `numMother`. The operator outputs these two variables along with a generation number.

Example 3.8: Evaluate a expression and statements in a population's local namespace.

```

>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(1000, loci=1,
...     infoFields=['mother_idx', 'father_idx']),
...     sim.randomMating())
>>> simu.evolve(
...     initOps = sim.initSex(),
...     duringOps = sim.parentsTagger(),
...     postOps = [
...         sim.stat(alleleFreq=0),
...         sim.pyEval(r'"gen %d, #father %d, #mother %d\n" \
...             ' % (gen, numFather, numMother)',
...         stmts="numFather = len(set(pop.indInfo('father_idx')))\n"
...             "numMother = len(set(pop.indInfo('mother_idx')))",
...         exposePop='pop')
...     ],
...     gen=3
... )
gen 0, #father 439, #mother 433
gen 1, #father 433, #mother 432
gen 2, #father 449, #mother 420
(3,)

```

Note that the function form of this operator (`PyEval`) returns the result of the expression rather than writing it to an output.

### 3.2.4 Expression and statement involving individual information fields (operator `infoEval` and `infoExec`) \*

Operators `pyEval` and `pyExec` work at the population level, using the local namespace of populations. Operator `infoEval` and `infoExec`, on the contrarary, work at the individual level, using individual information fields.

Because there is no individual-specific namespace, these two operators make use of either a temporary namespace for every individual, or the population namespace (parameter *usePopVars*). In the first case, a namespace is created

for each individual, with variables being the information fields of this individual. In the second case, individual information fields are copied to the population namespace one by one. Expressions and statements can make use of population variables in this case. Optionally, the individual object can be exposed to these namespace using a user-specified name (parameter *exposeInd*).

Operator `infoEval` evaluates an expression and outputs its value. Operator `infoExec` executes one or more statements and does not produce any output. The major difference between them is that `infoEval` does not change individual information fields while `infoExec` update individual information fields from the namespace after the statements are executed.

Operator `infoEval` is usually used to output individual information fields and properties in batch mode. It is faster and sometimes easier to use than corresponding for loop plus individual level operations. For example

- `infoEval(r'%.2f\t' % a')` outputs the value of information field *a* for all individuals, separated by tabs.
- `infoEval('ind.sexChar()', exposeInd='ind')` outputs the sex of all individuals using an exposed individual object *ind*.
- `infoEval('a+b*2')` outputs  $a + b^2$  for information fields *a* and *b* for all individuals.

Example 3.9 demonstrates the use of this operator.

Example 3.9: Evaluate expressions using individual information fields

```
>>> import simuPOP as sim
>>> import random
>>> pop = sim.population(20, loci=1, infoFields='a')
>>> pop.setVirtualSplitter(sim.infoSplitter('a', cutoff=[3]))
>>> sim.InitByFreq(pop, [0.2, 0.8])
>>> pop.setIndInfo([random.randint(2, 5) for x in range(20)], 'a')
>>> sim.InfoEval(pop, 'a', subPops=[(0, 0)]);print
2.02.0
>>> sim.InfoEval(pop, 'ind.allele(0, 0)', exposeInd='ind');print
11011111111100111111
>>> # use sim.population variables
>>> pop.dvars().b = 5
>>> sim.InfoEval(pop, '%d ' % (a+b)', usePopVars=True);print
8 10 8 9 10 8 10 8 9 7 10 10 8 10 8 9 8 7 8 9
```

Operator `infoExec` is usually used to set individual information fields. For example

- `infoExec('age += 1')` increases the age of all individuals by one.
- `infoExec('risk = 2 if packPerYear > 10 else 1.5')` sets information field *risk* to 2 if *packPerYear* is greater than 10, and 1.5 otherwise. Note that conditional expression is only available for Python version 2.5 or later.
- `infoExec('a = b*c')` sets the value of information field *a* to the product of *b* and *c*.

Example 3.10 demonstrates the use of this operator, using its function form `InfoExec`.

Example 3.10: Execute statements using individual information fields

```
>>> import simuPOP as sim
>>> pop = sim.population(100, loci=1, infoFields=['a', 'b', 'c'])
>>> sim.InitByFreq(pop, [0.2, 0.8])
>>> sim.InfoExec(pop, 'a=1')
>>> print pop.indInfo('a')[:10]
(1.0, 1.0, 1.0, 1.0, 1.0, 1.0, 1.0, 1.0, 1.0, 1.0)
```

```

>>> sim.InfoExec(pop, 'b=ind.sex()', exposeInd='ind')
>>> print pop.indInfo('b')[:10]
(1.0, 1.0, 1.0, 1.0, 1.0, 1.0, 1.0, 1.0, 1.0, 1.0)
>>> sim.InfoExec(pop, 'c=a+b')
>>> print pop.indInfo('c')[:10]
(2.0, 2.0, 2.0, 2.0, 2.0, 2.0, 2.0, 2.0, 2.0, 2.0)
>>> pop.dvars().d = 5
>>> sim.InfoExec(pop, 'c+=d', usePopVars=True)
>>> print pop.indInfo('c')[:10]
(7.0, 7.0, 7.0, 7.0, 7.0, 7.0, 7.0, 7.0, 7.0, 7.0)

```

**Note:** Except for the local (temporary) namespace, operator `infoEval` and `infoExec` can also access variables and functions in a global namespace, which is the module namespace of your script. However, use of global variables in these operators are strongly discouraged.

### 3.3 Demographic changes

A mating scheme controls the size of an offspring generation using parameter `subPopSize`. This parameter has been described in detail in section 2.6.1. In summary,

- The subpopulation sizes of the offspring generation will be the same as the parental generation if `subPopSize` is not set.
- The offspring generation will have a fixed size if `subPopSize` is set to a number (no subpopulation) or a list of subpopulation sizes.
- The subpopulation sizes of an offspring generation will be determined by the return value of a demographic function if `subPopSize` is set to such a function (a function that returns subpopulation sizes at each generation).

**Note:** Parameter `subPopSize` only controls subpopulation sizes of an offspring generation immediately after it is generated. Population or subpopulation sizes could be changed by other operators. During mating, a mating scheme goes through each parental subpopulation and populates its corresponding offspring subpopulation. This implies that

- Parental and offspring populations should have the same number of subpopulations.
- Mating happens strictly within each subpopulation.

This section will introduce several operators that allow you to move individuals across the boundary of subpopulations (migration), and change the number of subpopulations during evolution (split and merge).

#### 3.3.1 Migration (operator `migrator`)

##### Migration by probability

Operator `migrator` (and its function form `Migrate`) migrates individuals from one subpopulation to another. The key parameters are

- *from* subpopulations (parameter `subPops`). A list of subpopulations from which individuals migrate. Default to all subpopulations.
- *to* subpopulations (parameter `toSubPops`). A list of subpopulations to which individuals migrate. Default to all subpopulations. **A new subpopulation ID can be specified to create a new subpopulation from migrants.**

- A migration rate matrix (parameter `rate`). A  $m$  by  $n$  matrix ( a nested list in Python) that specifies migration rate from each source to each destination subpopulation.  $m$  and  $n$  are determined by the number of *from* and *to* subpopulations.

Example 3.11 demonstrate the use of a `migrator` to migrate individuals between three subpopulations. Note that

- Operator `migrator` relies on an information field `migrate_to` (configurable) to record destination subpopulation of each individual so this information field needs to be added to a population before migration.
- Migration rates to subpopulation themselves are determined automatically so they can be left unspecified.

Example 3.11: Migration by probability

```
>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(size=[1000]*3, infoFields='migrate_to'),
...     sim.randomMating())
>>> simu.evolve(
...     initOps = sim.initSex(),
...     preOps = sim.migrator(rate=[
...         [0, 0.1, 0.1],
...         [0, 0, 0.1],
...         [0, 0.1, 0]
...     ]),
...     postOps = [
...         sim.stat(popSize=True),
...         sim.pyEval('subPopSize'),
...         sim.pyOutput('\n')
...     ],
...     gen = 5
... )
[762, 1108, 1130]
[601, 1175, 1224]
[490, 1233, 1277]
[395, 1282, 1323]
[320, 1300, 1380]
(5,)
```

## Migration by proportion and counts

Migration rate specified in the `rate` parameter in Example 3.11 is interpreted as probabilities. That is to say, a migration rate  $r_{m,n}$  is interpreted as the probability at which any individual in subpopulation  $m$  migrates to subpopulation  $n$ . The exact number of migrants are randomly distributed.

If you would like to specify exactly how many migrants migrate from a subpopulation to another, you can specify parameter `mode` of operator `migrator` to `BY_PROPORTION` or `BY_COUNTS`. The `BY_PROPORTION` mode interpret  $r_{m,n}$  as proportion of individuals who will migrate from subpopulation  $m$  to  $n$  so the number of  $m \rightarrow n$  migrant will be exactly  $r_{m,n} \times \text{subPopSize}(m)$ . In the `BY_COUNTS` mode,  $r_{m,n}$  is interpreted as number of migrants, regardless the size of subpopulation  $m$ . Example 3.12 demonstrates these two migration modes, as well as the use of parameters `subPops` and `toSubPops`.

Example 3.12: Migration by proportion and count

```
>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(size=[1000]*3, infoFields='migrate_to'),
...     sim.randomMating())
```



```

>>> simu.evolve(
...     initOps = sim.initSex(),
...     preOps = sim.migrator(rate=[[0.1], [0.2]],
...                             mode=sim.BY_PROPORTION,
...                             subPops=[1, 2],
...                             toSubPops=[3]),
...     postOps = [
...         sim.stat(popSize=True),
...         sim.pyEval('subPopSize'),
...         sim.pyOutput('\n')
...     ],
...     gen = 5
... )
[1000, 900, 800, 300]
[1000, 810, 640, 550]
[1000, 729, 512, 759]
[1000, 657, 410, 933]
[1000, 592, 328, 1080]
(5,)
>>> #
>>> simu.evolve(
...     preOps = sim.migrator(rate=[[50, 50], [100, 50]],
...                             mode=sim.BY_COUNTS,
...                             subPops=[3, 2],
...                             toSubPops=[2, 1]),
...     postOps = [
...         sim.stat(popSize=True),
...         sim.pyEval('subPopSize'),
...         sim.pyOutput('\n')
...     ],
...     gen = 5
... )
[1000, 692, 328, 980]
[1000, 792, 328, 880]
[1000, 892, 328, 780]
[1000, 992, 328, 680]
[1000, 1092, 328, 580]
(5,)

```

### Theoretical migration models

To facilitate the use of widely used theoretical migration models, a few functions are defined in module `simuUtil`.

- `MigrIslandRates(r, n)` returns a  $n \times n$  migration matrix

$$\begin{pmatrix} 1-r & \frac{r}{n-1} & \dots & \dots & \frac{r}{n-1} \\ \frac{r}{n-1} & 1-r & \dots & \dots & \frac{r}{n-1} \\ & & \dots & & \\ \frac{r}{n-1} & \dots & \dots & 1-r & \frac{r}{n-1} \\ \frac{r}{n-1} & \dots & \dots & \frac{r}{n-1} & 1-r \end{pmatrix}$$

for a traditional island model where individuals have equal probability of migrating to any other subpopulations.

- `MigrHierarchicalIslandRates(r1, r2, n)` models a hierarchical island model in which local populations are grouped into neighborhoods within which there is considerable gene flow and between which there is less gene flow.  $n$  should be a list of group size.  $r_1$  is the within-group migration rate and  $r_2$  is the cross-group migration rate. That is to say, an individual in an island has probability  $1 - r_1 - r_2$  to stay,  $r_1$  to be a migrant to

other islands in the group (migration rate depending on the size of group), and  $r_2$  to be a migrant to other islands in another group (migration rate depending on the number of islands in other groups). Both  $r_1$  and  $r_2$  can vary across groups of islands. For example, `MigrHierarchicalIslandRates([r11, r12], r2, [3, 2])` returns a  $5 \times 5$  migration matrix

$$\begin{pmatrix} 1 - r_{11} - r_2 & \frac{r_{11}}{2} & \frac{r_{11}}{2} & \frac{r_2}{2} & \frac{r_2}{2} \\ \frac{r_{11}}{2} & 1 - r_{11} - r_2 & \frac{r_{11}}{2} & \frac{r_2}{2} & \frac{r_2}{2} \\ \frac{r_{11}}{2} & \frac{r_{11}}{2} & 1 - r_{11} - r_2 & \frac{r_2}{2} & \frac{r_2}{2} \\ \frac{r_2}{3} & \frac{r_2}{3} & \frac{r_2}{3} & 1 - r_{12} - r_2 & r_{12} \\ \frac{r_2}{3} & \frac{r_2}{3} & \frac{r_2}{3} & r_{12} & 1 - r_{12} - r_2 \end{pmatrix}$$

- `MigrSteppingStoneRates(r, n, circular=False)` returns a  $n \times n$  migration matrix

$$\begin{pmatrix} 1 - r & r & & & \\ r/2 & 1 - r & r/2 & & \\ & & \dots & & \\ & & r/2 & 1 - r & r/2 \\ & & & r & 1 - r \end{pmatrix}$$

and if `circular=True`, returns

$$\begin{pmatrix} 1 - r & r/2 & & & r/2 \\ r/2 & 1 - r & r/2 & & \\ & & \dots & & \\ & & r/2 & 1 - r & r/2 \\ r/2 & & & r/2 & 1 - r \end{pmatrix}$$

Many more migration models have been proposed and studied, sometimes under different names with slightly different definitions. Please refer to the *operators* section of the simuPOP online cookbook for the implementation of more migration models. If you cannot find your model there, it should not be too difficult to construct a migration rate matrix for it and please consider adding your model to the cookbook.

### Migrate from virtual subpopulations \*

Under a realistic eco-social settings, individuals in a subpopulation rarely have the same probability to migrate. Genetic evidence has shown that female has a higher migrate rate than male in humans, perhaps due to migration patterns related to inter-population marriages. Such sex-biased migration also happens in other large migration events such as slave trade.

It is easy to simulate most of such complex migration models by migrating from virtual subpopulations. For example, if you define virtual subpopulations by sex, you can specify different migration rates for males and females and control the proportion of males among migrants. Example 3.13 demonstrate a sex-biased migration model where males dominate migrants from subpopulation 0.

To avoid confusing, this example uses the proportion migration mode. At the beginning of the first generation, there are 500 males and 500 females in each subpopulation. A 10% male migration rate and 5% female migration rate leads to 50 male migrants and 25 female migrants. Subpopulation sizes and number of males in each subpopulation before mating are therefore:

- Subpopulation 0: male 500-50, female 500-25, total 925
- Subpopulation 1: male 500+50, female 500+25, total 1075

Note that the unspecified *to* subpopulations are subpopulation 0 and 1, which cannot be virtual.

### Example 3.13: Migration from virtual subpopulations

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[1000]*2, infoFields='migrate_to')
>>> pop.setVirtualSplitter(sim.sexSplitter())
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     # 500 males and 500 females
...     initOps = sim.initSex(sex=[sim.MALE, sim.FEMALE]),
...     preOps = [
...         sim.migrator(rate=[
...             [0, 0.10],
...             [0, 0.05],
...             ],
...         mode = sim.BY_PROPORTION,
...         subPops=[(0, 0), (0, 1)]),
...     sim.stat(popSize=True, numOfMales=True, vars='numOfMales_sp'),
...     sim.pyEval(r"'%d/%d\t%d/%d\n' % (subPop[0]['numOfMales'], subPopSize[0], "
...         "subPop[1]['numOfMales'], subPopSize[1]))"),
...     ],
...     postOps = [
...         sim.stat(popSize=True, numOfMales=True, vars='numOfMales_sp'),
...         sim.pyEval(r"'%d/%d\t%d/%d\n' % (subPop[0]['numOfMales'], subPopSize[0], "
...             "subPop[1]['numOfMales'], subPopSize[1]))"),
...     ],
...     gen = 2
... )
450/925 550/1075
426/925 520/1075
384/859 562/1141
425/859 582/1141
(2,)
```

### Arbitrary migration models \*\*

If none of the described migration methods fits your need, you can always resort to manual migration. One such example is when you need to mimick an existing evolutionary scenario so you know exactly which subpopulation each individual will migrate to.

Manual migration is actually very easy. All you need to do is specifying the destination subpopulation of all individuals in the *from* subpopulations (parameter `subPops`), using an information field (usually `migrate_to`). You can then call the `migrator` using `mode=BY_IND_INFO`. Example 3.14 shows how to manually move individuals around. This example uses the function form of `migrator`. You usually need to use a Python operator to set destination subpopulations if you would like to manually migrate individuals during an evolutionary process.

### Example 3.14: Manual migration

```
>>> import simuPOP as sim
>>> pop = sim.population([10]*2, infoFields='migrate_to')
>>> pop.setIndInfo([0, 1, 2, 3]*5, 'migrate_to')
>>> sim.Migrate(pop, mode=sim.BY_IND_INFO)
>>> pop.subPopSizes()
(5, 5, 5, 5)
```

**Note:** Individuals with an invalid destination subpopulation ID (e.g. an negative number) will be discarded silently. Although not recommended, this feature can be used to remove individuals from a subpopulation.

### 3.3.2 Split subpopulations (operators `splitSubPops`)

Operator `splitSubPops` splits one or more subpopulations into finer subpopulations. It can be used to simulate populations that originate from the same founder population. For example, a population of size 1000 in Example 3.15 is split into three subpopulations of sizes 300, 300 and 400 respectively, after evolving as a single population for two generations.

Example 3.15: Split subpopulations by size

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(1000), sim.randomSelection())
>>> simu.evolve(
...     preOps = [
...         sim.splitSubPops(subPops=0, sizes=[300, 300, 400], at=2),
...         sim.stat(popSize=True),
...         sim.pyEval(r'"Gen %d:\t%s\n" % (gen, subPopSize)')
...     ],
...     gen = 4
... )
Gen 0: [1000]
Gen 1: [1000]
Gen 2: [300, 300, 400]
Gen 3: [300, 300, 400]
(4,)
```

Operator `splitSubPops` splits a subpopulation by sizes of the resulting subpopulations. It is often easier to do so with proportions. In addition, if a demographic function is used, you should make sure that the number of subpopulations will be the same before and after mating at any generation. One way of doing this is to apply a `splitSubPops` operator at the right generation. Example 3.16 demonstrates such an evolutionary scenario. However, it is often easier to split the population in the demographic function in such case (see section 2.6.2 for details).

Example 3.16: Split subpopulations by proportion

```
>>> import simuPOP as sim
>>> def demo(gen, pop=None):
...     if gen < 2:
...         return 1000 + 100 * gen
...     else:
...         return [x + 50 * gen for x in pop.subPopSizes()]
...
>>> simu = sim.simulator(sim.population(1000),
...     sim.randomSelection(subPopSize=demo))
>>> simu.evolve(
...     preOps = [
...         sim.splitSubPops(subPops=0, proportions=[.5]*2, at=2),
...         sim.stat(popSize=True),
...         sim.pyEval(r'"Gen %d:\t%s\n" % (gen, subPopSize)')
...     ],
...     gen = 4
... )
Gen 0: [1000]
Gen 1: [1000]
Gen 2: [550, 550]
Gen 3: [650, 650]
(4,)
```

Either by *sizes* or by *proportions*, individuals in a subpopulation are divided randomly. It is, however, also possible to split subpopulations according to individual information fields. In this case, individuals with different values at a given information field will be split into different subpopulations. This is demonstrated in Example 3.17 where the function form of operator `splitSubPops` is used.

Example 3.17: Split subpopulations by individual information field

```
>>> import simuPOP as sim
>>> import random
>>> pop = sim.population([1000]*3, subPopNames=['a', 'b', 'c'], infoFields='x')
>>> pop.setIndInfo([random.randint(0, 3) for x in range(1000)], 'x')
>>> print pop.subPopSizes()
(1000, 1000, 1000)
>>> print pop.subPopNames()
('a', 'b', 'c')
>>> sim.SplitSubPops(pop, subPops=[0, 2], infoFields=['x'])
>>> print pop.subPopSizes()
(268, 227, 237, 268, 1000, 268, 227, 237, 268)
>>> print pop.subPopNames()
('a', 'a', 'a', 'a', 'b', 'c', 'c', 'c', 'c')
```

### 3.3.3 Merge subpopulations (operator `mergeSubPops`)

Operator `mergeSubPops` merges specified subpopulations into a single subpopulation. This operator can be used to simulate admixed populations where two or more subpopulations merged into one subpopulation and continue to evolve for a few generations. Example 3.18 simulates such an evolutionary scenario. A demographic model could be added similar to Example 3.16.

Example 3.18: Merge multiple subpopulations into a single subpopulation

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population([500]*2),
...     sim.randomSelection())
>>> simu.evolve(
...     preOps = [
...         sim.mergeSubPops(subPops=[0, 1], at=3),
...         sim.stat(popSize=True),
...         sim.pyEval(r'"Gen %d:\t%s\n" % (gen, subPopSize)')
...     ],
...     gen = 5
... )
Gen 0: [500, 500]
Gen 1: [500, 500]
Gen 2: [500, 500]
Gen 3: [1000]
Gen 4: [1000]
(5,)
```

### 3.3.4 Resize subpopulations (operator `resizeSubPops`)

Whenever possible, it is recommended that subpopulation sizes are changed naturally, namely through the population of an offspring generation. However, it is sometimes desired to change the size of a population forcefully. Examples of such applications include immediate expansion of a small population before evolution, and the simulation of sudden population size change caused by natural disaster. By default, new individuals created by such sudden population expansion get their genotype from existing individuals. Example 3.19 shows a scenario where two subpopulations expand instantly at generation 3.

Example 3.19: Resize subpopulation sizes

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population([500]*2),
...     sim.randomSelection())
```

```

>>> simu.evolve(
...     preOps = [
...         sim.resizeSubPops(proportions=(1.5, 2), at=3),
...         sim.stat(popSize=True),
...         sim.pyEval(r'"Gen %d:\t%s\n" % (gen, subPopSize)')
...     ],
...     gen = 5
... )
Gen 0: [500, 500]
Gen 1: [500, 500]
Gen 2: [500, 500]
Gen 3: [750, 1000]
Gen 4: [750, 1000]
(5,)

```

## 3.4 Genotype transmitters

### 3.4.1 Generic genotype transmitters (operators `genoTransmitter`, `cloneGenoTransmitter`, `mendelianGenoTransmitter`, `selfingGenoTransmitter`, `haplodiploidGenoTransmitter`, and `mitochondrialGenoTransmitter`) \*

A number of during-mating operators are defined to transmit genotype from parent(s) to offspring. They are rarely used or even seen directly because they are used as genotype transmitters of mating schemes.

- `genoTransmitter`: This genotype transmitter is usually used by customized genotype transmitters because it provides some utility functions that are more efficient than their Pythonic counterparts.
- `cloneGenoTransmitter`: Copy all genotype from a parent to an offspring. It also copies parental sex to the offspring because sex can be genotype determined. This genotype transmitter is used by mating scheme `cloneMating`. This genotype transmitter can be applied to populations of **any ploidy** type.
- `mendelianGenoTransmitter`: Copy genotypes from two parents (a male and a female) to an offspring following Mendel's laws, used by mating scheme `randomMating`. This genotype transmitter can only be applied to **diploid** populations.
- `selfingGenoTransmitter`: Copy genotypes from one parent to an offspring using self-fertilization, used by mating scheme `selfMating`. This genotype transmitter can only be applied to **diploid** populations.
- `haplodiploidGenoTransmitter`: Set genotype to male and female offspring differently in a haplodiploid population, used by mating scheme `haplodiploidMating`. This genotype transmitter can only be applied to **haplodiploid** populations.
- `mitochondrialGenoTransmitter`: Treat all customized chromosomes or specified chromosomes as mitochondrial chromosomes and transmit maternal mitochondrial chromosomes randomly to an offspring. This genotype transmitter can be applied to populations of **any ploidy** type. It trasmits the first homologous copy of chromosomes maternally and clears alleles on other homologous copies of chromosomes of an offspring.

### 3.4.2 Recombination (Operator `recombinator`)

The generic genotype transmitters do not handle genetic recombination. A genotype transmitter recombinator is provided for such purposes, and can be used with `randomMating` and `selfMating` (replace `mendelianGenoTransmitter` and `selfingGenoTransmitter` used in these mating schemes).

Recombination rate is implemented **between adjacent markers**. There can be only one recombination event between adjacent markers no matter how far apart they are located on a chromosome. In practise, a `recombinator` goes along chromosomes and determine, between each adjacent loci, whether or not a recombination happens.

Recombination rates could be specified in the following ways:

1. If a single recombination rate is specified through parameter `rates`, it will be the recombination rate between all adjacent loci, regardless of loci position.
2. If recombination happens only after certain loci, you can specify these loci using parameter `loci`. For example,

```
recombinator(rates=0.1, loci=[2, 5])
```

recombines a chromosome only **after** loci 2 (between 2 and 3) and 5 (between 5 and 6).

3. If parameter `loci` is given, different recombination rate can be given to each of them. For example

```
recombinator(rates=[0.1, 0.05], loci=[2, 5])
```

uses two different recombination rates after loci 2 and 5.

4. If recombination rates vary across your chromosomes, a long list of `rate` and `loci` may be needed to specify recombination rates one by one. An alternative method is to specify a **recombination intensity**. Recombination rate between two adjacent loci is calculated as the product of this intensity and distance between them. For example, if you apply operator

```
recombinator(intensity=0.1)
```

to a population

```
population(size=100, loci=[4], lociPos=[0.1, 0.2, 0.4, 0.8])
```

The recombination rates between adjacent markers will be  $0.1 \times 0.1$ ,  $0.1 \times 0.2$  and  $0.1 \times 0.4$  respectively.

#### Example 3.20: Genetic recombination at all and selected loci

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(size=[1000], loci=[100]),
...     sim.randomMating(ops = [
...         sim.recombinator(rates=0.01, reps=0),
...         sim.recombinator(rates=[0.01]*10, loci=range(50, 60), reps=1),
...     ]), rep=2)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([0]*100 + [1]*100)
...     ],
...     postOps = [
...         sim.stat(LD=[[40, 55], [60, 70]]),
...         sim.pyEval(r' "%d:\t%.3f\t%.3f\t" % (rep, LD_prime[40][55], LD_prime[60][70])'),
...         sim.pyOutput('\n', reps=-1)
...     ],
...     gen = 5
... )
0:      0.769   0.805   1:      0.933   1.000
0:      0.660   0.742   1:      0.861   1.000
0:      0.547   0.694   1:      0.829   1.000
0:      0.488   0.592   1:      0.792   1.000
0:      0.431   0.572   1:      0.729   1.000
(5, 5)
```

Example 3.20 demonstrates how to specify recombination rates for all loci or for specified loci. In this example, two replicates of a population are evolved, subject to two different recombinators. The first recombinator applies the same recombination rate between all adjacent loci, and the second recombinator recombines only after loci 50 - 59. Because there is no recombination event between loci 60 and 70 for the second replicate, linkage disequilibrium values between these two loci does not decrease as what happens in the first replicate.

Example 3.21: Genetic recombination rates specified by intensity

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(size=[1000], loci=3, lociPos=[0, 1, 1.1]),
...     sim.randomMating(ops=sim.recombinator(intensity=0.01)))
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([0]*3 + [1]*3)
...     ],
...     postOps = [
...         sim.stat(LD=[[0, 1], [1, 2]]),
...         sim.pyEval(r' "%.3f\t%.3f\n" % (LD_prime[0][1], LD_prime[1][2])', step=10)
...     ],
...     gen = 50
... )
0.986 1.000
0.890 0.994
0.859 0.990
0.784 0.969
0.769 0.959
(50,)
```

Example 3.21 demonstrates the use of the `intensity` parameter. In this example, the distances between the first two loci and the latter two loci are 1 and 0.1 respectively. This leads recombination rates 0.01 and 0.001 respectively with a recombination intensity 0.01. Consequently, LD between the first two loci decay much faster than the latter two.

If more advanced recombination model is desired, a customized genotype transmitter can be used. For example, Example 2.53 uses two recombinators to implement sex-specific recombination. **Note:** Both loci positions and recombination intensity are unitless. You can assume different unit for loci position and recombination intensity as long as the resulting recombination rate makes sense.

### 3.4.3 Gene conversion (Operator `recombinator`) \*

simuPOP uses the Holliday junction model to simulate gene conversion. This model treats recombination and conversion as a unified process. The key features of this model is

- Two (out of four) chromatids pair and a single strand cut is made in each chromatid
- Strand exchange takes place between the chromatids
- Ligation occurs yielding two completely intact DNA molecules
- Branch migration occurs, giving regions of heteroduplex DNA
- Resolution of the Holliday junction gives two DNA molecules with heteroduplex DNA. Depending upon how the holliday junction is resolved, we either observe no exchange of flanking markers, or an exchange of flanking markers. The former forms a conversion event, which can be considered as a double recombination.

In practise, gene conversion can be considered as a double recombination event. That is to say, when a recombination event happens, it has certain probability to trigger a second recombination event along the chromosome. The distance between the two locations where recombination events happen is the tract length of this conversion event.



The probability at which gene conversion happens, and how tract length is determined is specify using parameter `convMode` of a recombinator. This parameter can be

- `NoConversion` No gene conversion. (default)
- `(NUM_MARKERS, prob, N)` Convert a fixed number `N` of markers at probability `prob`.
- `(TRACT_LENGTH, prob, N)` Convert a fixed length `N` of chromosome regions at probability `prob`. This can be used when markers are not equally spaced on chromosomes.
- `(GEOMETRIC_DISTRIBUTION, prob, p)` When a conversion event happens at probability `prob`, convert a random number of markers, with a geometric distribution with parameter `p`.
- `(EXPONENTIAL_DISTRIBUTION, prob, p)` When a conversion event happens at probability `prob`, convert a random length of chromosome region, using an exponential distribution with parameter `p`.

Note that

- If tract length is determined by length (`TractLength` or `ExponentialDistribution`), the starting point of the flanking region is uniformly distributed between marker  $i-1$  and  $i$ , if the recombination happens at marker  $i$ . That is to say, it is possible that no marker is converted with a positive tract length.
- A conversion event will act like a recombination event if its flanking region exceeds the end of a chromosome, or if another recombination event happens before the end of the flanking region.

Example 3.22 compares two recombinators. The first recombinator is a regular recombinator that recombine between loci 50 and 51. The second recombinator is a conversion operator because every recombination event will become a conversion event (`prob=1`). Because a second recombination event will surely happen between loci 60 and 61, there will be either no or double recombination events between loci 40, 70. LD between these two loci therefore does not decrease, although LD between locus 55 and these two loci will decay.

Example 3.22: Gene conversion

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(size=[1000], loci=[100]),
...     sim.randomMating(ops=[
...         sim.recombinator(rates=0.01, loci=50, reps=0),
...         sim.recombinator(rates=0.01, loci=50, reps=1, convMode=(sim.NUM_MARKERS, 1, 10)),
...     ]), rep=2)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([0]*100 + [1]*100)
...     ],
...     postOps = [
...         sim.stat(LD=[[40, 55], [40, 70]]),
...         sim.pyEval(r' "%d:\t%.3f\t%.3f\t" % (rep, LD_prime[40][55], LD_prime[40][70])'),
...         sim.pyOutput('\n', reps=-1)
...     ],
...     gen = 5
... )
0:      0.980      0.980      1:      0.978      1.000
0:      0.968      0.968      1:      0.970      1.000
0:      0.968      0.968      1:      0.960      1.000
0:      0.952      0.952      1:      0.944      1.000
0:      0.956      0.956      1:      0.935      1.000
(5, 5)
```

### 3.4.4 Tracking all recombination events \*\*

To understand the evolutionary history of a simulated population, it is sometimes needed to track down all ancestral recombination events. In order to do that, you will first need to give a unique ID to each individual so that you could make sense of the dumped recombination events. Although this is routinely done using operator `idTagger` (see example 3.53 for details), it is a little tricky here because you need to place the during-mating `idTagger` before a `recombinator` in the `ops` parameter of a mating scheme so that offspring ID could be set and outputted correctly.

After setting the name of the ID field (usually `ind_id`) to the `infoField` parameter of a `recombinator`, it can dump a list of recombination events (loci after which recombination events happened) for each set of homologous chromosomes of an offspring. Each line is in the format of

```
offspringID parentID startingPloidy rec1 rec2 ....
```

Example 3.23 gives an example how the output looks like.

Example 3.23: Tracking all recombination events

```
>>> import simuPOP as sim
>>> pop = sim.population(1000, loci=[1000, 2000], infoFields='ind_id')
>>> simu = sim.simulator(pop, sim.randomMating(ops = [
...     sim.idTagger(),
...     sim.recombinator(rates=0.001, output='>>rec.log', infoFields='ind_id')])
... )
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.idTagger(),
...     ],
...     gen = 5
... )
(5,)
>>> rec = open('rec.log')
>>> # print the first three lines of the log file
>>> print ''.join(rec.readlines()[:4])
10021 9662 0 385 1039 1424 1967
10021 9270 0 919 1425 1788 2619
10022 9180 0
10022 9184 0 986 999 1716
```

## 3.5 Mutation

A mutator (a mutation operator) mutates alleles at certain loci from one allele to another. Because alleles are simple non-negative numbers that can be interpreted as nucleotides, codons, sequences of nucleotides or even genetic deletions, appropriate mutation models have to be chosen for different types of loci. Please refer to Section 2.2 for a few examples.

A mutator will mutate alleles at all loci unless parameter `loci` is used to specify a subset of loci. Different mutators have different concepts and forms of mutation rates. If a mutator accepts only a single mutation rate (which can be in the form of a list or a matrix), it uses parameter `rate` and applies the same mutation rate to all loci. If a mutator accepts a list of mutation rates (each of which is a single number), it uses parameter `rates` and applies different mutation rates to different loci if multiple loci are specified. Note that parameter `rates` also accepts single form inputs (e.g. `rates=0.01`) in which case the same mutation rate will be applied to all loci.

### 3.5.1 Mutation models specified by rate matrixes (**matrixMutator**)

A mutation model can be defined as a **mutation rate matrix**  $(p_{ij})_{n \times n}$  where  $p_{ij}$  is the probability that an allele  $i$  mutates to  $j$  per generation per locus. Although mathematical formulation of  $p_{ij}$  are sometimes unscaled, simuPOP assumes  $\sum_{j=0}^{n-1} p_{ij} = 1$  for all  $i$  and requires such rate matrixes in the specification of a mutation model.  $p_{ii}$  of such a matrix are ignored because they are automatically calculated from  $p_{ii} = 1 - \sum_{j \neq i} p_{ij}$ .

A **matrixMutator** is defined to mutate between alleles 0, 1, ...,  $n-1$  according to a given rate matrix. Conceptually speaking, this mutator goes through each mutable allele and mutates it to allele 0, 1, ...,  $n-1$  according to probabilities  $p_{ij}$ ,  $j = 0, \dots, n-1$ . Most alleles will be kept intact because mutations usually happen at low probability (with  $p_{ii}$  close to 1). For example, Example 3.24 simulates a locus with 3 alleles. Because the rate at which allele 2 mutates to alleles 0 and 1 is higher than the rate alleles 0 and 1 mutate to allele 2, the frequency of allele 2 decreases over time.

Example 3.24: General mutator specified by a mutation rate matrix

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(size=[2000], loci=1),
...     sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.2, 0.3, 0.5])
...     ],
...     preOps = sim.matrixMutator(rate = [
...         [0, 1e-5, 1e-5],
...         [1e-4, 0, 1e-4],
...         [1e-3, 1e-3, 0]
...     ]),
...     postOps = [
...         sim.stat(alleleFreq=0, step=100),
...         sim.pyEval(r'', '.join(['%.3f' % alleleFreq[0][x] for x in range(3)]) + '\n',
...             step=100),
...     ],
...     gen=1000
... )
0.195, 0.303, 0.502
0.160, 0.516, 0.324
0.275, 0.432, 0.292
0.304, 0.480, 0.215
0.245, 0.573, 0.181
0.283, 0.484, 0.232
0.289, 0.479, 0.232
0.297, 0.443, 0.260
0.384, 0.501, 0.115
0.283, 0.630, 0.086
(1000,)
```

### 3.5.2 k-allele mutation model (**kamMutator**)

A  $k$ -allele model assumes  $k$  alleles (0, ...,  $k-1$ ) at a locus and mutate between them using rate matrix

$$p_{ij} = \begin{pmatrix} 1 - \mu & \frac{\mu}{k-1} & \cdots & \frac{\mu}{k-1} \\ \frac{\mu}{k-1} & 1 - \mu & \cdots & \frac{\mu}{k-1} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{\mu}{k-1} & \frac{\mu}{k-1} & \cdots & 1 - \mu \end{pmatrix}$$

The only parameter  $\mu$  is the mutation rate, which is the rate at which an allele mutates to any other allele with equal probability.

This mutation model is a special case of the `matrixMutator` but a specialized `kamMutator` is recommended because it provides better performance, especially when  $k$  is large. In addition, this operator allows different mutation rates at different loci. When  $k$  is not specified, it is assumed to be the number of allowed alleles (e.g. 2 for binary modules). Example 3.25 demonstrates the use of this operator where parameters `rate` and `loci` are used to specify different mutation rates for different loci. Because this operator treats all alleles equally, all alleles will have the same allele frequency in the long run.

Example 3.25: A  $k$ -allele mutation model

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[2000], loci=1*3)
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = sim.initSex(),
...     postOps = [
...         sim.kamMutator(k=5, rates=[1e-2, 1e-3], loci=[0, 1]),
...         sim.stat(alleleFreq=range(3), step=100),
...         sim.pyEval(r"', '.join(['%.3f' % alleleFreq[x][0] for x in range(3)]) + '\n',
...             step=100),
...     ],
...     gen=500
... )
0.991, 0.999, 1.000
0.408, 0.895, 1.000
0.232, 0.793, 1.000
0.201, 0.752, 1.000
0.219, 0.674, 1.000
(500,)
```

### 3.5.3 Diallelic mutation models (`snpMutator`)

`matrixMutator` and `kamMutator` are general purpose mutators in the sense that they do not assume a type for the mutated alleles. This and the following sections describe mutation models for specific types of alleles.

If there are only two alleles at a locus, a diallelic mutation model should be used. Because single nucleotide polymorphisms (SNPs) are the most widely available diallelic markers, a `snpMutator` is provided to mutate such markers using a mutate rate matrix

$$R = \begin{pmatrix} 1-u & u \\ v & 1-v \end{pmatrix}.$$

Despite of its name, this mutator can be used in many theoretical models assuming  $\Pr(A \rightarrow a) = u$  and  $\Pr(a \rightarrow A) = v$ . If  $v = 0$ , mutations will be directional. Example 3.26 applies such a directional mutator model to two loci, but with a purifying selection applied to the first locus. Because of the selection pressure, the frequency of allele 1 at the first locus does not increase indefinitely as allele 1 at the second locus.

Example 3.26: A diallelic directional mutation model

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[2000], loci=[1, 1], infoFields='fitness')
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = sim.initSex(),
...     preOps = [
...         sim.snpMutator(u=0.001),
...         sim.maSelector(loci=0, fitness=[1, 0.99, 0.98]),
...     ],
...     postOps = [
```

```

...     sim.stat(alleleFreq=[0, 1], step=100),
...     sim.pyEval(r"'\t%.3f\n' % (alleleFreq[0][1], alleleFreq[1][1])",
...               step=100),
... ],
... gen=500
... )
0.001 0.001
0.077 0.087
0.099 0.192
0.099 0.300
0.085 0.400
(500,)

```

### 3.5.4 Nucleotide mutation models (acgtMutator)

Mutations in these models assume alleles 0, 1, 2, 3 as nucleotides A, C, G, and T. The operator is named `acgtMutator` to remind you the alphabetic order of these nucleotides. This mutation model is specified by a rate matrix

	A	C	G	T
A	—	$x_1$	$x_2$	$x_3$
C	$x_4$	—	$x_5$	$x_6$
G	$x_7$	$x_8$	—	$x_9$
T	$x_{10}$	$x_{11}$	$x_{12}$	—

which is determined by 12 parameters. However, several simpler models with fewer parameters can be used. In addition to parameters shared by all mutation operators, a nucleotide mutator is specified by a parameter list and a model name. For example:

```
acgtMutator(rate=[1e-5, 0.5], model='K80')
```

specifies a nucleotide mutator using Kimura's 2-parameter model with  $\mu = 10^{-5}$  and  $\kappa = 0.5$ . Because multiple parameters could be involved for a particular mutation model, **the definition of a mutation rate and other parameters are model dependent and may vary with different mathematical representation of the models.**

The names and acceptable parameters of acceptable models are listed below:

1. Jukes and Cantor 1969 model: `model='JC69'`, `rate=[ $\mu$ ]`

The Jukes and Cantor model is similar to a 4-allele model but its definition of  $\mu$  is different. More specifically, when a mutation event happens at rate  $\mu$ , an allele will have equal probability to mutate to any of the 4 allelic states.

$$R = \begin{pmatrix} - & \frac{\mu}{4} & \frac{\mu}{4} & \frac{\mu}{4} \\ \frac{\mu}{4} & - & \frac{\mu}{4} & \frac{\mu}{4} \\ \frac{\mu}{4} & \frac{\mu}{4} & - & \frac{\mu}{4} \\ \frac{\mu}{4} & \frac{\mu}{4} & \frac{\mu}{4} & - \end{pmatrix}$$

2. Kimura's 2-parameter 1980 model: `model='K80'`, `rate=[ $\mu$ ,  $\kappa$ ]`

Kimura's model distinguishes transitions ( $A \longleftrightarrow G$ , and  $C \longleftrightarrow T$  namely  $0 \longleftrightarrow 2$  and  $1 \longleftrightarrow 3$  with probability  $\frac{\mu}{4}\kappa$ ) and transversions (others) with probability  $\frac{\mu}{4}$ . It would be a Jukes and Cantor model if  $\kappa = 1$ .

$$R = \begin{pmatrix} - & \frac{\mu}{4} & \frac{\mu}{4}\kappa & \frac{\mu}{4} \\ \frac{\mu}{4} & - & \frac{\mu}{4}\kappa & \frac{\mu}{4} \\ \frac{\mu}{4}\kappa & \frac{\mu}{4} & - & \frac{\mu}{4}\kappa \\ \frac{\mu}{4} & \frac{\mu}{4}\kappa & \frac{\mu}{4} & - \end{pmatrix}$$

3. Felsenstein 1981 model: `model='F81'`, `rate=[μ, πA, πC, πG]`.

This model assumes different base frequencies but the same probabilities for transitions and transversions.  $\pi_T$  is calculated from  $\pi_A$ ,  $\pi_C$  and  $\pi_G$ .

$$R = \begin{pmatrix} - & \mu\pi_C & \mu\pi_G & \mu\pi_T \\ \mu\pi_A & - & \mu\pi_G & \mu\pi_T \\ \mu\pi_A & \mu\pi_C & - & \mu\pi_T \\ \mu\pi_A & \mu\pi_C & \mu\pi_G & - \end{pmatrix}$$

4. Hasegawa, Kishino and Yano 1985 model: `model='HKY85'`, `rate=[μ, κ, πA, πC, πG]`

This model replaces 1/4 frequency used in the Kimura's 2-parameter model with nucleotide-specific frequencies.

$$R = \begin{pmatrix} - & \mu\pi_C & \mu\kappa\pi_G & \mu\pi_T \\ \mu\pi_A & - & \mu\pi_G & \mu\kappa\pi_T \\ \mu\kappa\pi_A & \mu\pi_C & - & \mu\pi_T \\ \mu\pi_A & \mu\kappa\pi_C & \mu\pi_G & - \end{pmatrix}$$

5. Tamura 1992 model: `model='T92'`, `rate=[μ, πGC]`

This model is a HKY85 model with  $\pi_G = \pi_C = \pi_{GC}/2$  and  $\pi_A = \pi_T = \pi_{AT}/2 = (1 - \pi_{GC})/2$ ,

$$R = \begin{pmatrix} - & \frac{1}{2}\mu\pi_{GC} & \frac{1}{2}\mu\nu\pi_{GC} & \frac{1}{2}\mu\pi_{AT} \\ \frac{1}{2}\mu\pi_{AT} & - & \frac{1}{2}\mu\pi_{GC} & \frac{1}{2}\mu\nu\pi_{AT} \\ \frac{1}{2}\mu\nu\pi_{AT} & \frac{1}{2}\mu\pi_{GC} & - & \frac{1}{2}\mu\pi_{AT} \\ \frac{1}{2}\mu\pi_{AT} & \frac{1}{2}\mu\nu\pi_{GC} & \frac{1}{2}\mu\pi_{GC} & - \end{pmatrix}$$

6. Tamura and Nei 1993 model: `model='TN93'`, `rate=[μ, κ1, κ2, πA, πC, πG]`

This model extends the HKY1985 model by distinguishing  $A \longleftrightarrow G$  transitions (namely  $0 \longleftrightarrow 2$ ) and  $C \leftrightarrow T$  transitions ( $1 \longleftrightarrow 3$ ) with different  $\kappa$ .

$$R = \begin{pmatrix} - & \mu\pi_C & \mu\kappa_1\pi_G & \mu\pi_T \\ \mu\pi_A & - & \mu\pi_G & \mu\kappa_2\pi_T \\ \mu\kappa_1\pi_A & \mu\pi_C & - & \mu\pi_T \\ \mu\pi_A & \mu\kappa_2\pi_C & \mu\pi_G & - \end{pmatrix}$$

7. Generalized time reversible model: `model='GTR'`, `rate=[x1, x2, x3, x4, x5, x6, πA, πC, πG]`

The generalized time reversible model is the most general neutral, independent, finite-sites, time-reversible model possible. It is specified by six parameters and base frequencies. Its rate matrix is defined as

$$R = \begin{pmatrix} - & \frac{\pi_A x_1}{\pi_C} & \frac{\pi_A x_2}{\pi_G} & \frac{\pi_A x_3}{\pi_T} \\ x_1 & - & \frac{\pi_C x_4}{\pi_G} & \frac{\pi_C x_5}{\pi_T} \\ x_2 & x_4 & - & \frac{\pi_G x_6}{\pi_T} \\ x_3 & x_5 & x_6 & - \end{pmatrix}$$

8. General model: `model='general'` (default), `rate=[x1, x2, x3, x4, x5, x6, x7, x8, x9, x10, x11, x12]`.

This is the most general model with 12 parameters:

$$R = \begin{pmatrix} - & x_1 & x_2 & x_3 \\ x_4 & - & x_5 & x_6 \\ x_7 & x_8 & - & x_9 \\ x_{10} & x_{11} & x_{12} & - \end{pmatrix}$$

It is not surprising that all other models are implemented as special cases of this model.

Example 3.27 applies a Kimura's 2-parameter mutation model to a population with a single nucleotide marker.

### Example 3.27: A Kimura's 2 parameter mutation model

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[2000], loci=1,
...     alleleNames=['A', 'C', 'G', 'T'])
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([.1, .1, .1, .7])
...     ],
...     preOps = [
...         sim.acgtMutator(rate=[1e-4, 0.5], model='K80'),
...         sim.stat(alleleFreq=0, step=100),
...         sim.pyEval(r"','.join(['%.3f' % alleleFreq[0][x] for x in range(4)]) + '\n'",
...             step=100),
...     ],
...     gen=500
... )
0.093, 0.101, 0.094, 0.712
0.157, 0.063, 0.130, 0.650
0.227, 0.120, 0.168, 0.484
0.267, 0.048, 0.319, 0.366
0.315, 0.047, 0.326, 0.312
(500,)
```

### 3.5.5 Mutation model for microsatellite markers (`smmMutator`)

The **stepwise mutation model** (SMM) was proposed by [Ohta and Kimura \[1973\]](#) to model the mutation of Variable Number Tandem Repeat (VNTR), which consists of tandem repeat of sequences. VNTR markers consisting of short sequences (e.g. 5 basepair or less) are also called microsatellite markers. A mutation event of a VNTR marker either increase or decrease the number of repeats, as a result of slipped-strand mispairing or unequal sister chromatid exchange and genetic recombination.

A `smmMutator` assumes that alleles at a locus are the number of tandem repeats and mutates them by increasing or decreasing the number of repeats during a mutation event. By adjusting parameters `incProb`, `maxAllele` and `mutStep`, this operator can be used to simulate the standard neutral stepwise mutation model and a number of **generalized stepwise mutation models**. For example, Example 3.28 uses two `smmMutator` to mutate two microsatellite markers, using a standard and a generalized model where a geometric distribution is used to determine the number of steps.

### Example 3.28: A standard and a generalized stepwise mutation model

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(size=1000, loci=[1, 1]), sim.randomMating())
>>> simu.evolve(
...     # all start from allele 50
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0]*50 + [1])
...     ],
...     preOps = [
...         sim.smmMutator(rates=1e-3, loci=0),
...         sim.smmMutator(rates=1e-3, incProb=0.6, loci=1,
...             mutStep=(sim.GEOMETRIC_DISTRIBUTION, 0.2)),
...     ],
...     gen=100
... )
```

```
(100,)
>>> # count the average number tandem repeats at both loci
>>> cnt0 = cnt1 = 0
>>> for ind in simu.population(0).individuals():
...     cnt0 += ind.allele(0, 0) + ind.allele(0, 1)
...     cnt1 += ind.allele(1, 0) + ind.allele(1, 1)
...
>>> print 'Average number of repeats at two loci are %.2f and %.2f.' % \
...       (cnt0/2000., cnt1/2000.)
Average number of repeats at two loci are 50.06 and 50.49.
```

### 3.5.6 Simulating arbitrary mutation models using a hybrid mutator (pyMutator)\*

A hybrid mutator `pyMutator` mutates random alleles at selected loci (parameter `loci`), replicates (parameter `loci`), subpopulations (parameter `subPop`) with specified mutation rate (parameter `rate`). Instead of mutating the alleles by itself, it passes the alleles to a user-defined function and use it return values as the mutated alleles. Arbitrary mutation models could be implemented using this operator.

Example 3.29 applies a simple mutation model where an allele is increased by a random number between 1 and 5 when it is mutated. Two different mutation rates are used for two different loci so average alleles at these two loci are different.

Example 3.29: A hybrid mutation model

```
>>> import simuPOP as sim
>>> import random
>>> def incAllele(allele):
...     return allele + random.randint(1, 5)
...
>>> simu = sim.simulator(sim.population(size=1000, loci=[20]),
...     sim.randomMating())
>>> simu.evolve(
...     initOps = sim.initSex(),
...     postOps = sim.pyMutator(func=incAllele, rates=[1e-4, 1e-3],
...         loci=[2, 10]),
...     gen = 1000
... )
(1000,)
>>> # count the average number tandem repeats at both loci
>>> def avgAllele(pop, loc):
...     ret = 0
...     for ind in pop.individuals():
...         ret += ind.allele(loc, 0) + ind.allele(loc, 1)
...     return ret / (pop.popSize() * 2.)
...
>>> pop = simu.population(0)
>>> print 'Average number of repeats at two loci are %.2f and %.2f.' % \
...       (avgAllele(pop, 2), avgAllele(pop, 10))
Average number of repeats at two loci are 0.00 and 3.22.
```

### 3.5.7 Mixed mutation models (mixedMutator)\*\*

Mixed mutation models are sometimes used to model real data. For example, a  $k$ -allele model can be used to explain extremely large or small number of tandem repeats at a microsatellite marker which are hard to justify using a standard stepwise mutation model. A mixed mutation model would apply two or more mutation models at pre-specified probabilities.



A `mixedMutator` is constructed by a list of mutators and their respective probabilities. It accepts regular mutator parameters such as `rates`, `loci`, `subPops`, `mapIn` and `mapOut` and mutates alleles at specified rate. When a mutation event happens, it calls one of the mutators to mutate the allele. For example, Example 3.30 applies a mixture of  $k$ -allele model and stepwise model to mutate a microsatellite model.

Example 3.30: A mixed  $k$ -allele and stepwise mutation model

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(5000, loci=[1, 1]),
...     sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([50, 50])
...     ],
...     preOps = [
...         # the first locus uses a pure stepwise mutation model
...         sim.smmMutator(rates=0.001, loci=0),
...         # the second locus uses a mixed model
...         sim.mixedMutator(rates=0.001, loci=1, mutators=[
...             sim.kamMutator(rates=1, k=100),
...             sim.smmMutator(rates=1)
...         ], prob=[0.1, 0.9])),
...     gen = 20
... )
(20,)
>>> # what alleles are there?
>>> geno0 = []
>>> geno1 = []
>>> for ind in simu.population(0).individuals():
...     geno0.extend([ind.allele(0, 0), ind.allele(0, 1)])
...     geno1.extend([ind.allele(1, 0), ind.allele(1, 1)])
...
>>> print 'Locus 0 has alleles', ', '.join([str(x) for x in set(geno0)])
Locus 0 has alleles 49, 50, 51
>>> print 'Locus 1 has alleles', ', '.join([str(x) for x in set(geno1)])
Locus 1 has alleles 88, 49, 50, 51, 79
```

When a mutation event happens, mutators in Example 3.30 mutate the allele with probability (mutation rate) 1. If different mutation rates are specified, the overall mutation rates would be the product of mutation rate of `mixedMutator` and the passed mutators. However, it is extremely important to understand that although `mixedMutator(rates=mu)` with `smmMutator(rates=1)` and `mixedMutator(rates=1)` with `smmMutator(rates=mu)` mutate alleles at the same mutation rate, the former is much more efficient because it triggers far less mutation events.

### 3.5.8 Context-dependent mutation models (`contextMutator`)\*\*

All mutation models we have seen till now are context independent. That is to say, how an allele is mutated depends only on the allele itself. However, it is understood that DNA and amino acid substitution rates are highly sequence context-dependent, e.g.,  $C \rightarrow T$  substitutions in vertebrates may occur much more frequently at CpG sites. To simulate such models, a mutator must consider the context of a mutated allele, e.g. certain number of alleles to the left and right of this allele, and mutate the allele accordingly.

A `contextMutator` can be used to mutate an allele depending on its surrounding loci. This mutator is constructed by a list of mutators and their respective contexts. It accepts regular mutator parameters such as `rates`, `loci`, `subPops`, `mapIn` and `mapOut` and mutates alleles at specified rate. When a mutation event happens, it checks the context of the mutated allele and choose a corresponding mutator to mutate the allele. An additional mutator can be

specified to mutate alleles with unknown context. Example 3.31 applies two `snpMutator` at different rates under different contexts.

Example 3.31: A context-dependent mutation model

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(5000, loci=[3, 3]),
...     sim.randomMating())
>>> simu.evolve(
...     # initialize locus by 0, 0, 0, 1, 0, 1
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([1, 1], loci=[3, 5])
...     ],
...     preOps = [
...         sim.contextMutator(mutators=[
...             sim.snpMutator(u=0.1),
...             sim.snpMutator(u=1),
...         ],
...         contexts=[(0, 0), (1, 1)],
...         loci=[1, 4],
...         rates=0.01
...     ),
...     sim.stat(alleleFreq=[1, 4], step=5),
...     sim.pyEval(r'''Gen: %2d freq1: %.3f, freq2: %.3f\n''' +
...         " % (gen, alleleFreq[1][1], alleleFreq[4][1])", step=5)
...     ],
...     gen = 20
... )
Gen: 0 freq1: 0.001, freq2: 0.010
Gen: 5 freq1: 0.008, freq2: 0.060
Gen: 10 freq1: 0.011, freq2: 0.113
Gen: 15 freq1: 0.015, freq2: 0.156
(20,)
```

Note that although

```
contextMutator(mutators=[
    snpMutator(u=0.1),
    snpMutator(u=1)],
contexts=[(0, 0), (1, 1)],
rates=0.01
)
```

and

```
contextMutator(mutators=[
    snpMutator(u=0.001),
    snpMutator(u=0.01)],
contexts=[(0, 0), (1, 1)],
rates=1
)
```

both apply two `snpMutator` at mutation rates 0.001 and 0.01, the former is more efficient because it triggers less mutation events.

Context-dependent mutator can also be implemented by a `pyMutator`. When a non-zero parameter `context` is specified, this mutator will collect `context` number of alleles to the left and right of a mutated allele and pass them as a second parameter of the user-provided mutation function. Example 3.32 applies the same mutation model as Example 3.31 using a `pyMutator`.

Example 3.32: A hybrid context-dependent mutation model

```
>>> import simuPOP as sim
>>> import random
>>> simu = sim.simulator(sim.population(5000, loci=[3, 3]),
...     sim.randomMating())
>>> def contextMut(allele, context):
...     if context == [0, 0]:
...         if allele == 0 and random.random() < 0.1:
...             return 1
...     elif context == [1, 1]:
...         if allele == 0:
...             return 1
...     # do not mutate
...     return allele
>>> simu.evolve(
...     # initialize locus by 0, 0, 0, 1, 0, 1
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([1, 1], loci=[3, 5])
...     ],
...     preOps = [
...         sim.pyMutator(func=contextMut, context=1,
...             loci=[1, 4], rates=0.01
...         ),
...         #sim.snpMutator(u=0.01, v= 0.01, loci=[1, 4]),
...         sim.stat(alleleFreq=[1, 4], step=5),
...         sim.pyEval(r"'Gen: %2d freq1: %.3f, freq2: %.3f\n'" +
...             " % (gen, alleleFreq[1][1], alleleFreq[4][1])", step=5)
...     ],
...     gen = 20
... )
Gen:  0 freq1: 0.001, freq2: 0.010
Gen:  5 freq1: 0.006, freq2: 0.056
Gen: 10 freq1: 0.008, freq2: 0.090
Gen: 15 freq1: 0.015, freq2: 0.144
(20,)
```

### 3.5.9 Manually-introduced mutations (pointMutator)

Operator `pointMutator` is different from all other mutators in that it mutates specified alleles of specified individuals. It is usually used to manually introduce one or more mutants to a population. Although it is not a recommended method to introduce a disease predisposing allele, the following example (Example 3.33) demonstrates an evolutionary process where mutants are repeatedly introduced and raised by positive selection until it reaches an appreciable allele frequency. This example uses two `ifElse` operators. The first one introduces a mutant when there is no mutant in the population, and the second one terminate the evolution when the frequency of the mutant reaches 0.05.

Example 3.33: Use a point mutator to introduce a disease predisposing allele

```
>>> import simuPOP as sim
>>> pop = sim.population(1000, loci=1, infoFields='fitness')
>>> simu = sim.simulator(pop, sim.randomSelection())
>>> simu.evolve(
...     initOps = sim.pyOutput('Introducing alleles at generation'),
...     preOps = sim.maSelector(loci=0, wildtype=0, fitness=[1, 1.05, 1.1]),
...     postOps = [
...         sim.stat(alleleFreq=0),
```

```

...     sim.ifElse('alleleNum[0][1] == 0', ifOps=[
...         sim.pyEval(r"' %d' % gen"),
...         sim.pointMutator(inds=0, loci=0, allele=1),
...     ]),
...     sim.ifElse('alleleFreq[0][1] > 0.05', ifOps=[
...         sim.pyEval(r"'\nTerminate at generation %d at allele freq %.3f.\n'" +
...             " % (gen, alleleFreq[0][1])"),
...         sim.terminateIf('True'),
...     ])
... ]
... )
Introducing alleles at generation 0 1 2 16 17 18 22 30 32 33 34 41 81 82 83.
Terminate at generation 111 at allele freq 0.051.
(112,)

```

### 3.5.10 Apply mutation to (virtual) subpopulations \*

A mutator is usually applied to all individuals in a population. However, you can restrict its use to specified subpopulations and/or virtual subpopulations using parameter `subPop`. For example, you can use `subPop=[0, 2]` to apply the mutator only to individuals in subpopulations 0 and 2.

Virtual subpopulations can also be specified in this parameter. For example, you can apply different mutation models to male and female individuals, to unaffected or affected individuals, to patients at different stages of a cancer. Example 3.34 demonstrate a mutation model where individuals with more tandem repeats at a disease predisposing locus are more likely to develop a disease (e.g. fragile-X). Affected individuals are then subject to a non-neutral mutation model at an accelerated mutation rate.

Example 3.34: Applying mutation to virtual subpopulations.

```

>>> import simuPOP as sim
>>> def fragileX(geno, gen):
...     '''A disease model where an individual has increased risk of
...     affected if the number of tandem repeats exceed 75.
...     '''
...     # Alleles A1, A2.
...     maxRep = max(geno)
...     if maxRep < 50:
...         return 0
...     else:
...         # individuals with allele >= 70 will surely be affected
...         return min(1, (maxRep - 50)*0.05)
...
>>> def avgAllele(pop):
...     'Get average allele by affection sim.status.'
...     sim.Stat(pop, alleleFreq=(0,1), subPops=[(0,0), (0,1)],
...         numOfAffected=True, vars=['alleleNum', 'alleleNum_sp'])
...     avg = []
...     for alleleNum in [\
...         pop.dvars((0,0)).alleleNum[0], # first locus, unaffected
...         pop.dvars((0,1)).alleleNum[0], # first locus, affected
...         pop.dvars().alleleNum[1],      # second locus, overall
...     ]:
...         alleleSum = numAllele = 0
...         for idx,cnt in enumerate(alleleNum):
...             alleleSum += idx * cnt
...             numAllele += cnt
...         if numAllele == 0:
...             avg.append(0)

```

```

...         else:
...             avg.append(alleleSum * 1.0 / numAllele)
...             # unaffected, affected, loc2
...             pop.dvars().avgAllele = avg
...         return True
...
>>> pop = sim.population(10000, loci=[1, 1])
>>> pop.setVirtualSplitter(sim.affectionSplitter())
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([50, 50])
...     ],
...     postOps = [
...         # determine affection sim.status for each offspring (duringMating)
...         sim.pyPenetrance(func=fragileX, loci=0),
...         # unaffected offspring, mutation rate is high to save some time
...         sim.smmMutator(rates=1e-3, loci=1),
...         # unaffected offspring, mutation rate is high to save some time
...         sim.smmMutator(rates=1e-3, loci=0, subPops=[(0, 0)]),
...         # affected offspring have high probability of mutating upward
...         sim.smmMutator(rates=1e-2, loci=0, subPops=[(0, 1)],
...             incProb=0.7, mutStep=3),
...         # number of affected
...         sim.pyOperator(func=avgAllele, step=20),
...         sim.pyEval(r'''Gen: %3d #Aff: %d AvgRepeat: %.2f (unaff), %.2f (aff), %.2f (unrelated)\n
...             + " % (gen, numOfAffected, avgAllele[0], avgAllele[1], avgAllele[2])",
...             step=20),
...     ],
...     gen = 101
... )
Gen:  0 #Aff: 0 AvgRepeat: 1.01 (unaff), 0.00 (aff), 1.01 (unrelated)
Gen: 20 #Aff: 6 AvgRepeat: 1.53 (unaff), 0.50 (aff), 1.52 (unrelated)
Gen: 40 #Aff: 25 AvgRepeat: 2.56 (unaff), 1.53 (aff), 1.01 (unrelated)
Gen: 60 #Aff: 47 AvgRepeat: 2.57 (unaff), 1.03 (aff), 2.04 (unrelated)
Gen: 80 #Aff: 40 AvgRepeat: 2.56 (unaff), 1.02 (aff), 2.04 (unrelated)
Gen: 100 #Aff: 53 AvgRepeat: 3.08 (unaff), 2.05 (aff), 2.04 (unrelated)
(101,)

```

At the beginning of a simulation, all individuals have 50 copies of a tandem repeat and the mutation follows a standard neutral stepwise mutation model. Individuals with more than 50 repeats will have an increasing probability to develop a disease ( $\Pr(\text{affected} | n) = (n - 50) * 0.05$  for  $50 \leq n \leq 70$ ). The average repeat number therefore increases for affected individuals. In contrast, the mean number of repeats at locus 1 on a separate chromosome oscillate around 50.

### 3.5.11 Allele mapping \*\*

If alleles in your simulation do not follow the convention of a mutation model, you may want to use the `pop.recodeAlleles()` function to recode your alleles so that appropriate mutation models could be applied. If this is not possible, you can use a general mutation model with your own mutation matrix, or an advanced feature called **allele mapping**.

Allele mapping is done through two parameters *mapIn* and *mapOut*, which map alleles in your population to and from alleles assumed in a mutation model. For example, an `acgtMutator` mutator assumes alleles A, C, G and T for alleles 0, 1, 2, and 3 respectively. If for any reason the alleles in your application does not follow this order, you will need to map these alleles to the alleles assumed in the mutator. For example, if you assumes C, G, A, T for alleles 0, 1, 2, and 3 respectively, you can use parameters

```
mapIn=[1, 2, 0, 3], mapOut=[2, 0, 1, 3]
```

to map your alleles (C (0) → C (1), G (1) → G (2), A (2) → A (0), T (3) → T (3)) to alleles `acgtMutator` assumes, and then map mutated alleles (A (0) → A (2), C (1) → C (0), G (2) → G (1), T (3) → T (3)) back. Example 3.35 gives another example where alleles 4, 5, 6 and 7 are mutated using a 4-allele model.

Example 3.35: Allele mapping for mutation operators

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[2000], loci=1)
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0]*4 + [0.1, 0.2, 0.3, 0.4])
...     ],
...     postOps = [
...         sim.kamMutator(k=4, rates=1e-4, mapIn=[0]*4 + range(4),
...             mapOut=[4, 5, 6, 7]),
...         sim.stat(alleleFreq=0, step=100),
...         sim.pyEval(r"','.join(['%.2f' % alleleFreq[0][x] for x in range(8)]) + '\n'",
...             step=100),
...     ],
...     gen=500
... )
0.00, 0.00, 0.00, 0.00, 0.09, 0.20, 0.30, 0.41
0.00, 0.00, 0.00, 0.00, 0.16, 0.14, 0.42, 0.28
0.00, 0.00, 0.00, 0.00, 0.18, 0.07, 0.41, 0.34
0.00, 0.00, 0.00, 0.00, 0.24, 0.11, 0.42, 0.23
0.00, 0.00, 0.00, 0.00, 0.25, 0.07, 0.51, 0.17
(500,)
```

These two parameters also accept Python functions which should return corresponding mapped-in or out allele for a given allele. These two functions can be used to explore very fancy mutation models. For example, you can categorize a large number of alleles into alleles assumed in a mutation model, and emit random alleles from a mutated allele.

### 3.5.12 Mutation rate and transition matrix of a `matrixMutator` \*\*

A `matrixMutator` is specified by a mutation rate matrix. Although mutation rates of this mutator is typically allele-dependent, the `matrixMutator` is implemented as a two-step process where mutation events are triggered independent to allelic states. This section describes these two steps which can be useful if you need to use a `matrixMutator` in a `mixedMutator` or `contextMutator`, and would like to factor out an allele-independent mutation rate to the wrapper mutator.

Because alleles usually have different probabilities of mutating to other alleles, **a mutation process is usually allele dependent**. Given a mutation model ( $p_{ij}$ ), it is obviously inefficient to go through all mutable alleles and determine whether or not to mutate it using  $p_{ij}$ ,  $j = 0, \dots, 1 - n$ . `simuPOP` uses a two step procedure to mutate a large number of alleles. More specifically, for each mutation model, we determine  $\mu = \max_{i=0}^{n-1} (1 - p_{ii})$  as the overall mutation rate, and then

1. For each allele, trigger a mutation event with probability  $\mu$ . Because  $\mu$  is usually very small and is the same for all alleles, this step can be implemented efficiently.
2. When a mutation event happens, mutation allele  $i$  to allele  $j$  with probability

$$\Pr(i \rightarrow j) = \begin{cases} 1 - \frac{1}{\mu} (1 - p_{ii}) & \text{if } i = j \\ \frac{p_{ij}}{\mu} & \text{if } i \neq j \end{cases}$$

Because steps 1 and 2 are independent, it is easy to verify that

$$p_{ij} = \mu \Pr(i \rightarrow j)$$

if  $i \neq j$  and

$$p_{ii} = (1 - \mu) + \mu \Pr(i \rightarrow i)$$

where the first and second items are probabilities of no-mutation at steps 1 and 2.  $\mu$  was chosen as the smallest  $\mu$  that makes  $0 \leq \Pr(i \rightarrow i) \leq 1$  for all  $i$ .

For example, for a  $k$ -allele model with

$$p_{ij} = \begin{pmatrix} 1 - \mu & \frac{\mu}{k-1} & \cdots & \frac{\mu}{k-1} \\ \frac{\mu}{k-1} & 1 - \mu & \cdots & \frac{\mu}{k-1} \\ \vdots & \vdots & \ddots & \vdots \\ \frac{\mu}{k-1} & \frac{\mu}{k-1} & \cdots & 1 - \mu \end{pmatrix}$$

$\mu$  is directly  $\mu$  for the first step and

$$\Pr(i \rightarrow j) = \begin{cases} 0 & \text{if } i = j \\ \frac{1}{k-1} & \text{if } i \neq j \end{cases}$$

for the second step. Therefore, mutation rate  $\mu$  in a  $k$ -allele model could be interpreted as the probability of mutation, and a mutation event would mutate an allele to any other allele with equal probability.

For a classical mutation model with  $P(A \rightarrow a) = u$  and  $P(a \rightarrow A) = v$ ,

$$p_{ij} = \begin{pmatrix} 1 - u & u \\ v & 1 - v \end{pmatrix}$$

if  $u = 0.001$  and  $v = 0.0005$ ,  $\mu = \max(u, v) = 0.001$ ,

$$\Pr(i \rightarrow j) = \begin{pmatrix} 0 & 1 \\ \frac{v}{u} = 0.5 & 1 - \frac{v}{u} = 0.5 \end{pmatrix}$$

That is to say, we would mutate at a mutation rate  $u = 0.001$ , mutate allele  $A$  to  $a$  with probability 1 and mutate allele  $a$  to  $A$  with probability 0.5.

### 3.5.13 Infinite-sites model and other simulation techniques \*\*

Infinite-sites and infinite-alleles models have some similarities. In some cases, you can treat a long chromosomal region as a locus and use the infinite-alleles model, actually a  $k$ -allele model with large  $k$ , to mimic the infinite-site model. Because there is supposed to be only one mutant at each site, you can assign a unique *location* for each allele of an infinite-allele model and convert multi-allelic datasets simulated by an infinite-allele model to sequences of diallelic markers. It worth noting that mutation rates are interpreted differently for these two models, and there is no way to recombine in such a region because it is represented as a single allele.

If specific location of such a mutation is needed, it is possible to record the location of mutations during an evolution and mimic an infinite-sites model. For example, alleles in Example 3.36 are used to store location of a mutation event. When a mutation event happens, the location of the new allele (rather the allele itself) is recorded on the chromosome (actually list of mutation events) of an individual. The transmission of chromosomes proceed normally and effectively transmit mutants from parents to offspring. At the end of the simulation, each individual accumulates a number of mutation events and they are essentially alleles at their respective locations.

Example 3.36: Mimicking an infinite-sites model using mutation events as alleles

```
>>> import simuOpt
>>> simuOpt.setOptions(alleleType='long')
>>> import simuPOP as sim
```

```

>>>
>>> def infSitesMutate(pop, param):
...     '''Apply an infinite mutation model'''
...     (startPos, endPos, rate) = param
...     # for each individual
...     for ind in pop.individuals():
...         # for each homologous copy of chromosomes
...         for p in range(2):
...             # using a geometric distribution to determine
...             # the first mutation location
...             loc = sim.GetRNG().randGeometric(rate)
...             # if a mutation happens, record the mutated location
...             if startPos + loc < endPos:
...                 try:
...                     # find the first non-zero location
...                     idx = ind.genotype(p).index(0)
...                     # record mutation here
...                     ind.setAllele(startPos + loc, idx, ploidy=p)
...                 except:
...                     print 'Warning: more than %d mutations have accumulated' % pop.totNumLoci()
...                     pass
...     return True
...
>>> pop = sim.population(size=[2000], loci=[100])
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = sim.initSex(),
...     preOps = [
...         # recombine in a 10Mb region at rate 1e-8
...         sim.pyOperator(func=infSitesMutate, param=(1, 10000000, 1e-8)),
...     ],
...     gen = 100
... )
(100,)
>>> # now, we get a sim.population. Let us have a look at the 'alleles'.
>>> pop = simu.extract(0)
>>> # print the first five mutation locations
>>> print pop.individual(0).genotype()[1:5]
[1527502, 4774892, 7979220, 3671118, 395142]
>>> # how many alleles are there (does not count 0)?
>>> print len(set(pop.genotype())) - 1
2700
>>> # Allele count a simple count of alleles.
>>> cnt = {}
>>> for allele in pop.genotype():
...     if allele == 0:
...         continue
...     if cnt.has_key(allele):
...         cnt[allele] += 1
...     else:
...         cnt[allele] = 1
...
>>> # highest allele frequency?
>>> print max(cnt.values()) * 0.5 / pop.popSize()
0.05475

```

All mutation models in `simuPOP` apply to existing alleles at pre-specified loci. However, if the location of loci cannot be determined beforehand, it is sometimes desired to create new loci as a result of mutation. A customized operator can be used for this purpose (see Example 2.32), but extra attention is needed to make sure that other operators are



applied to the correct loci because loci indexes will be changed with the insertion of new loci. This technique could also be used to simulate mutations over long sequences.

## 3.6 Penetrance

Penetrance is the probability for an individual to be affected with a disease conditioning on his or her genotype and other risk factors. A penetrance model calculates such a probability for an individual and assign affection status randomly according to this probability. For example, if an individual with genotype 10 has probability 0.2 to be affected according to a penetrance model, he or she will be affected with probability 0.2. Note that simuPOP supports only one affection status. If there are multiple affection outcomes involved, you can treat them as binary quantitative traits and use information fields to store them.

A penetrance operator can be applied before or after mating, to assign affection status to all individuals in the parental or offspring generation, respectively. It can also be applied during mating and assign affection status to each offspring. The latter could be used to assist natural selection through the selection of offspring. You can also assign affection status to all individuals in a population using the function form of a penetrance operator (e.g. function `MapPenetrance` for operator `mapPenetrance`). Compared the penetrance operators that assign affection status to only the current generation, **these functions by default assign affection status to all ancestral generations as well.**

A penetrance operator usually do not store the penetrance values. However, if an information field is given, penetrance values will be saved to this information field before it is used to determine individual affection status.

### 3.6.1 Map penetrance model (operator `mapPenetrance`)

A map penetrance operator uses a Python dictionary to provide penetrance values for each type of genotype. For example, Example 3.37 uses a dictionary with keys (0,0), (0,1) and (1,1) to specify penetrance for individuals with these genotypes at locus 0.

Example 3.37: A penetrance model that uses pre-defined fitness value

```
>>> import simuPOP as sim
>>> pop = sim.population(size=2000, loci=2)
>>> sim.InitByFreq(pop, [.2, .8])
>>> sim.MapPenetrance(pop, loci=0,
...     penetrance={(0,0):0, (0,1):.2, (1,1):.3})
>>> sim.Stat(pop, genoFreq=0, numOfAffected=1, vars='genoNum')
>>> # number of affected individuals
>>> pop.dvars().numOfAffected
519
>>> # which should be roughly (#01 + #10) * 0.2 + #11 * 0.3
>>> (pop.dvars().genoNum[0][(0,1)] + pop.dvars().genoNum[0][(1,0)]) * 0.2 \
... + pop.dvars().genoNum[0][(1,1)] * 0.3
514.10000000000002
```

The above example assumes that penetrance for individuals with genotypes (0,1) and (1,0) are the same. This assumption is usually valid but can be violated with imprinting. In that case, you can specify fitness for both types of genotypes. The underlying mechanism is that the `mapPenetrance` looks up a genotype in the dictionary first directly, and then without phase information if a genotype is not found.

This operator supports haplodiploid populations and sex chromosomes. In these cases, only valid alleles should be listed which can lead to dictionary keys with different lengths. In addition, although less used because of potentially a large number of keys, this operator can act on multiple loci. For example,

- keys (a1,a2) and (a1,) can be used to specify fitness values for female and male individuals in a haplodiploid population, respectively

- keys (x1,x2) and (x1,) can be used to specify fitness for female and male individuals according to a locus on the X chromosome in a diploid population, respectively. Similarly, keys (y) and (y,) for a locus on chromosome Y.
- keys (a1,a2,b1,b2) can be used to specify fitness values according to genotype at two loci in a diploid population.

### 3.6.2 Multi-allele penetrance model (operator `maPenetrance`)

A multi-allele penetrance model divides alleles into two groups, wildtype *A* and mutants *a*, and treat alleles within each group as the same. The penetrance model is therefore simplified to

- Two fitness values for genotype *A*, *a* in the haploid case
- Three fitness values for genotype *AA*, *Aa* and *aa* in the diploid single locus case. Genotype *Aa* and *aA* are assumed to have the same impact on fitness.

The default wildtype group contains allele 0 so the two allele groups are zero and non-zero alleles. Example 3.38 demonstrates the use of this operator.

Example 3.38: A multi-allele penetrance model

```
>>> import simuPOP as sim
>>> pop = sim.population(5000, loci=3)
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.9] + [0.02]*5)
...     ],
...     postOps = [
...         sim.maPenetrance(loci=0, penetrance=(0.01, 0.2, 0.3)),
...         sim.stat(numOfAffected=True, vars='propOfAffected'),
...         sim.pyEval(r"Gen: %d Prevalence: %.1f%%\n" % (gen, propOfAffected*100)),
...     ],
...     gen = 5
... )
Gen: 0 Prevalence: 4.6%
Gen: 1 Prevalence: 4.7%
Gen: 2 Prevalence: 4.7%
Gen: 3 Prevalence: 4.1%
Gen: 4 Prevalence: 4.2%
(5,)
```

Operator `maPenetrance` also supports multiple loci by specifying fitness values for all combination of genotype at specified loci. In the case of two loci, this operator requires

- Four fitness values for genotype *AB*, *Ab*, *aB* and *ab* in the haploid case,
- Nine fitness values for genotype *AABB*, *AABb*, *AAbb*, *AaBB*, *AaBb*, *Aabb*, *aaBB*, *aaBb*, and *aabb* in the haploid case.

In general,  $2^n$  values are needed for haploid populations and  $3^n$  values are needed for diploid populations where  $n$  is the number of loci. This operator does not yet support haplodiploid populations and sex chromosomes.

### 3.6.3 Multi-loci penetrance model (operator `mlPenetrance`)

Although an individual's affection status can be affected by several factors, each of which can be modeled individually, **only one penetrance value is used to determine a person's affection status** and we have to use a multi-locus penetrance model to combine single-locus models.

This multi-loci penetrance model applies several penetrance models to each individual and computes an overall penetrance value from the penetrance values provided by these operators. Although this selector is designed to obtain multi-loci penetrance values from several single-locus penetrance models, any penetrance operator, including those obtain their penetrance values from multiple disease predisposing loci, can be used in this operator. This operator uses parameter `mode` to control how individual penetrance values are combined. More specifically, if  $f_i$  are penetrance values obtained from individual selectors, this selector returns

- $\prod_i f_i$  if `mode=MULTIPLICATIVE`, and
- $\sum_i f_i$  if `mode=ADDITIVE`, and
- $1 - \prod_i (1 - f_i)$  if `mode=HETEROGENEITY`

0 or 1 will be returned if the returned fitness value is out of range of  $[0, 1]$ .

Example 3.39 demonstrates the use of this operator using an multiplicative multi-locus model over three additive single-locus models at three disease predisposing loci.

Example 3.39: A multi-loci penetrance model

```
>>> import simuPOP as sim
>>> pop = sim.population(5000, loci=3)
>>> sim.InitByFreq(pop, [0.2]*5)
>>> # the multi-loci penetrance
>>> sim.MlPenetrance(pop, mode=sim.MULTIPLICATIVE,
...     ops = [sim.maPenetrance(loci=loc,
...     penetrance=[0, 0.3, 0.6]) for loc in range(3)])
>>> # count the number of affected individuals.
>>> sim.Stat(pop, numOfAffected=True)
>>> pop.dvars().numOfAffected
537
```

### 3.6.4 Hybrid penetrance model (operator `pyPenetrance`)

When your selection model involves multiple interacting genetic and environmental factors, it might be easier to calculate a penetrance value explicitly using a Python function. A hybrid penetrance operator can be used for this purpose. If your penetrance model depends solely on genotype, you can define a function such as

```
def pfunc(genotype, gen):
    # calculate penetrance according to genotype at specified loci
    return val
```

and use this function in an operator `pySelector(func=pfunc, loci=loci)`. If your penetrance model depends on genotype as well as some information fields, you can define a function in the form of

```
def pfunc(genotype, fields, gen):
    # calculate penetrance according to genotype at specified loci
    # and values at specified informaton fields.
    return val
```

and use this function in an operator `pySelector(func=pfunc, loci=loci, paramFields=fields)`.

When a `pyPenetrance` operator is used to calculate penetrance for an individual, it will collect his or her genotype at specified loci, optional values at specified information fields, and the generation number to a user-specified Python function, and take its return value as penetrance. As you can imagine, the incorporation of information fields and generation number allow the implementation of very complex penetrance scenarios such as gene environment interaction and varying selection pressures. Note that this operator does not pass sex and affection status to the user-defined function. If your selection model is sex-dependent, you can define an information field `sex`, synchronize its value with individual sex (e.g. using operator `infoExec('sex=ind.sex()', exposeInd='ind')`) and pass this information to the user-defined function (`pySelector(func=func, paramFields='sex')`).

Example 3.48 demonstrates how to use a `pyPenetrance` to specify penetrance values according to a fitness table and the smoking status of each individual. In this example, individual risk is doubled when he or she smokes. The disease prevalence is therefore much higher in smokers than in non-smokers.

Example 3.40: A hybrid penetrance model

```
>>> import simuPOP as sim
>>> import random
>>> pop = sim.population(size=2000, loci=[1]*2, infoFields=['p', 'smoking'])
>>> pop.setVirtualSplitter(sim.infoSplitter(field='smoking', values=[0,1]))
>>> simu = sim.simulator(pop, sim.randomMating())
>>> # the second parameter gen can be used for varying selection pressure
>>> def penet(arr, smoking, gen):
...     #      BB      Bb      bb
...     # AA  0.01   0.01   0.01
...     # Aa  0.01   0.03   0.03
...     # aa  0.01   0.03   0.05
...     #
...     # arr is (A1 A2 B1 B2)
...     if arr[0] + arr[1] == 1 and arr[2] + arr[3] != 0:
...         v = 0.03 # case of AaBb
...     elif arr[0] + arr[1] == 2 and arr[2] + arr[3] == 1:
...         v = 0.03 # case of aaBb
...     elif arr[0] + arr[1] == 2 and arr[2] + arr[3] == 2:
...         v = 0.05 # case of aabb
...     else:
...         v = 0.01 # other cases
...     if smoking[0]:
...         return v * 2
...     else:
...         return v
...
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq(alleleFreq=[.5, .5]),
...         sim.pyOutput('Calculate prevalence in smoker and non-smokers'),
...     ],
...     postOps = [
...         # set smoking status randomly
...         sim.initInfo(lambda : random.randint(0,1), infoFields='smoking'),
...         # assign affection status
...         sim.pyPenetrance(loci=[0, 1], func=penet, paramFields='smoking'),
...         sim.stat(numOfAffected=True, subPops=[(0,0), (0,1)],
...             vars='propOfAffected_sp', step=20),
...         sim.pyEval(r'''Non-smoker: %.2f%%\tSmoker: %.2f%%\n' % "
...             "(subPop[(0,0)]['propOfAffected']*100, subPop[(0,1)]['propOfAffected']*100)",
...             step=20)
...     ],
...     gen = 50
```

```

... )
Calculate prevalence in smoker and non-smokersNon-smoker: 1.88% Smoker: 4.94%
Non-smoker: 2.39%      Smoker: 4.12%
Non-smoker: 1.86%      Smoker: 4.91%
(50,)
>>>

```

## 3.7 Quantitative trait

Quantitative traits are naturally stored in information fields of each individual. A quantitative trait operator assigns quantitative trait fields according to individual genetic (genotype) and environmental (other information fields) information. Although a large number of quantitative trait models have been used in theoretical and empirical studies, no model is popular enough to deserve a specialized operator. Therefore, only one hybrid operator is currently provided in simuPOP.

### 3.7.1 A hybrid quantitative trait operator (operator `pyQuanTrait`)

Operator `pyQuanTrait` accepts a user defined function that returns quantitative trait values for specified information fields. This operator uses parameter `infoFields` to specify one or more trait fields, and `paramFields` to specify additional information that will be passed to the user-defined function. Depending on the value of parameter `paramFields`, the function can have form `func(genotype, gen)` or `func(genotype, fields, gen)`.

A quantitative trait operator can be applied before or after mating and assign values to the trait fields of all parents or offspring, respectively. It can also be applied during mating to assign trait values to offspring. Example 3.41 demonstrates the use of this operator, using two trait fields `trait1` and `trait2` which are determined by individual genotype and age. This example also demonstrates how to calculate statistics within virtual subpopulations (defined by age).

Example 3.41: A hybrid quantitative trait model

```

>>> import simuPOP as sim
>>> import random
>>> pop = sim.population(size=5000, loci=2, infoFields=['qtrait1', 'qtrait2', 'age'])
>>> pop.setVirtualSplitter(sim.infoSplitter(field='age', cutoff=[40]))
>>> simu = sim.simulator(pop, sim.randomMating())
>>> def qtrait(geno, age, gen):
...     'Return two traits that depends on genotype and age'
...     return random.normalvariate(age[0] * sum(geno), 10), random.randint(0, 10*sum(geno))
...
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.2, 0.8]),
...     ],
...     postOps = [
...         # use random age for simplicity
...         sim.initInfo(lambda: random.randint(20, 75), infoFields='age'),
...         sim.pyQuanTrait(loci=(0,1), func=qtrait, paramFields='age',
...             infoFields=['qtrait1', 'qtrait2']),
...         sim.stat(meanOfInfo=['qtrait1'], subPops=[(0,0), (0,1)],
...             vars='meanOfInfo_sp'),
...         sim.pyEval(r'''Mean of trait1: %.3f (age < 40), %.3f (age >=40)\n' % "
...             "(subPop[(0,0)]['meanOfInfo'] ['qtrait1'], subPop[(0,1)] ['meanOfInfo'] ['qtrait1'])"
...         ],
...     ),
...     gen = 5

```

```

... )
Mean of trait1: 93.004 (age < 40), 182.701 (age >=40)
Mean of trait1: 94.130 (age < 40), 185.562 (age >=40)
Mean of trait1: 94.580 (age < 40), 185.927 (age >=40)
Mean of trait1: 95.694 (age < 40), 185.856 (age >=40)
Mean of trait1: 96.662 (age < 40), 187.308 (age >=40)
(5,)
>>>

```

## 3.8 Natural Selection

### 3.8.1 Natural selection through the selection of parents

In the simplest scenario, natural selection is implemented in two steps:

- Before mating happens, an operator (called a **selector**) goes through a populations and assign each individual a fitness value. The fitness values are stored in an information field called `fitness`.
- When mating happens, parents are chosen with probabilities that are proportional to their fitness values. For example, assuming that a parental population consists of four individuals with fitness values 1, 2, 3, and 4, respectively, the probability that they are picked to produce offspring are  $1/(1+2+3+4) = 0.1, 0.2, 0.3,$  and  $0.4$  respectively. As you can image, if the offspring population has 10 individuals, the four parents will on average parent 1, 2, 3 and 4 offspring.

Because parents with lower fitness values have less chance to be produce offspring, their genotypes have less chance to be passed to an offspring generation. If the decreased fitness is caused by the presence of certain mutant (e.g. a mutant causing a serious disease), individuals with that mutant will have less change to survive and effectivly reduce or eliminate that mutant from the population.

Example 3.42 gives an example of natural selection. In this example, a `mapSelector` is used to explicitly assign fitness value to genotypes at the first locus. The fitness values are 1, 0.98, 0.97 for genotypes 00, 01 and 11 respectively. The selector set individual fitness values to information field `fitness` before mating happens. The `randomMating` mating scheme then selects parents according to parental fitness values.

Example 3.42: Natural selection through the selection of parents

```

>>> import simuPOP as sim
>>> pop = sim.population(4000, loci=1, infoFields='fitness')
>>> simu = sim.simulator(pop, sim.randomMating(), rep=3)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5])
...     ],
...     preOps = sim.mapSelector(loci=0, fitness={(0,0):1, (0,1):0.98, (1,1):0.97}),
...     postOps = [
...         sim.stat(alleleFreq=0, step=10),
...         sim.pyEval('"Gen:%3d ' % gen", reps=0, step=10),
...         sim.pyEval(r'"%.3f\t' % alleleFreq[0][1]", step=10),
...         sim.pyOutput('\n', reps=-1, step=10)
...     ],
...     gen = 50
... )
Gen: 0 0.490 0.492 0.487
Gen: 10 0.433 0.430 0.431
Gen: 20 0.403 0.390 0.419

```

```
Gen: 30 0.343    0.325    0.383
Gen: 40 0.303    0.297    0.334
(50, 50, 50)
```

**Note:** The selection algorithm used in simuPOP is called *fitness proportionate selection*, or *roulette-wheel selection*. simuPOP does not use the more efficient *stochastic universal sampling* algorithm because the number of needed offspring is unknown in advance.

### 3.8.2 Natural selection through the selection of offspring \*

Natural selection can also be implemented as selection of offspring. Remember that an individual will be discarded if one of the during-mating operators fails (return `False`), **a during-mating selector discards offspring according to fitness values of offspring**. Instead of relative fitness that will be compared against other individuals during the selection of parents, **fitness values of a during-mating selector are considered as absolute fitness which are probabilities to survive** and have to be between 0 and 1.

A during-mating selector works as follows:

1. During evolution, parents are chosen randomly to produce one or more offspring. (Nothing prevents you from choosing parents according to their fitness values, but it is rarely justifiable to apply natural selection to both parents and offspring.)
2. A selection operator is applied to each offspring during mating and determines his or her fitness value. The fitness value is considered as probability to survive so an offspring will be discarded (operator returns `False`) if the fitnessvalue is larger than an uniform random number.
3. Repeat steps 1 and 2 until the offspring generation is populated.

Because many offspring will be generated and discarded, especially when offspring fitness values are low, selection through offspring is less efficient than selection through parents. In addition, absolute fitness is usually more difficult to estimate than relative fitness. So, unless there are compelling reasons (e.g. simulating realistic scenarios of survival competition among offspring), selection through parents are recommended.

Example 3.43 gives an example of natural selection through the selection of offspring. This example looks almost identical to Example 3.42 but the underlying selection mechanism is quite different. Note that selection through offspring does not need an information field to hold fitness values.

Example 3.43: Natural selection through the selection of offspring

```
>>> import simuPOP as sim
>>> pop = sim.population(10000, loci=1)
>>> simu = sim.simulator(pop, sim.randomMating(), rep=3)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5])
...     ],
...     duringOps = sim.mapSelector(loci=0, fitness={(0,0):1, (0,1):0.98, (1,1):0.97}),
...     postOps = [
...         sim.stat(alleleFreq=0, step=10),
...         sim.pyEval("'Gen:%3d ' % gen", reps=0, step=10),
...         sim.pyEval(r"'%.3f\t' % alleleFreq[0][1]", step=10),
...         sim.pyOutput('\n', reps=-1, step=10)
...     ],
...     gen = 50
... )
Gen: 0 0.493    0.493    0.496
Gen: 10 0.461    0.464    0.465
```

Gen: 20	0.436	0.445	0.442
Gen: 30	0.389	0.386	0.385
Gen: 40	0.370	0.345	0.348
(50, 50, 50)			

### 3.8.3 Are two selection scenarios equivalent? \*\*

If you look closely at Examples 3.42 and 3.43, you will notice that their results are quite similar. This is actually what you should expect in most cases. Let us look at the theoretical consequence of selection through parents or offspring in a simple case with asexual mating.

Assuming a diallelic marker with three genotypes  $g_{AA}$ ,  $g_{Aa}$  and  $g_{aa}$ , with frequencies  $P_{AA}$ ,  $P_{Aa}$  and  $P_{aa}$ , and relative fitness values  $w_{AA}$ ,  $w_{Aa}$ , and  $w_{aa}$  respectively. If we select through offspring, the proportion of genotype  $g_{AA}$  etc., should be

$$P'_{AA} = \frac{P_{AA}w_{AA}}{P_{AA}w_{AA} + P_{Aa}w_{Aa} + P_{aa}w_{aa}}$$

$$P'_{Aa} = \frac{P_{Aa}w_{Aa}}{P_{AA}w_{AA} + P_{Aa}w_{Aa} + P_{aa}w_{aa}}$$

$$P'_{aa} = \frac{P_{aa}w_{aa}}{P_{AA}w_{AA} + P_{Aa}w_{Aa} + P_{aa}w_{aa}}$$

because offspring genotypes are randomly drawn from the parental generation, and each offspring has certain probability to survive.

Now, if we select through parents, the proportion of parents with genotype  $AA$  will be the number of  $AA$  individuals times its probability to be chosen:

$$n_{AA} \frac{w_{AA}}{\sum_{n=1}^N w_n}$$

This is, however, exactly

$$n_{AA} \frac{w_{AA}}{\sum_{n=1}^N w_n} = \frac{n_{AA}w_{AA}}{n_{AA}w_{AA} + n_{Aa}w_{Aa} + n_{aa}w_{aa}} = \frac{P_{AA}w_{AA}}{P_{AA}w_{AA} + P_{Aa}w_{Aa} + P_{aa}w_{aa}} = P'_{AA}$$

which corresponds to the proportion of offspring with such genotype. That is to say, **in this simple case, two types of selection scenarios yield identical results.**

These two types of selection scenarios do not have to always yield identical results. Exceptions may be found in cases with more than one offspring or sexual mating with sex-specific survival rate. simuPOP provides both selection implementations and you should choose one of them for your particular simulation.

### 3.8.4 Map selector (operator mapSelector)

A map selector uses a Python dictionary to provide fitness values for each type of genotype. For example, Example 3.44 uses a dictionary with keys  $(0, 0)$ ,  $(0, 1)$  and  $(1, 1)$  to specify fitness values for individuals with these genotypes at locus 0. This example is a typical example of heterozygote advantage. When  $w_{11} < w_{12} > w_{22}$ , the genotype frequencies will go to an equilibrium state. Theoretically, if  $s_1 = w_{12} - w_{11}$  and  $s_2 = w_{12} - w_{22}$ , the stable allele frequency of allele 0 is

$$p = \frac{s_2}{s_1 + s_2}$$

which is  $\frac{2}{3}$  in the example ( $s_1 = .1$ ,  $s_2 = .2$ ).



Example 3.44: A selector that uses pre-defined fitness value

```
>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(size=1000, loci=1, infoFields='fitness'),
...     sim.randomMating())
>>> s1 = .1
>>> s2 = .2
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq(alleleFreq=[.2, .8])
...     ],
...     preOps = sim.mapSelector(loci=0, fitness={(0,0):1-s1, (0,1):1, (1,1):1-s2}),
...     postOps = [
...         sim.stat(alleleFreq=0),
...         sim.pyEval(r"'%.4f\n' % alleleFreq[0][0]", step=100)
...     ],
...     gen=301
... )
0.2250
0.6605
0.6530
0.6870
(301,)
>>>
```

The above example assumes that the fitness value for individuals with genotypes (0,1) and (1,0) are the same. This assumption is usually valid but can be violated with imprinting. In that case, you can specify fitness for both types of genotypes. The underlying mechanism is that the `mapSelector` looks up a genotype in the dictionary first directly, and then without phase information if a genotype is not found.

This operator supports haplodiploid populations and sex chromosomes. In these cases, only valid alleles should be listed which can lead to dictionary keys with different lengths. In addition, although less used because of potentially a large number of keys, this operator can act on multiple loci. Please refer to `mapPenetrance` for details.

### 3.8.5 Multi-allele selector (operator `maSelector`)

A multi-allele selector divides alleles into two groups, wildtype *A* and mutants *a*, and treat alleles within each group as the same. The fitness model is therefore simplified to

- Two fitness values for genotype *A*, *a* in the haploid case
- Three fitness values for genotype *AA*, *Aa* and *aa* in the diploid single locus case. Genotype *Aa* and *aA* are assumed to have the same impact on fitness.

The default wildtype group contains allele 0 so the two allele groups are zero and non-zero alleles. Example 3.45 demonstrates the use of this operator. This example is identical to Example 3.44 except that there are five alleles at locus 0 and alleles 1, 2, 3, 4 are treated as a single non-wildtype group.

Example 3.45: A multi-allele selector

```
>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(size=1000, loci=1, infoFields='fitness'),
...     sim.randomMating())
>>> s1 = .1
>>> s2 = .2
```

```

>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq(alleleFreq=[.2] * 5)
...     ],
...     preOps = sim.maSelector(loci=0, fitness=[1-s1, 1, 1-s2]),
...     postOps = [
...         sim.stat(alleleFreq=0),
...         sim.pyEval(r"'%.4f\n' % alleleFreq[0][0]", step=100)
...     ],
...     gen = 301)
0.2250
0.6605
0.6530
0.6870
(301,)

```

Operator `maSelector` also supports multiple loci by specifying fitness values for all combination of genotype at specified loci. In the case of two loci, this operator requires

- Four fitness values for genotype AB, Ab, aB and ab in the haploid case,
- Nine fitness values for genotype AABB, AABb, AAbb, AaBB, AaBb, Aabb, aaBB, aaBb, and aabb in the haploid case.

In general,  $2^n$  values are needed for haploid populations and  $3^n$  values are needed for diploid populations where  $n$  is the number of loci. This operator does not yet support haplodiploid populations and sex chromosomes. Example 3.46 demonstrates the use of a multi-locus model in a haploid population.

Example 3.46: A multi-locus multi-allele selection model in a haploid population

```

>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(size=10000, ploidy=1, loci=[1,1], infoFields='fitness'),
...     sim.randomSelection())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq(alleleFreq=[.5, .5])
...     ],
...     # fitness values for AB, Ab, aB and ab
...     preOps = sim.maSelector(loci=[0,1], fitness=[1, 1, 1, 0.95]),
...     postOps = [
...         sim.stat(haploFreq=[0, 1], step=25),
...         sim.pyEval(r"'%.3f\t%.3f\t%.3f\t%.3f\n' % (haploFreq[(0,1)][(0,0)],"
...             "haploFreq[(0,1)][(0,1)], haploFreq[(0,1)][(1,0)],"
...             "haploFreq[(0,1)][(1,1)])", step=25)
...     ],
...     gen = 100
... )
0.264 0.243 0.252 0.240
0.292 0.294 0.321 0.093
0.339 0.330 0.303 0.027
0.310 0.383 0.297 0.009
(100,)

```

### 3.8.6 Multi-locus selection models (operator `mlSelector`)

Although an individual's fitness can be affected by several factors, each of which can be modeled individually, **only one fitness value is used to determine a person's ability to pass all these factors to his or her offspring**. Although in theory we sometimes assume independent evolution of disease predisposing loci (mostly for mathematical reasons), in practise we have to use a multi-locus selection model to combine single-locus models.

This multi-loci selector applies several selectors to each individual and computes an overall fitness value from the fitness values provided by these selectors. Although this selector is designed to obtain multi-loci fitness values from several single-locus fitness models, any selector, including those obtain their fitness values from multiple disease predisposing loci, can be used in this selector. This selector uses parameter `mode` to control how individual fitness values are combined. More specifically, if  $f_i$  are fitness values obtained from individual selectors, this selector returns

- $\prod_i f_i$  if `mode=MULTIPLICATIVE`, and
- $1 - \sum_i (1 - f_i)$  if `mode=ADDITIVE`, and
- $1 - \prod_i (1 - f_i)$  if `mode=HETEROGENEITY`

0 will be returned if the returned fitness value is less than 0.

This operator simply combines individual fitness values and it is your responsibility to apply and interpret these models. For example, if relative fitness values are greater than one, the heterogeneity model hardly makes sense. Example 3.47 demonstrates the use of this operator using an additive multi-locus model over an additive and a recessive single-locus model at two disease predisposing loci. For comparison, we simulate two additional replicates with selection only applying to one of the two loci. It would be interesting to see if these two loci evolve more or less independently by comparing allele frequency trajectories of these two replicates to those in the first replicate.

Example 3.47: A multi-loci selector

```
>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(size=10000, loci=2, infoFields='fitness'),
...     sim.randomMating(), rep=3)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq(alleleFreq=[.5, .5])
...     ],
...     preOps = [
...         sim.mlSelector([
...             sim.mapSelector(loci=0, fitness={(0,0):1, (0,1):1, (1,1):.8}),
...             sim.mapSelector(loci=1, fitness={(0,0):1, (0,1):0.9, (1,1):.8}),
...         ], mode = sim.ADDITIVE, reps=0),
...         sim.mapSelector(loci=0, fitness={(0,0):1, (0,1):1, (1,1):.8}, reps=1),
...         sim.mapSelector(loci=1, fitness={(0,0):1, (0,1):0.9, (1,1):.8}, reps=2)
...     ],
...     postOps = [
...         sim.stat(alleleFreq=[0,1]),
...         sim.pyEval(r"'REP %d:\t%.3f\t%.3f\t' % (rep, alleleFreq[0][1], alleleFreq[1][1])"),
...         sim.pyOutput('\n', reps=-1),
...     ],
...     gen = 5
... )
REP 0:  0.461   0.463   REP 1:  0.478   0.502   REP 2:  0.502   0.468
REP 0:  0.436   0.433   REP 1:  0.455   0.504   REP 2:  0.503   0.438
REP 0:  0.414   0.404   REP 1:  0.429   0.504   REP 2:  0.505   0.416
REP 0:  0.394   0.382   REP 1:  0.403   0.503   REP 2:  0.510   0.389
REP 0:  0.371   0.354   REP 1:  0.390   0.499   REP 2:  0.514   0.362
(5, 5, 5)
```

### 3.8.7 A hybrid selector (operator pySelector)

When your selection model involves multiple interacting genetic and environmental factors, it might be easier to calculate a fitness value explicitly using a Python function. A hybrid selector can be used for this purpose. If your selection model depends solely on genotype, you can define a function such as

```
def fitness_func(genotype, gen):
    # calculate fitness according to genotype at specified loci
    return val
```

and use this function in an operator `pySelector(func=fitness_func, loci=loci)`. If your selection model depends on genotype as well as some information fields, you can define a function in the form of

```
def fitness_func(genotype, fields, gen):
    # calculate fitness according to genotype at specified loci
    # and values at specified information fields.
    return val
```

and use this function in an operator `pySelector(func=fitness_func, loci=loci, paramFields=fields)`.

When a `pySelector` is used to calculate fitness for an individual (parents if applied pre-mating, offspring if applied during-mating), it will collect his or her genotype at specified loci, optional values at specified information fields, and the generation number to a user-specified Python function, and take its return value as fitness. As you can imagine, the incorporation of information fields and generation number allow the implementation of very complex selection scenarios such as gene environment interaction and varying selection pressures. Note that this operator does not pass sex and affection status to the user-defined function. If your selection model is sex-dependent, you can define an information field `sex`, synchronize its value with individual sex (e.g. using operator `infoExec('sex=ind.sex()', exposeInd='ind')`) and pass this information to the user-defined function (`pySelector(func=func, paramFields='sex')`).

Example 3.48 demonstrates how to use a `pySelector` to specify fitness values according to a fitness table and the smoking status of each individual.

Example 3.48: A hybrid selector

```
>>> import simuPOP as sim
>>> import random
>>> simu = sim.simulator(
...     sim.population(size=2000, loci=[1]*2, infoFields=['fitness', 'smoking']),
...     sim.randomMating()
... )
>>> s1 = .02
>>> s2 = .03
>>> # the second parameter gen can be used for varying selection pressure
>>> def sel(arr, smoking, gen):
...     #      BB  Bb  bb
...     # AA  1   1   1
...     # Aa  1   1-s1 1-s2
...     # aa  1   1   1-s2
...     #
...     # arr is (A1 A2 B1 B2)
...     if arr[0] + arr[1] == 1 and arr[2] + arr[3] == 1:
...         v = 1 - s1 # case of AaBb
...     elif arr[2] + arr[3] == 2:
...         v = 1 - s2 # case of ??bb
...     else:
...         v = 1 # other cases
...     if smoking[0]:
...         return v * 0.9
```

```

...     else:
...         return v
...
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq(alleleFreq=[.5, .5])
...     ],
...     preOps = sim.pySelector(loci=[0, 1], func=sel, paramFields='smoking'),
...     postOps = [
...         # set smoking status randomly
...         sim.initInfo(lambda : random.randint(0,1), infoFields='smoking'),
...         sim.stat(alleleFreq=[0, 1], step=20),
...         sim.pyEval(r"%.4f\t%.4f\n" % (alleleFreq[0][1], alleleFreq[1][1])), step=20)
...     ],
...     gen = 50
... )
0.4953 0.4930
0.5530 0.4420
0.5938 0.3755
(50,)

```

### 3.8.8 Alternative implementations of natural selection

If you know how natural selection works in simuPOP, you do not have to use a selector to perform natural selection in simuPOP. All you need to do is

- Set individual fitness values to individuals who will be involved in mating. You do not have to use information field fitness because you can specify which information field to use in a mating scheme using parameter `selectionField`. Or,
- Using a during-mating operator as a filter to remove some offspring. Because during-mating operators other than selectors usually do not return `False`, a `pyOperator(func=func, offspringOnly=True)` is usually used in this case.

A number of operators could then be used to implement natural selection. Example 3.49 demonstrates a commonly used case where parents who are affected with certain disease are excluded from producing offspring. In this example, a penetrance model (operator `maPenetrance`) is applied to the parental generation to determine who will be affected. An `infoExec` operator is used to set individual fitness to 1 if he or she is unaffected, and 0 if he or she is affected. Due to the way parents are selected, affected parents will not be able to produce offspring as long as there is any unaffected individual. Because individual affection status is determined by his or her genotype, this genotype - affection status - fitness relationship could be implemented using an equivalent `maSelector`. This method could be extended to `infoExec('fitness = 1 - 0.01*ind.affected()', exposeInd='ind')` to select against, but not remove, affected parents, and similarly `infoExec('fitness = 1 - 0.01*(LDL > 250)')` to select against individuals according to a quantitative trait.

Example 3.49: Natural selection according to individual affection status

```

>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(size=2000, loci=1, infoFields='fitness'),
...     sim.randomMating()
... )
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),

```

```

...     sim.initByFreq(alleleFreq=[.5, .5])
... ],
... preOps = [
...     sim.maPenetrance(loci=0, penetrance=[0.01, 0.1, 0.2]),
...     sim.stat(numOfAffected=True, step=25, vars='propOfAffected'),
...     sim.pyEval(r"'Percent of affected: %.3f\t' % propOfAffected", step=50),
...     sim.infoExec('fitness = not ind.affected()', exposeInd='ind')
... ],
... postOps = [
...     sim.stat(alleleFreq=0),
...     sim.pyEval(r"'%.4f\n' % alleleFreq[0][1]", step=50)
... ],
... gen=151
... )
Percent of affected: 0.110      0.4713
Percent of affected: 0.009      0.0095
Percent of affected: 0.013      0.0000
Percent of affected: 0.008      0.0000
(151,)

```

### 3.8.9 Support for virtual subpopulations \*

Support for virtual subpopulations allows you to use different selectors for different (virtual) subpopulations. Because virtual subpopulations may overlap, and they do not have to cover all individuals in a subpopulation, it is important to remember that

- If virtual subpopulations overlap, the fitness value set by the last selector will be used.
- If an individual is not included in any of the virtual subpopulation, its fitness value will be zero which will prevent them from producing any offspring.

Example 3.50 demonstrates how to apply selectors to virtual subpopulations. This example has two subpopulations, each having two virtual subpopulations defined by sex. Natural selection is applied to male individuals in the first subpopulation, and female individuals in the second subpopulation. However, because the sex of offspring is randomly determined, the selection actually decreases the disease allele frequency for all individuals. Note that the second selector that set fitness `[1, 1, 1]` to females in the first subpopulation and males in the second subpopulation is, strictly speaking, not needed because `randomMating` performs naturally selection separately in males and females so females will be handled correctly in the first subpopulation if their fitness values are all zero.

Example 3.50: Selector in virtual subpopulations

```

>>> import simuPOP as sim
>>> pop = sim.population(size=[5000, 5000], loci=1, infoFields='fitness')
>>> pop.setVirtualSplitter(sim.sexSplitter())
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq(alleleFreq=[.5, .5])
...     ],
...     preOps = [
...         sim.maSelector(loci=0, fitness=[1, 1, 0.98], subPops=[(0,0), (1,1)]),
...         sim.maSelector(loci=0, fitness=[1, 1, 1], subPops=[(0,1), (1,0)]),
...     ],
...     postOps = [
...         sim.stat(alleleFreq=[0], subPops=[(0,0), (0,1), (1,0), (1,1)],
...             vars='alleleFreq_sp', step=50),
...     ]
... )

```

```

...         sim.pyEval(r"'\%.4f\t%.4f\t%.4f\t%.4f\n' % "
...             "tuple([subPop[x]['alleleFreq'][0][1] for x in ((0,0),(0,1),(1,0),(1,1))])",
...             step=50)
...     ],
...     gen=151
... )
0.5034 0.5097 0.4986 0.5037
0.4651 0.4635 0.4826 0.4864
0.3889 0.3717 0.4019 0.4042
0.3411 0.3553 0.3802 0.3680
(151,)

```

### 3.8.10 Natural selection in heterogeneous mating schemes \*\*

Multiple mating schemes could be applied to the same subpopulation in a heterogeneous mating scheme (heteroMating). These mating schemes may or may not support natural selection, may be applied to different virtual subpopulations of population, and they may see individuals differently in terms of individual fitness. Parameter `fitnessField` of a mating scheme could be used to handle such cases. More specifically,

- You can turn off the natural selection support of a mating scheme by setting `fitnessField=""`.
- If a mating scheme uses a different set of fitness values, you can add an information field (e.g. `fitness1`), setting individual fitness to this information field using a selector (with parameter `infoFields='fitness1'`) and tells a mating scheme to look in this information field for fitness values (using parameter `fitnessField='fitness1'`).

## 3.9 Tagging operators

In `simuPOP`, tagging refers to the action of setting various information fields of offspring, usually using various parental information during the production of offspring. `simuPOP` provides a number of tagging operators (called taggers) for various purposes. Because tagging operators are during-mating operators, they do not support parameter `subPops`. If you would like to apply different taggers to different (virtual) subpopulations, you can use them in the homogeneous mating schemes of a heterogeneous mating scheme.

### 3.9.1 Inheritance tagger (operator `inheritTagger`)

An inheritance tagger passes values of parental information field(s) to the corresponding offspring information field(s). Depending on the parameters, an `inheritTagger` can

- For asexual mating schemes, pass one or more information fields from parent to offspring.
- Pass one or more information fields from father to offspring (`mode=PATERNAL`).
- Pass one or more information fields from mother to offspring (`mode=MATERNAL`).
- Pass the maximal, minimal, sum, multiplication or average of values of one or more information fields of both parents (`mode=MAXIMUM, MINIMUM, ADDITION, MULTIPLICATION` or `MEAN`).

This can be used to track the spread of certain information during evolution. For example, [Example3.51](#) tags the first individuals of ten subpopulations of size 1000. Individuals in the offspring generation inherits the maximum value of field `x` from his/her parents so `x` is inherited regardless of the sex of parents. A `stat` operator is used to calculate the number of offspring having this tag in each subpopulation. The results show that some tagged ancestors have

many offspring, and some have none. If you run this simulation long enough, you can see that all ancestors become the ancestor of either none or all individuals in a population. Note that this simulation only considers genealogical inheritance and ancestors do not have to pass any genotype to the last generation.

Example 3.51: Use an inherit tagger to track offspring of individuals

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[1000]*10, loci=1, infoFields='x')
>>> # tag the first individual of each subpopulation.
>>> for sp in range(pop.numSubPop()):
...     pop.individual(0, sp).x = 1
...
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = sim.initSex(),
...     duringOps = sim.inheritTagger(mode=sim.MAXIMUM, infoFields='x'),
...     postOps = [
...         sim.stat(sumOfInfo='x', vars=['sumOfInfo_sp']),
...         sim.pyEval(r' ".join(["%3d" % subPop[i]["sumOfInfo"]["x"] for i in range(10)])+"\n"'
...     ],
...     gen = 5
... )
2, 1, 0, 1, 1, 2, 3, 3, 1, 1
5, 1, 0, 1, 1, 3, 3, 5, 3, 0
9, 2, 0, 2, 2, 7, 9, 5, 13, 0
21, 4, 0, 2, 5, 18, 11, 9, 27, 0
39, 5, 0, 6, 8, 36, 23, 20, 67, 0
(5,)
```

### 3.9.2 Summarize parental information fields (operator summaryTagger)

A `summaryTagger` summarizes values of one or more parental information fields and places the result in an offspring information field. If mating is sexual, two sets of values will be involved. Summarization methods include `MEAN`, `MINIMUM`, `MAXIMUM`, `SUMMATION` and `MULTIPLICATION`. The operator is usually used to summarize certain characteristics of parents of each offspring. For example, a `summaryTagger` is used in Example 3.52 to calculate the mean fitness of parents during each mating event. The results are saved in the `avgFitness` field of offspring. Because allele 1 at locus 0 is under purifying selection, the allele frequency of this allele decreases. In the mean time, fitness of parents increases because less and less parents have this allele.

Example 3.52: Using a summary tagger to calculate mean fitness of parents.

```
>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(1000, loci=1, infoFields=['fitness', 'avgFitness']),
...     sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5]),
...     ],
...     preOps = sim.maSelector(loci=0, wildtype=0, fitness=[1, 0.99, 0.95]),
...     duringOps = sim.summaryTagger(mode=sim.MEAN, infoFields=['fitness', 'avgFitness']),
...     postOps = [
...         sim.stat(alleleFreq=0, meanOfInfo='avgFitness', step=10),
...         sim.pyEval(r'"gen %d: allele freq: %.3f, average fitness of parents: %.3f\n' % "
...             "(gen, alleleFreq[0][1], meanOfInfo['avgFitness'])", step=10)
...     ],
...     gen = 50,
```



```

... )
gen 0: allele freq: 0.473, average fitness of parents: 0.984
gen 10: allele freq: 0.421, average fitness of parents: 0.986
gen 20: allele freq: 0.388, average fitness of parents: 0.988
gen 30: allele freq: 0.288, average fitness of parents: 0.991
gen 40: allele freq: 0.256, average fitness of parents: 0.993
(50,)

```

### 3.9.3 Tracking parents (operator `parentsTagger`)

A parents tagger is used to record the indexes of parents (in the parental population) in the information fields (default to `father_idx`, `mother_idx`) of their offspring. These indexes provide a way to track down an individual's parents, offspring and consequently all relatives in a multi-generation population. Because this operator has been extensively used in this guide, please refer to other sections for an Example (e.g. Example 2.6).

As long as parental generations do not change after the offspring generation is created, recorded parental indexes can be used to locate parents of an individual. However, in certain applications when parental generations change (e.g. to draw a pedigree from a large population), or when individuals can not be looked up easily using indexes (e.g. after individuals are saved to a file), giving every individual a unique ID and refer to them using ID will be a better choice.

### 3.9.4 Assign unique IDs to individuals (operator `idTagger`)

Although it is possible to use generation number and individual indexes to locate individuals in an evolving population, a unique ID makes it much easier to identify individuals when migration is involved, and to analyze an evolutionary process outside of `simuPOP`. An operator `idTagger` (and its function form `TagID`) is provided by `simuPOP` to assign a unique ID to all individuals during evolution.

The IDs of individuals are usually stored in an information field named `ind_id`. To ensure uniqueness across populations, a single source of ID is used for this operator. Individual IDs are assigned consecutively starting from 0. If you would like to reset the sequence or start from a different number, you can call the `reset(startID)` function of any `idTagger`.

An `idTagger` is usually used during-mating to assign ID to each offspring. However, if it is applied directly to a population, it will assign unique IDs to all individuals in this population. This property is usually used in the `preOps` parameter of function `simulator.evolve` to assign initial ID to a population. For example, three `idTagger` operators are used in Example 3.53 to assign IDs to individuals before, during and after evolution. Although different operators are used, different IDs are assigned to individuals.

Example 3.53: Assign unique IDs to individuals

```

>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(10, infoFields='ind_id', ancGen=1),
...     sim.randomSelection())
>>> simu.evolve(
...     initOps = sim.idTagger(),
...     duringOps = sim.idTagger(),
...     gen = 1
... )
(1,)
>>> pop = simu.extract(0)
>>> print [int(ind.ind_id) for ind in pop.individuals()]
[11, 12, 13, 14, 15, 16, 17, 18, 19, 20]
>>> pop.useAncestralGen(1)
>>> print [int(ind.ind_id) for ind in pop.individuals()]
[1, 2, 3, 4, 5, 6, 7, 8, 9, 10]

```

```
>>> sim.TagID(pop) # re-assign ID
>>> print [int(ind.ind_id) for ind in pop.individuals()]
[21, 22, 23, 24, 25, 26, 27, 28, 29, 30]
```

### 3.9.5 Tracking pedigrees (operator pedigreeTagger)

A `pedigreeTagger` is similar to a `parentsTagger` in that it records parental information in offspring's information fields. However, instead of indexes of parents, this operator records a unique ID of each parent to make it easier to study and reconstruct a complete pedigree of a whole evolutionary process. The default information fields are `father_id` and `mother_id`.

By default, the `pedigreeTagger` does not produce any output. However, if a valid output string (or function) is specified, it will output the ID of offspring and all available parents. Such information is enough to reconstruct the complete pedigree of an evolutionary process.

Example 3.54 demonstrates how to output the complete pedigree of an evolutionary process. Note that `idTagger` has to be applied before `pedigreeTagger` so that IDs of offspring could be assigned before they are outputted.

Example 3.54: Output a complete pedigree of an evolutionary process

```
>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(100, infoFields=['ind_id', 'father_id', 'mother_id']),
...     sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.idTagger()
...     ],
...     duringOps = [
...         sim.idTagger(),
...         sim.pedigreeTagger(output=">>sim.pedigree.txt")
...     ],
...     gen = 100
... )
(100,)
>>> ped = open('sim.pedigree.txt')
>>> print ''.join(ped.readlines()[100:105])
201 145 118
202 119 194
203 122 189
204 182 195
205 191 103
```

### 3.9.6 A hybrid tagger (operator pyTagger)

A `pyTagger` uses a user-defined function to pass parental information fields to offspring. When a mating event happens, this operator collect values of specified information fields of parents, pass them to a user-provided function, and use the return values to set corresponding offspring information fields. A typical usage of this operator is to set random environmental factors that are affected by parental values. Example 3.55 demonstrates such an example where the location of each offspring (x, y) is randomly assigned around the middle position of his or her parents.

Example 3.55: Use of a hybrid tagger to pass parental information to offspring

```
>>> import simuPOP as sim
>>> import random
>>> def randomMove(values):
```

```

...     '''Pass parental information fields to offspring'''
...     x1, y1, x2, y2 = values
...     # shift right with high concentration of alleles...
...     x = random.normalvariate((x1+x2)/2., 0.1)
...     y = random.normalvariate((y1+y2)/2., 0.1)
...     return (x, y)
...
>>> pop = sim.population(1000, loci=[1], infoFields=['x', 'y'])
>>> pop.setVirtualSplitter(sim.genotypeSplitter(loci=0, alleles=[[0, 0], [0,1], [1, 1]]))
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5]),
...         sim.initInfo(random.random, infoFields=['x', 'y'])
...     ],
...     duringOps = sim.pyTagger(func=randomMove, infoFields=['x', 'y']),
...     postOps = [
...         sim.stat(minOfInfo='x', maxOfInfo='x'),
...         sim.pyEval(r'''Range of x: %.2f, %.2f\n' % (minOfInfo['x'], maxOfInfo['x'])''')
...     ],
...     gen = 5
... )
Range of x: -0.14, 1.12
Range of x: -0.09, 1.07
Range of x: -0.09, 1.04
Range of x: -0.02, 1.08
Range of x: 0.08, 0.98
(5,)
>>>

```

### 3.9.7 Tagging that involves other parental information

If the way how parental information fields pass to their offspring is affected by parental genotype, sex, or affection status, you could use a Python operator (`pyOperator`) during mating to explicitly obtain parental information and set offspring information fields.

Alternatively, you can add another information field, translate needed information to this field and pass the genotype information in the form of information field. Operator `infoExec` could be helpful in this case. Example 3.56 demonstrates such an example where the number of affected parents are recorded in an information field. Before mating happens, a penetrance operator is used to assign affection status to parents. The affection status is then copied to an information field affected so that operator `summaryTagger` could be used to count the number of affected parents. Two `maPenetrance` operators are used both before and after mating to assign affection status to both parental and offspring generations. This helps dividing the offspring generation into affected and unaffected virtual subpopulations. Not surprisingly, the average number of affected parents is larger for affected individuals than unaffected individuals.

Example 3.56: Tagging that involves other parental information

```

>>> import simuPOP as sim
>>> pop = sim.population(1000, loci=[1], infoFields=['aff', 'numOfAff'])
>>> # define virtual subpopulations by affection sim.status
>>> pop.setVirtualSplitter(sim.affectionSplitter())
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5]),
...     ],
...

```

```

...     preOps = [
...         # get affection sim.status for parents
...         sim.maPenetrance(loci=0, wildtype=0, penetrance=[0.1, 0.2, 0.4]),
...         # set 'aff' of parents
...         sim.infoExec('aff = ind.affected()', exposeInd='ind'),
...     ],
...     # get number of affected parents for each offspring and store in numOfAff
...     duringOps = sim.summaryTagger(mode=sim.SUMMATION, infoFields=['aff', 'numOfAff']),
...     postOps = [
...         # get affection sim.status for offspring
...         sim.maPenetrance(loci=0, wildtype=0, penetrance=[0.1, 0.2, 0.4]),
...         # calculate mean 'numOfAff' of offspring, for unaffected and affected subpopulations.
...         sim.stat(meanOfInfo='numOfAff', subPops=[(0,0), (0,1)], vars=['meanOfInfo_sp']),
...         # print mean number of affected parents for unaffected and affected offspring.
...         sim.pyEval(r'''sim.MEAN number of affected parents: %.2f (unaff), %.2f (aff)\n' % "
...             "(subPop[(0,0)]['meanOfInfo'] ['numOfAff'], subPop[(0,1)] ['meanOfInfo'] ['numOfAff'])
...         ]),
...     ],
...     gen = 5
... )
sim.MEAN number of affected parents: 0.41 (unaff), 0.44 (aff)
sim.MEAN number of affected parents: 0.41 (unaff), 0.54 (aff)
sim.MEAN number of affected parents: 0.47 (unaff), 0.55 (aff)
sim.MEAN number of affected parents: 0.47 (unaff), 0.55 (aff)
sim.MEAN number of affected parents: 0.42 (unaff), 0.45 (aff)
(5,)
>>>

```

## 3.10 Statistics calculation (operator stat)

### 3.10.1 How statistics calculation works

A `stat` operator calculates specified statistics of a population when it is applied to this population. This operator can be applied to specified replicates (parameter *rep*) at specified generations (parameter *begin*, *end*, *step*, and *at*). This operator does not produce any output (ignore parameter *output*) after statistics are calculated. Instead, it stores results in the local namespace of the population being applied. Other operators can retrieve these variables or evaluate expression directly in this local namespace.

The `stat` operator is usually used in conjunction with a `pyEval` or `pyExec` operator which execute Python statements and/or expressions in a population's local namespace. For example, operators

```

ops = [
    stat(alleleFreq[0]),
    pyEval("'%.2f' % alleleFreq[0][0]")
]

```

in the `ops` parameter of the `simulator.evolve` function will be applied to populations during evolution. The first operator calculates allele frequency at the first locus and store the results in each population's local namespace. The second operator formats and outputs one of the variables. Because of the flexibility of the `pyEval` operator, you can output statistics, even simple derived statistics, in any format. For example, you can output expected heterozygosity ( $1 - \sum p_i^2$ ) using calculated allele frequencies as follows:

```

pyEval("'H_exp=%.2f' % (1-sum([x*x for x in alleleFreq[0].values()])))")

```

Note that `alleleFreq[0]` is a dictionary.

You can also retrieve variables in a population directly using functions `population.vars()` or `population.dvars()`. The only difference between these functions is that `vars()` returns a dictionary and

`dvars()` returns a Python object that uses variable names as attributes (`vars()[ 'alleleFreq' ]` is equivalent to `dvars().alleleFreq`). This method is usually used when the function form of the `stat` operator is used. For example,

```
Stat(pop, alleleFreq=[0])
H_exp = 1 - sum([x*x for x in pop.dvars().alleleFreq[0].values()])
```

uses the `Stat` function (note the capital S) to count frequencies of alleles for a given population and calculates expected heterozygosity using these variables.

### 3.10.2 Support for virtual subpopulations

The `stat` operator supports parameter `subPops` and can calculate statistics in specified subpopulations. For example

```
stat(alleleFreq=[0], subPops=[(0, 0), (1, 0)])
```

will calculate the frequencies of alleles at locus 0, among individuals in two virtual subpopulations. If the virtual subpopulation is defined by sex (using a `sexSplitter`), the above operator will calculate allele frequency among all males in the first and second subpopulations. If `subPops` is not specified, allele frequency of the whole population (all subpopulations) will be calculated.

Although many statistics could be calculated and outputted, the `stat` operator by default outputs a selected number of variables for each statistic calculated. Other statistics could be calculated and outputted if their names are specified in parameter `vars`. Variable names ending with `_sp` is interpreted as variables that will be calculated and outputted in all or specified (virtual) subpopulations. For example, parameter `vars` in

```
stat(alleleFreq=[0], subPops=[0, (1, 0)], vars=['alleleFreq_sp', 'alleleNum_sp'])
```

tells this operator to output numbers and frequencies of alleles at locus 0 in subpopulation 0 and virtual subpopulation (1,0). These variables will be saved in dictionaries `subPop[sp]` of the local namespace. For example, the above operator will write variables such as `subPop[0]['alleleFreq']`, `subPop[(1,0)]['alleleFreq']` and `subPop[(1,0)]['alleleNum']`. Functions `population.vars(sp)` and `population.dvars(sp)` are provided as shortcuts to access these variables but the full variable names have to be specified if these variables are used in expressions.

By default, the same variables will be set for a statistic, regardless of the values of the `subPops` parameter. This can be a problem if multiple `stat` operators are used to calculate the same statistics for different sets of subpopulations. To avoid name conflict, you can use parameter `suffix` to add a suffix to all variables outputted by a `stat` operator. For example, Example 3.57 uses 4 `stat` operators to calculate overall and pairwise  $F_{ST}$  values for three subpopulations. Different suffixes are used for pairwise  $F_{ST}$  estimators so that variables set by these operators will not override each other.

Example 3.57: Add suffixes to variables set by multiple `stat` operators

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population([5000]*3, loci=5), sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5])
...     ],
...     postOps = [
...         sim.stat(structure=range(5), subPops=(0, 1), suffix='_01', step=40),
...         sim.stat(structure=range(5), subPops=(1, 2), suffix='_12', step=40),
...         sim.stat(structure=range(5), subPops=(0, 2), suffix='_02', step=40),
...         sim.stat(structure=range(5), step=40),
...         sim.pyEval(r'"Fst=%.3f (pairwise: %.3f %.3f %.3f)\n' % (F_st, F_st_01, F_st_12, F_st_02)
...             step=40),
...     ],
```

```

...     gen = 200
... )
Fst=0.000 (pairwise: 0.000 -0.000 0.000)
Fst=0.004 (pairwise: 0.005 0.005 0.003)
Fst=0.009 (pairwise: 0.009 0.008 0.009)
Fst=0.008 (pairwise: 0.008 0.007 0.008)
Fst=0.010 (pairwise: 0.005 0.012 0.014)
(200,)

```

**Note:** The `stat` operator accepts overlapping or even duplicate virtual subpopulations. During the calculation of summary statistics, these subpopulations are treated as separate subpopulations so some individuals can be counted more than once. For example, individuals in virtual subpopulation (0, 1) will be counted twice during the calculation of allele frequency and population size in operator

```
stat(alleleFreq=[0], popSize=True, subPops=[0, (0, 1)])
```

### 3.10.3 Counting individuals by sex and affection status

Parameters `popSize`, `numOfMales` and `numOfAffected` provide basic individual counting statistics. They count the number of all, male/female, affected/unaffected individuals in all or specified (virtual) subpopulations, and set variables such as `popSize`, `numOfMales`, `numOfFemales`, `numOfAffected`, `numOfUnaffected`. Proportions and statistics for subpopulations are available if variables such as `propOfMales`, `numOfAffected_sp` are specified in parameter vars. Another variable `subPopSize` is defined for parameter `popSize=True`. It is a list of sizes of all or specified subpopulations and is easier to use than referring to variable `popSize` from individual subpopulations.

Example 3.58 demonstrates how to use these parameters in operator `stat`. It defines four VSPs by sex and affection status (using a `stackedSplitter`) and count individuals by sex and affection status. It is worth noting that `pop.dvars().popSize` in the first example is the total number of individuals in two virtual subpopulations (0, 0) and (0, 2), which are all male individuals, and all unaffected individuals. Because these two VSPs overlap, this variable can be larger than actual population size.

Example 3.58: Count individuals by sex and/or affection status

```

>>> import simuPOP as sim
>>> pop = sim.population(10000, loci=1)
>>> pop.setVirtualSplitter(sim.combinedSplitter(
...     [sim.sexSplitter(), sim.affectionSplitter()])))
>>> sim.InitSex(pop)
>>> sim.InitByFreq(pop, [0.2, 0.8])
>>> sim.MaPenetrance(pop, loci=0, penetrance=[0.1, 0.2, 0.5])
>>> # Count sim.population size
>>> sim.Stat(pop, popSize=True, subPops=[(0, 0), (0, 2)])
>>> # popSize is the size of two VSPs, does not equal to total sim.population size.
>>> # Because two VSPs overlap (all males and all unaffected), popSize can be
>>> # greater than real sim.population size.
>>> print pop.dvars().subPopSize, pop.dvars().popSize
[5052, 6080] 11132
>>> # print popSize of each virtual subpopulation.
>>> sim.Stat(pop, popSize=True, subPops=[(0, 0), (0, 2)], vars='popSize_sp')
>>> # Note the two ways to access variable in (virtual) subpopulations.
>>> print pop.dvars((0,0)).popSize, pop.dvars().subPop[(0,2)]['popSize']
5052 6080
>>> # Count number of male (should be the same as the size of VSP (0,0)).
>>> sim.Stat(pop, numOfMales=True)
>>> print pop.dvars().numOfMales
5052
>>> # Count the number of affected and unaffected male individual
>>> sim.Stat(pop, numOfMales=True, subPops=[(0, 2), (0, 3)], vars='numOfMales_sp')

```

```

>>> print pop.dvars((0,2)).numOfMales, pop.dvars((0,3)).numOfMales
3056 1996
>>> # or number of affected male and females
>>> sim.Stat(pop, numOfAffected=True, subPops=[(0, 0), (0, 1)], vars='numOfAffected_sp')
>>> print pop.dvars((0,0)).numOfAffected, pop.dvars((0,1)).numOfAffected
1996 1924
>>> # These can also be done using a sim.productSplitter...
>>> pop.setVirtualSplitter(sim.productSplitter(
...     [sim.sexSplitter(), sim.affectionSplitter()])))
>>> sim.Stat(pop, popSize=True, subPops=[(0, x) for x in range(4)])
>>> # counts for male unaffected, male affected, female unaffected and female affected
>>> print pop.dvars().subPopSize
[3056, 1996, 3024, 1924]

```

### 3.10.4 Allele count and frequency

Parameter *alleleFreq* accepts a list of markers at which allele frequencies in all or specified (virtual) subpopulations will be calculated. This statistic sets variables `alleleFreq[loc][allele]` and `alleleNum[loc][allele]` which are frequencies and numbers of allele *allele* at locus *loc*, respectively. If variables `alleleFreq_sp` and `alleleNum_sp` are specified in parameter *vars*, these variables will be set for all or specified (virtual) subpopulations. **At the Python level, these variables of dictionaries of default dictionaries.** That is to say, `alleleFreq[loc]` at a unspecified locus will raise a `KeyError` exception, and `alleleFreq[loc][allele]` of an invalid allele will return 0.

Example 3.59 demonstrates an advanced usage of allele counting statistic. In this example, two virtual subpopulations are defined by individual affection status. During evolution, a multi-allele penetrance operator is used to determine individual affection status and a `stat` operator is used to calculate allele frequencies in these two virtual subpopulations, and in the whole population. Because the simulated disease is largely caused by the existence of allele 1 at the first locus, it is expected that the frequency of allele 1 is higher in the case group than in the control group. It is worth noting that `alleleFreq[0][1]` in this example is the frequency of allele 1 in the whole population because these two virtual subpopulations add up to the whole population.

Example 3.59: Calculate allele frequency in affected and unaffected individuals

```

>>> import simuPOP as sim
>>> pop = sim.population(10000, loci=1)
>>> pop.setVirtualSplitter(sim.affectionSplitter())
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq(loci=0, alleleFreq=[0.8, 0.2])
...     ],
...     postOps = [
...         sim.maPenetrance(penetrance=[0.1, 0.4, 0.6], loci=0),
...         sim.stat(alleleFreq=0, subPops=[(0, 0), (0, 1)],
...             vars=['alleleFreq', 'alleleFreq_sp']),
...         sim.pyEval(r'''Gen: %d, freq: %.2f, freq (aff): %.2f, freq (unaff): %.2f\n' % " + \
...             "(gen, alleleFreq[0][1], subPop[(0,1)]['alleleFreq'][0][1], " + \
...             "subPop[(0,0)]['alleleFreq'][0][1])"'''),
...     ],
...     gen = 5
... )
Gen: 0, freq: 0.20, freq (aff): 0.41, freq (unaff): 0.14
Gen: 1, freq: 0.20, freq (aff): 0.40, freq (unaff): 0.14
Gen: 2, freq: 0.20, freq (aff): 0.41, freq (unaff): 0.14
Gen: 3, freq: 0.20, freq (aff): 0.41, freq (unaff): 0.14

```

```
Gen: 4, freq: 0.19, freq (aff): 0.41, freq (unaff): 0.14
(5,)
```

### 3.10.5 Genotype count and frequency

Parameter *genoFreq* accepts a list of loci at which genotype counts and frequencies are calculated and outputted. A genotype is represented as a tuple of alleles at a locus. The length of the tuples is determined by the number of homologous copy of chromosomes in a population. For example, genotypes in a diploid population are ordered pairs such as (1, 2) where 1 and 2 are alleles at a locus on, respectively, the first and second homologous copies of chromosomes. (1, 2) and (2, 1) are different genotypes. This statistic sets dictionaries (with locus indexes as keys) of default dictionaries (with genotypes as keys) *genoFreq* and *genoNum*.

Example 3.60 creates a small population and initializes a locus with rare alleles 0, 1 and a common allele 2. A function *Stat* (the function form of operator *stat*) is used to count the available genotypes. Note that `pop.dvars().genoFreq[0][(i, j)]` can be used to print frequencies of all genotypes even when not all genotypes are available in the population.

Example 3.60: Counting genotypes in a population

```
>>> import simuPOP as sim
>>> pop = sim.population(100, loci=[1, 1, 1], chromTypes=[sim.AUTOSOME, sim.CHROMOSOME_X, sim.CHROMOSOME_Y])
>>> sim.InitByFreq(pop, [0.01, 0.05, 0.94])
>>> sim.Stat(pop, genoFreq=[0, 1])
>>> print 'Available genotypes on autosome:', pop.dvars().genoFreq[0].keys()
Available genotypes on autosome: [(1, 2), (2, 1), (1, 1), (2, 0), (2, 2), (0, 2)]
>>> for i in range(3):
...     for j in range(3):
...         print '%d-%d: %.3f' % (i, j, pop.dvars().genoFreq[0][(i, j)])
...
0-0: 0.000
0-1: 0.000
0-2: 0.020
1-0: 0.000
1-1: 0.010
1-2: 0.090
2-0: 0.020
2-1: 0.020
2-2: 0.840
>>> print 'Genotype frequency on chromosome X:\n', \
...       '\n'.join(['%s: %.3f' % (x, y) for x, y in pop.dvars().genoFreq[1].iteritems()])
Genotype frequency on chromosome X:
(2,): 0.970
(1,): 0.030
```

### 3.10.6 Homozygote and heterozygote count and frequency

In a diploid population, a heterozygote is a genotype with two different alleles and a homozygote is a genotype with two identical alleles. Parameter *heteroFreq* accepts a list of loci and outputs variables *heteroFreq* which is a dictionary of heterozygote frequencies at specified loci. Optional variables *heteroNum*, *homoFreq* and *homoNum* can be outputted for all and each (virtual) subpopulations. Example 3.61 demonstrates the decay of heterozygosity of a locus due to genetic drift.

Example 3.61: Counting homozygotes and heterozygotes in a population

```
>>> import simuPOP as sim
>>> pop = sim.population(100, loci=1)
```



```

>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5])
...     ],
...     postOps = [
...         sim.stat(heteroFreq=0, step=10),
...         sim.pyEval(r"'Gen: %d, HeteroFreq: %.2f\n' % (gen, heteroFreq[0])", step=20)
...     ],
...     gen = 100
... )
Gen: 0, HeteroFreq: 0.45
Gen: 20, HeteroFreq: 0.44
Gen: 40, HeteroFreq: 0.55
Gen: 60, HeteroFreq: 0.46
Gen: 80, HeteroFreq: 0.40
(100,)

```

### 3.10.7 Haplotype count and frequency

Haplotypes refer to alleles on the same homologous copy of a chromosome at specified loci. For example, an diploid individual can have haplotypes (0, 2, 1) and (0, 1, 1) at loci (2, 3, 5) if he or she has genotype (0, 0), (2, 1) and (1, 1) at loci 2, 3 and 5 respectively. Parameter *haploFreq* accept one or more lists of loci specifying one or more haplotype sites (e.g. *haploFreq*=[(0,1,2), (2,3)] specifies two haplotype sites). The results are saved to dictionaries (with haplotype site as keys) of default dictionaries (with haplotype as keys). For example, *haploFreq*[(0,1,2)][(0,1,1)] will be the frequency of haplotype (0, 1, 1) at loci (0, 1, 2). Example 3.62 prints the numbers of genotypes and haplotypes at loci 0, 1 and 2 of a small population. Note that the *ViewVars* function defined in module *simuUtil* can make use of a wxPython window to view all variables if it is called in GUI mode.

Example 3.62: Counting haplotypes in a population

```

>>> import simuPOP as sim
>>> from simuPOP.utils import ViewVars
>>> pop = sim.population(100, loci=3)
>>> sim.InitByFreq(pop, [0.2, 0.4, 0.4], loci=0)
>>> sim.InitByFreq(pop, [0.2, 0.8], loci=2)
>>> sim.Stat(pop, genoFreq=[0, 1, 2], haploFreq=[0, 1, 2],
...     vars=['genoNum', 'haploFreq'])
>>> ViewVars(pop.vars(), gui=False)
{'genoNum': {0: {(0, 0): 3.0,
                 (0, 1): 7.0,
                 (0, 2): 5.0,
                 (1, 0): 9.0,
                 (1, 1): 14.0,
                 (1, 2): 16.0,
                 (2, 0): 8.0,
                 (2, 1): 14.0,
                 (2, 2): 24.0},
              1: {(0, 0): 100.0},
              2: {(0, 0): 4.0, (0, 1): 19.0, (1, 0): 15.0, (1, 1): 62.0}},
'haploFreq': {(0, 1, 2): {(0, 0, 0): 0.029999999999999999,
                           (0, 0, 1): 0.14499999999999999,
                           (1, 0, 0): 0.055,
                           (1, 0, 1): 0.315,
                           (2, 0, 0): 0.125,

```

```
(2, 0, 1): 0.33000000000000002}}}
```

**Note:** *haploFreq* does not check if loci in a haplotype site belong to the same chromosome, or if loci are duplicated or in order. It faithfully assemble alleles at specified loci as haplotypes although these haplotypes might not be biologically meaningful.

**Note:** Counting a large number of haplotypes on long haplotype sites may exhaust the RAM of your computer.

### 3.10.8 Summary statistics of information fields

Parameter `sumOfInfo`, `meanOfInfo`, `varOfInfo`, `maxOfInfo` and `minOfInfo` are used to calculate the sum, mean, sample variance ( $\frac{1}{n-1} \sum_{i=1}^n (x_i - \bar{x})^2$ ), max and min of specified information fields of individuals in all or specified (virtual) subpopulations. The results are saved in dictionaries `sumOfInfo`, `meanOfInfo`, `varOfInfo`, `maxOfInfo` and `minOfInfo` with information fields as keys. For example, parameter `meanOfInfo='age'` calculates the mean age of all individuals and set variable `meanOfInfo['age']`.

Example 3.63 demonstrates a mixing process of two populations. The population starts with two types of individuals with ancestry values 0 or 1 (information field `anc`). During the evolution, parents mate randomly and the ancestry of offspring is the mean of parental ancestry values. A `stat` operator is used to calculate the mean and variance of individual ancestry values, and the number of individuals in five ancestry groups. It is not surprising that whereas population mean ancestry does not change, more and more people have about the same number of ancestors from each group and have an ancestry value around 0.5. The variance of ancestry values therefore decreases gradually.

Example 3.63: Calculate summary statistics of information fields

```
>>> import simuPOP as sim
>>> import random
>>> pop = sim.population([500], infoFields='anc')
>>> # Defines VSP 0, 1, 2, 3, 4 by anc.
>>> pop.setVirtualSplitter(sim.infoSplitter('anc', cutoff=[0.2, 0.4, 0.6, 0.8]))
>>> #
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         # anc is 0 or 1
...         sim.initInfo(lambda : random.randint(0, 1), infoFields='anc')
...     ],
...     duringOps = sim.inheritTagger(mode=sim.MEAN, infoFields='anc'),
...     postOps = [
...         sim.stat(popSize=True, meanOfInfo='anc', varOfInfo='anc',
...             subPops=[(0,x) for x in range(5)]),
...         sim.pyEval(r'''Anc: %.2f (%.2f), #inds: %s\n' %" + \
...             "(meanOfInfo['anc'], varOfInfo['anc'], " + \
...             "'", '.join(['%4d' % x for x in subPopSize]))")
...     ],
...     gen = 5,
... )
Anc: 0.53 (0.13), #inds: 112, 0, 247, 0, 141
Anc: 0.52 (0.06), #inds: 23, 117, 188, 137, 35
Anc: 0.54 (0.03), #inds: 12, 124, 129, 210, 25
Anc: 0.54 (0.02), #inds: 2, 76, 245, 167, 10
Anc: 0.54 (0.01), #inds: 0, 19, 371, 109, 1
(5,)
```

### 3.10.9 Linkage disequilibrium

Parameter *LD* accepts a list of loci-pairs (e.g.  $LD = [(0, 1), (2, 3)]$ ) with optional primary alleles at two loci (e.g.  $LD = [(0, 1, 0, 0), (2, 3)]$ ). For each pair of loci, this operator calculates linkage disequilibrium and optional association measures between them.

Assuming that two loci are both diallelic, one with alleles *A* and *a*, and the other with alleles *B* and *b*. If we denote  $P_x, P_{xy}$  as allele and haplotype frequencies for allele *x* and haplotype *xy*, respectively, the linkage disequilibrium measures **with respect to primaries alleles** *A* and *B* are

- Basic LD measure *D*:

$$D = P_{AB} - P_A P_B$$

*D* ranges from -0.25 to 0.25. The sign depends on the choice of alleles (*A* and *B*) at two loci.

- Lewontin's  $D' = D/D_{max}$  where

$$D_{max} = \begin{cases} \min(P_A(1 - P_B), (1 - P_A)P_B) & \text{if } D > 0 \\ \min(P_A P_B, (1 - P_A)(1 - P_B)) & \text{if } D < 0 \end{cases}$$

$D'$  ranges from -1 to 1. The sign depends on the choice of alleles (*A* and *B*) at two loci.

- $r^2$  ( $\Delta^2$  in [Devlin and Risch \[1995\]](#))

$$r^2 = \frac{D^2}{P_A(1 - P_A)P_B(1 - P_B)}$$

If one or both loci have more than 2 alleles, or if no primary allele is specified, the LD measures are calculated as follows:

- If primary alleles are specified, all other alleles are considered as minor alleles with combined frequency (e.g.  $1 - P_A$ ). The same formulas apply which lead to signed *D* and  $D'$  measures.
- If primary alleles are not specified, these LD measures are calculated as the average of the absolute value of diallelic measures of all allele pairs. For example, the multi-allele version of  $r^2$  is

$$r^2 = \sum_i \sum_j P_i P_j |r_{ij}^2| = \sum_i \sum_j \frac{D_{ij}^2}{(1 - P_i)(1 - P_j)}$$

where *i* and *j* iterate through all alleles at the two loci. **In the diallelic case, LD measures will be the absolute value of the single measures** because  $D_{ij}$  and  $D'_{ij}$  only differ by signs.

In another word,

- $LD = [loc1, loc2]$  will yield positive *D* and  $D'$  measures.
- $LD = [loc1, loc2, allele1, allele2]$  will yield signed *D* and  $D'$  measures.
- In the diallelic case, both cases yield identical results except for signs of *D* and  $D'$ .
- In the multi-allelic case, the results can be different because  $LD = [loc1, loc2, allele1, allele2]$  combines non-primary alleles and gives a single diallelic measure.

**Note:** A large number of linkage disequilibrium measures have been used in different disciplines but not all of them are well-accepted. Requests of adding a particular LD measure will be considered when a reliable reference is provided. Association tests between specified loci could also be calculated using a *m* by *n* table of haplotype frequencies. If primary alleles are specified, non-primary alleles are combined to form a 2 by 2 table ( $m = n = 2$ ). Otherwise, *m* and *n* are respective numbers of alleles at two loci.

- $\chi^2$  and its  $p$ -value (variable LD\_ChiSq and LD\_ChiSq\_p, respectively). A one-side  $\chi^2$  test with  $(m - 1) \times (n - 1)$  degrees of freedom will be used.
- Cramer V statistic (variable CramerV):

$$V = \sqrt{\frac{\chi^2}{N \times \min(m - 1, n - 1)}}$$

where  $N$  equals the total number of haplotypes ( $2 \times \text{popSize}$  for autosomes in diploid populations).

This statistic sets variables LD, LD\_prime, R2, and optionally ChiSq, ChiSq\_p and CramerV. Subpopulation specific variables can be calculated by specifying variables such as LD\_sp and R2\_sp. Example 3.64 demonstrates how to calculate various LD measures and output selected variables. Note that the significant overall LD between two loci is an artifact of population structure because loci are in linkage equilibrium in each subpopulation.

Example 3.64: Linkage disequilibrium measures

```
>>> import simuPOP as sim
>>> pop = sim.population([1000]*2, loci=3)
>>> sim.InitByFreq(pop, [0.2, 0.8], subPops=0)
>>> sim.InitByFreq(pop, [0.8, 0.2], subPops=1)
>>> sim.Stat(pop, LD=[[0, 1, 0, 0], [1, 2]],
...     vars=['LD', 'LD_prime', 'R2', 'LD_ChiSq', 'LD_ChiSq_p', 'CramerV',
...     'LD_prime_sp', 'LD_ChiSq_p_sp'])
>>> from pprint import pprint
>>> pprint(pop.vars())
{'CramerV': {0: {1: 0.35647022676475704}, 1: {2: 0.39096888549996384}},
 'LD': {0: {1: 0.08908268749999998}, 1: {2: 0.097704625000000017}},
 'LD_ChiSq': {0: {1: 508.28409027886926}, 1: {2: 611.42667771633535}},
 'LD_ChiSq_p': {0: {1: 0.0}, 1: {2: 0.0}},
 'LD_prime': {0: {1: 0.37027887761042649}, 1: {2: 0.40591087520649011}},
 'R2': {0: {1: 0.12707102256971725}, 1: {2: 0.15285666942908391}},
 'subPop': {0: {'LD_ChiSq_p': {0: {1: 0.87538050335969242},
                                1: {2: 0.9505876724892719}},
                 'LD_prime': {0: {1: 0.0039555147901857643},
                                1: {2: 0.0060501296456351179}}},
             1: {'LD_ChiSq_p': {0: {1: 0.48765795867496775},
                                1: {2: 0.4455410002324468}},
                 'LD_prime': {0: {1: -0.061118731900625944},
                                1: {2: 0.018223156154191452}}}}}
```

### 3.10.10 Genetic association

Genetic association refers to association between individual genotype (alleles or genotype) and phenotype (affection status). There are a large number of statistics tests based on different study designs (e.g. case-control, pedigree, longitudinal) with different covariate variables. Although specialized software applications should be used for sophisticated statistical analysis, simuPOP provides a number of simple genetic association tests for convenience. These tests

- Are single-locus tests that test specified loci separately.
- Are based on individual affection status. Associations between genotype and quantitative traits are currently unsupported.
- Apply to all individuals in specified (virtual) subpopulations. Because a population usually has much more unaffected individuals than affected ones, it is a common practice to draw certain types of samples (e.g. a case-control sample with the same number of cases and controls) before statistical tests are applied.

simuPOP currently supports the following tests:

- **Allele-based Chi-square test:** This is the basic allele-based  $\chi^2$  test that can be applied to diploid as well as haploid populations. Basically, a 2 by  $n$  contingency table is set up for each locus with  $n_{ij}$  being the number of alleles  $j$  in cases ( $i = 0$ ) and controls ( $i = 1$ ). A  $\chi^2$  test is applied to each locus and set variables `Allele_ChiSq` and `Allele_ChiSq_p` to the  $\chi^2$  statistic and its two-sided  $p$  value (with degrees freedom  $n - 1$ ). Note that genotype information is not preserved in such a test.
- **Genotype-based Chi-square test:** This is the genotype-based  $\chi^2$  test for diploid populations. Basically, a 2 by  $n$  contingency table is set up for each locus with  $n_{ij}$  being the number of genotype  $j$  (unordered pairs of alleles) in cases ( $i = 0$ ) and controls ( $i = 1$ ). A  $\chi^2$  test is applied to each locus and set variables `Geno_ChiSq` and `Geno_ChiSq_p` to the  $\chi^2$  statistic and its two-sided  $p$  value (with degrees freedom  $n - 1$ ). This test is usually applied to diallelic loci with 3 genotypes ( $AA$ ,  $Aa$  and  $aa$ ) but it can be applied to loci with more than two alleles as well.
- **Genotype-based trend test:** This Cochran-Armitage test can only be applied to diallelic loci in diploid populations. For each locus, a 2 by 3 contingency table is set up with  $n_{ij}$  being the number of genotype  $j$  ( $AA$ ,  $Aa$  and  $aa$  with  $A$  being the wildtype allele) in cases ( $i = 0$ ) and controls ( $i = 1$ ). A Cochran-Armitage trend test is applied to each locus and set variables `Armitage_p` to its two-sided  $p$  value.

Example 3.65 demonstrates how to apply a penetrance model, draw a case-control sample and apply genetic association tests to an evolving population. In this example, a penetrance model is applied to a locus (locus 3). A Python operator is then used to draw a case-control sample from the population and test genetic association at two surrounding loci. Because these two loci are tightly linked to the disease predisposing locus, they are in strong association with the disease initially. However, because of recombination, such association decays with time at rates depending on their genetic distances to the disease predisposing locus.

Example 3.65: Genetic association tests

```
>>> import simuPOP as sim
>>> from simuPOP.utils import *
>>> from simuPOP.sampling import DrawCaseControlSample
>>> def assoTest(pop):
...     'Draw case-control sample and apply association tests'
...     sample = DrawCaseControlSample(pop, cases=500, controls=500)
...     sim.Stat(sample, association=(0, 2), vars=['Allele_ChiSq_p', 'Geno_ChiSq_p', 'Armitage_p'])
...     print 'Allele test: %.2e, %.2e, Geno test: %.2e, %.2e, Trend test: %.2e, %.2e' \
...           % (sample.dvars().Allele_ChiSq_p[0], sample.dvars().Allele_ChiSq_p[2],
...             sample.dvars().Geno_ChiSq_p[0], sample.dvars().Geno_ChiSq_p[2],
...             sample.dvars().Armitage_p[0], sample.dvars().Armitage_p[2])
...     return True
...
>>> simu = sim.simulator(sim.population(size=100000, loci=3),
...     sim.randomMating(ops=sim.recombinator(loci=[0, 1], rates=[0.01, 0.005])))
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([[0]*3, [1]*3], proportions=[0.5, 0.5])
...     ],
...     postOps = [
...         sim.maPenetrance(loci=1, penetrance=[0.1, 0.2, 0.4]),
...         sim.pyOperator(func=assoTest, step=20),
...     ],
...     gen = 100
... )
Allele test: 0.00e+00, 0.00e+00, Geno test: 0.00e+00, 0.00e+00, Trend test: 0.00e+00, 0.00e+00
Allele test: 1.78e-14, 0.00e+00, Geno test: 9.21e-15, 0.00e+00, Trend test: 1.99e-14, 0.00e+00
Allele test: 6.95e-09, 1.21e-13, Geno test: 1.33e-07, 1.61e-12, Trend test: 2.17e-08, 1.90e-13
```

```
Allele test: 1.08e-06, 2.02e-13, Geno test: 3.24e-06, 1.74e-12, Trend test: 6.60e-07, 2.83e-13
Allele test: 3.22e-06, 1.99e-07, Geno test: 1.33e-05, 1.17e-06, Trend test: 2.37e-06, 1.96e-07
(100,)
```

### 3.10.11 Population structure

Parameter `structure` measures the structure of a population using the following statistics:

- The  $G_{ST}$  statistic developed by Nei [1973]. This statistic is equivalent to Wright's fixation index  $F_{ST}$  in the diallelic case so it can be considered as the multi-allele and multi-locus extension of Wright's  $F_{ST}$ . It assumes known genotype frequency so it can be used to calculate true  $F_{ST}$  of a population when all genotype information is available. This statistic sets a dictionary of locus level  $G_{ST}$  (variable `g_st`) and a summary statistics for all loci (variable `G_st`).
- Wright's fixation index  $F_{ST}$  calculated using an algorithm developed by Weir and Cockerham [1984]. This statistic considers existing populations as random samples from an infinite pool of populations with the same ancestral population so it is best to be applied to random samples where true genotype frequencies are unknown. This statistic sets dictionaries of locus level  $F_{ST}$ ,  $F_{IT}$  and  $F_{IS}$  (variables `f_st`, `f_is` and `f_it`), and summary statistics for all loci (variables `F_st`, `F_is` and `F_it`).

These statistics by default uses all existing subpopulations, but it can also be applied to a subset of subpopulations, or even virtual subpopulations using parameter `subPops`. That is to say, you can measure the genetic difference between males and females using `subPops=[(0,0), (0,1)]` if a `sexSplitter` is used to define two virtual subpopulations with male and female individuals respectively.

Example 3.66 demonstrate a simulation with two replicates. In the first replicate, three subpopulations evolve separately without migration and become more and more genetically distinct. In the second replicate, a low level migration is applied between subpopulations so the population structure is kept at a low level.

Example 3.66: Measure of population structure

```
>>> import simuPOP as sim
>>> from simuPOP.utils import MigrIslandRates
>>> simu = sim.simulator(sim.population([5000]*3, loci=10, infoFields='migrate_to'),
...     sim.randomMating(), rep=2)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5])
...     ],
...     preOps = sim.migrator(rate=MigrIslandRates(0.01, 3), reps=1),
...     postOps = [
...         sim.stat(structure=range(10), step=40),
...         sim.pyEval("'Fst=%.3f (rep=%d without migration) ' % (F_st, rep)", step=40, reps=0),
...         sim.pyEval("'Fst=%.3f (rep=%d with migration) ' % (F_st, rep)", step=40, reps=1),
...         sim.pyOutput('\n', reps=-1, step=40)
...     ],
...     gen = 200
... )
Fst=0.000 (rep=0 without migration) Fst=0.000 (rep=1 with migration)
Fst=0.003 (rep=0 without migration) Fst=0.004 (rep=1 with migration)
Fst=0.008 (rep=0 without migration) Fst=0.002 (rep=1 with migration)
Fst=0.009 (rep=0 without migration) Fst=0.002 (rep=1 with migration)
Fst=0.012 (rep=0 without migration) Fst=0.001 (rep=1 with migration)
(200, 200)
```

### 3.10.12 Hardy-Weinberg equilibrium test

Parameter `HWE` accepts a list of loci at which exact Hardy Weinberg equilibrium tests are applied. The  $p$ -values of the tests are assigned to a dictionary `HWE`. Example 3.67 demonstrates how Hardy Weinberg equilibrium is reached in one generation.

Example 3.67: Hardy Weinberg Equilibrium test

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population([1000], loci=1), sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([[0,0], [0, 1], [1,1]], proportions=[0.4, 0.4, 0.2])
...     ],
...     preOps = [
...         sim.stat(HWE=0, genoFreq=0),
...         sim.pyEval(r'"HWE p-value: %.5f (AA: %.2f, Aa: %.2f, aa: %.2f)\n" % (HWE[0], '
...             'genoFreq[0][(0,0)], genoFreq[0][(0,1)] + genoFreq[0][(1,0)], genoFreq[0][(1,1)])')
...     ],
...     postOps = [
...         sim.stat(HWE=0, genoFreq=0),
...         sim.pyEval(r'"HWE p-value: %.5f (AA: %.2f, Aa: %.2f, aa: %.2f)\n" % (HWE[0], '
...             'genoFreq[0][(0,0)], genoFreq[0][(0,1)] + genoFreq[0][(1,0)], genoFreq[0][(1,1)])')
...     ],
...     gen = 1
... )
HWE p-value: 0.00000 (AA: 0.37, Aa: 0.41, aa: 0.21)
HWE p-value: 0.23092 (AA: 0.33, Aa: 0.51, aa: 0.16)
(1,)
```

### 3.10.13 Other statistics

If you need other statistics, a popular approach is to define them using Python operators. If your statistics is based on existing statistics such as allele frequency, it is a good idea to calculate existing statistics using a `Stat` function and derive your statistics from population variables. Please refer to the last chapter of this guide on an example.

If performance becomes a problem, you might want to have a look at the source code of `simuPOP` and implement your statistics at the C++ level. If you believe that your statistics are popular enough, please send your implementation to the `simuPOP` mailinglist for possible inclusion of your statistics into `simuPOP`.

## 3.11 Miscellaneous operators

### 3.11.1 An operator that does nothing (operator `noneOp`)

Operator `noneOp` does nothing when it is applied to a population. It provides a placeholder when an operator is needed but no action is required. Example 3.11.1 demonstrates a typical usage of this operator

```
if hasSelection:
    sel = mapSelector(loci=[0], fitness=[1, 0.99, 0.98])
else:
    sel = noneOp()
#
simu.evolve(
    ops = [sel], # and other operators
)
```

### 3.11.2 Dump the content of a population (operator dumper)

Operator `dumper` and its function form `Dump` has been used extensively in this guide. They are perfect for demonstration and debugging purposes because they display all properties of a population in a human readable format. They are, however, rarely used in realistic settings because outputting a large population to your terminal can be disastrous.

Even with modestly-sized populations, it is a good idea to dump only parts of the population that you are interested. For example, you can use parameter `genotype=False` to stop outputting individual genotype, `structure=False` to stop outputting genotypic and population structure information, `loci=range(5)` to output genotype only at the first five loci, `max=N` to output only the first N individuals (default to 100), `subPops=[(0, 0)]` to output, for example, only the first virtual subpopulation in subpopulation 0. This operator by default only dump the present generation but you can set `ancGen` to a positive number or `-1` to dump part or all ancestral generations. Finally, if there are more than 10 alleles, you can set the `width` at which each allele will be printed. The following example (Example 3.68) presents a rather complicated usage of this operator.

Example 3.68: Dump the content of a population

```
>>> import simuPOP as sim
>>> pop = sim.population(size=[10, 10], loci=[20, 30], infoFields='gen',
...     ancGen=-1)
>>> pop.setVirtualSplitter(sim.sexSplitter())
>>> pop1 = pop.clone()
>>> sim.InitByFreq(pop, [0]*20 + [0.1]*10)
>>> pop.setIndInfo(1, 'gen')
>>> sim.InitByFreq(pop1, [0]*50 + [0.1]*10)
>>> pop1.setIndInfo(2, 'gen')
>>> pop.push(pop1)
>>> sim.Dump(pop, width=3, loci=[5, 6, 30], subPops=([0, 0], [1, 1]),
...     max=10, structure=False, ancGen=-1)
Subpopulation 0,0 (MALE), 10 individuals:
 0: MU  57 53 53 |  51 52 55 |  2
 1: MU  53 58 53 |  54 58 59 |  2
 2: MU  53 55 55 |  51 52 53 |  2
 3: MU  54 54 55 |  57 54 56 |  2
 4: MU  54 51 58 |  55 59 59 |  2
 5: MU  55 53 52 |  57 55 53 |  2
 6: MU  51 58 57 |  56 57 55 |  2
 7: MU  50 50 52 |  53 56 53 |  2
 8: MU  57 57 54 |  59 58 57 |  2
 9: MU  51 57 50 |  52 56 58 |  2
Subpopulation 1,1 (FEMALE), 0 individuals:

Ancestry population 1
Subpopulation 0,0 (MALE), 10 individuals:
 0: MU  29 27 20 |  27 27 22 |  1
 1: MU  22 27 27 |  27 21 29 |  1
 2: MU  28 20 27 |  27 21 21 |  1
 3: MU  26 24 20 |  23 24 21 |  1
 4: MU  21 28 25 |  20 29 25 |  1
 5: MU  24 27 22 |  28 23 24 |  1
 6: MU  26 24 26 |  27 20 23 |  1
 7: MU  27 29 20 |  26 20 23 |  1
 8: MU  28 28 29 |  29 22 20 |  1
 9: MU  26 29 25 |  22 27 23 |  1
Subpopulation 1,1 (FEMALE), 0 individuals:
```



### 3.11.3 Save a population during evolution (operator `savePopulation`)

Because it is usually not feasible to store all parental generations of an evolving population, it is a common practise to save snapshots of a population during an evolutionary process for further analysis. Operator `savePopulation` is designed for this purpose. When it is applied to a population, it will save the population to a file specified by parameter `output`.

The tricky part is that populations at different generations need to be saved to different filenames so the expression version of parameter `output` needs to be used (see operator `baseOperator` for details). For example, expression `'snapshot_%d_%d.pop' % (rep, gen)` is used in Example 3.69 to save population to files such as `snapshot_5_20.pop` during the evolution.

Example 3.69: Save snapshots of an evolving population

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(100, loci=2),
...     sim.randomMating(), rep=5)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.2, 0.8])
...     ],
...     postOps = sim.savePopulation(output="!'snapshot_%d_%d.pop' % (rep, gen)",
...         step = 10),
...     gen = 50
... )
(50, 50, 50, 50, 50)
```

### 3.11.4 Change ancestral depth of populations (operator `setAncestralDepth`)

Example 2.63 describes a two-stage evolutionary process where a random mating scheme is used in the first stage and another mating scheme is used in the second stage to prepare for pedigree ascertainment. The ancestral depth of each population is changed to 1 before the second `simulator.evolve` call. This step can also be done using a `setAncestralDepth` operator, which simply set the ancestral depth of each population to a given depth (please refer to class `population` for a detailed explanation for *ancestral depth*). Example 3.70 demonstrates a tpical usage of this operator.

Example 3.70: Change ancestral depth during the evolution

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(100, infoFields=['father_idx', 'mother_idx']),
...     sim.randomMating(), rep=5)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.3, 0.7])
...     ],
...     preOps = sim.setAncestralDepth(2, at=-2),
...     duringOps = sim.parentsTagger(begin=-2),
...     gen = 100
... )
(100, 100, 100, 100, 100)
>>> pop = simu.population(3)
>>> print pop.ancestralGens()
2
>>> print pop.ancestor(10, 1).father_idx
26.0
```

### 3.11.5 Conditional operator (operator `ifElse`) \*

Operator `ifElse` provides a simple way to conditionally apply an operator. The condition can be a fixed condition or an expression that will be evaluated in a population's local namespace when it is applied to the population.

The first case is used to control the execution of certain operators depending on user input. For example, Example 3.71 determines whether or not some outputs should be given depending on a variable `verbose`. Note that the applicability of the conditional operators are determined by the `ifElse` operator and individual operators. That is to say, the parameters `begin`, `step`, `end`, `at`, and `reps` of operators in `ifOps` and `elseOps` are only honored when operator `ifElse` is applied.

Example 3.71: A conditional operator with fixed condition

```
>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(size=1000, loci=1),
...     sim.randomMating())
>>> verbose = True
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5]),
...     ],
...     postOps = sim.ifElse(verbose,
...         ifOps = [
...             sim.stat(alleleFreq=0),
...             sim.pyEval(r'''Gen: %3d, allele freq: %.3f\n' % (gen, alleleFreq[0][1])'',
...                 step=5)
...         ],
...         begin=10),
...     gen = 30
... )
Gen: 10, allele freq: 0.483
Gen: 15, allele freq: 0.455
Gen: 20, allele freq: 0.481
Gen: 25, allele freq: 0.481
(30,)
```

The expression form of this operator is more useful. For example, you can re-introduce a mutant if it gets lost in the population, output a warning when certain condition is met, or record the occurrence of certain events in a population. For example, Example 3.72 records the number of generations the frequency of an allele goes below 0.4 and beyond 0.6 before it gets lost or fixed in the population. Note that an `else`-operator can also be executed when the condition is not met. If more complicated logic is involved, a Python operator (`pyOperator`) should be used.

Example 3.72: A conditional operator with dynamic condition

```
>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(size=1000, loci=1),
...     sim.randomMating(), rep=4)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5]),
...         sim.pyExec('below40, above60 = 0, 0')
...     ],
...     postOps = [
...         sim.stat(alleleFreq=0),
...         sim.ifElse('alleleFreq[0][1] < 0.4',
...             sim.pyExec('below40 += 1')),
...     ]
... )
```

```

...     sim.ifElse('alleleFreq[0][1] > 0.6',
...               sim.pyExec('above60 += 1')),
...     sim.ifElse('len(alleleFreq[0]) == 1',
...               sim.pyExec('stoppedAt = gen')),
...     sim.terminateIf('len(alleleFreq[0]) == 1')
... ]
... )
(892, 1898, 4001, 2946)
>>> for pop in simu.populations():
...     print 'Overall: %4d, below 40%%: %4d, above 60%%: %4d' % \
...           (pop.dvars().stoppedAt, pop.dvars().below40, pop.dvars().above60)

```

### 3.11.6 Conditionally terminate an evolutionary process (operator `terminateIf`)

Operator `terminateIf` has been described and used in several examples such as Example 2.60, 2.21 and 3.72. This operator accept an Python expression and terminate the evolution of the population being applied if the expression is evaluated to be `True`. This operator is well suited for situations where the number of generations to evolve cannot be determined in advance.

If a `terminateIf` operator is applied to the offspring generation (post-mating, default), the evolutionary cycle is considered to be completed. If the evolution is terminated before mating, the evolutionary cycle is condered to be imcomplete. Such a difference can be important if the number of generations that have been involved is important for your analysis.

A less-known feature of operator `terminateIf` is its ability to terminate the evolution of all replicates, using parameter `stopAll=True`. For example, Example 3.73 terminates the evolution of all populations when one of the populations gets fixed. The return value of `simu.evolve` shows that some populations have evolved one generation less than the population being fixed.

Example 3.73: Terminate the evolution of all populations in a simulator

```

>>> import simuPOP as sim
>>> simu = sim.simulator(
...     sim.population(size=100, loci=1),
...     sim.randomMating(), rep=10)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5]),
...     ],
...     postOps = [
...         sim.stat(alleleFreq=0),
...         sim.terminateIf('len(alleleFreq[0]) == 1', stopAll=True)
...     ]
... )
(88, 88, 88, 88, 87, 87, 87, 87, 87, 87)
>>>

```

### 3.11.7 Turn on and off debugging mode (operator `turnOnDebug` and `turnOffDebug`) \*

Debug information can be useful when something looks suspicious. By turnning on certain debug code, `simuPOP` will print out some internal information before and during evolution. The usually way to turn on and off debug information is to use functions `TurnOnDebug(code)` and `TurnOffDebug(code)`, or setting environmental variable `SIMUDEBBUG=code` where `code` is one of the debug codes listed by function `ListDebugCodes`. Note that debug information is only available in standard modules.

However, the amount of output can be overwhelming in some cases which makes it necessary to limit the debug information to certain generations. Example 3.74 demonstrates how to turn on debug information conditionally and turn it off afterwards, using operators `turnOnDebug` and `turnOffDebug`.

Example 3.74: Turn on and off debug information during evolution.

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(100, loci=1), sim.randomMating(), rep=5)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.1, 0.9])
...     ],
...     postOps = [
...         sim.stat(alleleFreq=0),
...         sim.ifElse('alleleNum[0][0] == 0',
...             ifOps = [
...                 sim.turnOnDebug("DBG_MUTATOR"),
...                 sim.pointMutator(loci=0, allele=0, inds=0),
...             ],
...             elseOps = sim.turnOffDebug("DBG_MUTATOR")),
...     ],
...     gen = 100
... )
```

### 3.11.8 Pause and resume an evolutionary process (operator pause) \*

If you are presenting an evolutionary process in public, you might want to temporarily stop the evolution so that your audience can have a better look at intermediate results or figures. If you have an exceptionally long evolutionary process, you might want to examine the status of the evolution process from time to time. These can be done using a `pause` operator.

The `pause` operator can stop the evolution at specified generations, or when you press a key. In the first case, you usually specify the generations to pause (e.g. `pause(step=1000)`) so that you can examine the status of a simulation from time to time. In the second case, you can apply the operator at each generation and pause the simulation when you press a key (e.g. `pause(stopOnKeyStroke=True)`). A specific key can be specified so that you can use different keys to stop different populations, as shown in Example 3.75.

Example 3.75: Pause the evolution of a simulation

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(100), sim.randomMating(), rep=10)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.5, 0.5])
...     ],
...     postOps = [sim.pause(stopOnKeyStroke=str(x), reps=x) for x in range(10)],
...     gen = 100
... )
(100, 100, 100, 100, 100, 100, 100, 100, 100, 100)
```

When a simulation is paused, you are given the options to resume evolution, stop the evolution of the paused population or all populations, or enter an interactive Python shell to examine the status of a population, which will be available in the Python shell as `pop_X_Y` where `X` and `Y` are generation and replicate number of the population, respectively. The evolution will resume after you exit the Python shell.

### 3.11.9 Measuring execution time of operators (operator `ticToc`) \*

The `ticToc` operator can be used to measure the time between two events during an evolutionary process. It outputs the elapsed time since the last time it is called, and the overall time since the operator is created. It is very flexible in that you can measure the time spent for mating in an evolutionary cycle if you apply it before and after mating, and you can measure time spent for several evolutionary cycles using generation applicability parameters such as `step` and `at`. The latter usage is demonstrated in Example 3.76.

Example 3.76: Monitor the performance of operators

```
>>> import simuPOP as sim
>>> simu = sim.simulator(sim.population(10000, loci=[100]*5), sim.randomMating(), rep=2)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.1, 0.9])
...     ],
...     postOps = [
...         sim.stat(alleleFreq=0),
...         sim.ticToc(step=50, reps=-1),
...     ],
...     gen = 101
... )
Start stopwatch.
Elapsed time: 3.22s      Overall time: 3.22s
Elapsed time: 3.34s      Overall time: 6.56s
(101, 101)
```



# Chapter 4

## Utility Modules

### 4.1 Module `simuOpt` (function `simuOpt.setOptions`)

Module `simuOpt` handles options to specify which `simuPOP` module to load and how this module should be loaded, using function `simuOpt.setOptions` with parameters *alleleType* (short, long, or binary), *optimized* (standard or optimized), *gui* (whether or not use a graphical user interface and which graphical toolkit to use), *revision* (minimal required version/revision), *quiet* (with or without banner message), and *debug* (which debug code to turn on). These options have been discussed in Example 2.1 and 2.2 and other related sections. Note that **most options can be set by environmental variables and command line options** which are sometimes more versatile to use.

#### 4.1.1 Class `simuOpt.simuParam`

The `simuOpt` module also provides a class `simuParam` to help users handle and manage script parameters. There are many other standard or third-party parameter handling modules in Python but this class is designed to help users run a `simuPOP` script in both batch and GUI modes, using a combination of parameter determination methods. More specifically, if a script uses the `simuOpt.simuParam` class to handle parameters,

- By default, a parameter input dialog is used to accept user input if the script is executed directly. Default values are given to each parameter and users are allowed to edit them using standard parameter input widgets (on/off button, edit box, dropdown list etc). Detailed explanations to parameters are available as tooltips of corresponding input widgets. A help button is provided that will display the usage of the script when clicked.
- If a configuration file is saved for a previous simulation, command line option `--config configFile` can be used to load all parameters from that configuration file. The parameter input dialog is still used to review and modify parameters.
- Each parameter can also be set using command line options. Command line inputs will override values read from a configuration file.
- If command line option `--gui=False` is given, the script will work in batch mode. If the value of a parameter cannot be determined through command line or a configuration file, and is set not to use its default value, users will be asked to enter its value interactively. For example, `myscript.py --gui=False --config configFile` will execute a previous simulation directly.

The following sections describes how to use the `simuOpt` class in a `simuPOP` script.

### 4.1.2 Define a parameter specification list.

A `simuParam` object is created from a list of parameter specification dictionaries, and optional short and long descriptions of a script. Each parameter specification dictionary consists of mandatory fields `longarg` (long command line argument) and `default` (default value for this parameter) and optional fields such as `label` (label to display in the parameter input dialog and as prompt for user input), `description` (a detailed description), `allowedTypes` (allowed types of input parameter), `validate` (a function that return tells if a user input is valid), `chooseOneOf` (tells the parameter input dialog to allow users to choose one of the provided values) and `chooseFrom` (tells the parameter input dialog to allow users to choose one or more values from the provided values). Although it can be lengthy to describe a parameter in this way, it is a self-documentary process from which your users and even yourself will benefit.

Example 4.3 shows a parameter specification list that defines parameter `help`, `rate`, `rep` and `pops`. What is special about each parameter is that `help` will not be listed in the parameter input dialog (no `label`) and setting `help` to `True` during interactive parameter input will ignore all other options (`jump`); `rate` has to be between 0 and 1 (using a validation function `valueBetween`), `rep` has to be a positive integer, and `pops` can be one of the three HapMap populations. Please refer to the `simuPOP` reference manual for details about each dictionary key. The description of parameter `pop` demonstrates a special rule in the formatting of such description texts, namely **lines with symbol `'` as the first non-space/tab character are outputted as a separate line without the leading `'` character**.

Example 4.1: A sample parameter specification list

```
import simuPOP as sim
import types, simuOpt
options = [
    {'arg': 'r:',
     'longarg': 'rate=',
     'default': [0.01],
     'useDefault': True,
     'label': 'Recombination rate',
     'allowedTypes': [types.ListType, types.TupleType],
     'description': '''Recombination rate for each replicate. If a single value
                       is given, it will be used for all replicates.'''},
    {'longarg': 'rep=',
     'default': 5,
     'label': 'Number of replicates',
     'allowedTypes': [types.IntType, types.LongType],
     'description': 'Number of replicates to simulate.',
     'validate': simuOpt.valueGT(0)},
    {'longarg': 'pop=',
     'default': 'CEU',
     'label': 'Initial sim.population',
     'allowedTypes': [types.StringType],
     'description': '''Use one of the HapMap sim.populations as the initial
                       sim.population for this simulation. You can choose from:
                       |YRI: 33 trios from the Yoruba people in Nigeria (Africa)
                       |CEU: 30 trios from Utah with European ancestry (European)
                       |CHB+JPT: 90 unrelated individuals from China and Japan (Asia)
                       ''',
     'chooseOneOf': ['CEU', 'YRI', 'CHB+JPT'],
     'validate': simuOpt.valueOneOf(['CEU', 'YRI', 'CHB+JPT'])}
]
```

If you dislike an explicit list of dictionaries, you can use function `simuOpt.param` with keyword arguments to return such a dictionary. Example 4.2 shows an equivalent parameter specification dictionaries using this style. **There**



is no functional difference between these two styles.

Example 4.2: Using `simuOpt.param` to specify parameters

```
import types, simuOpt
options = [
    simuOpt.param(
        arg = 'r:',
        longarg = 'rate=',
        default = [0.01],
        useDefault = True,
        label = 'Recombination rate',
        allowedTypes = [types.ListType, types.TupleType],
        description = '''Recombination rate for each replicate. If a single value
            is given, it will be used for all replicates.''' ,
        validate = simuOpt.valueListOf(simuOpt.valueBetween(0, 1))),
    simuOpt.param(
        longarg = 'rep=',
        default = 5,
        label = 'Number of replicates',
        allowedTypes = [types.IntType, types.LongType],
        description = 'Number of replicates to simulate.',
        validate = simuOpt.valueGT(0)),
    simuOpt.param(
        longarg = 'pop=',
        default = 'CEU',
        label = 'Initial sim.population',
        allowedTypes = [types.StringType],
        description = '''Use one of the HapMap sim.populations as the initial
            sim.population for this simulation. You can choose from:
            |YRI: 33 trios from the Yoruba people in Nigeria (Africa)
            |CEU: 30 trios from Utah with European ancestry (European)
            |CHB+JPT: 90 unrelated individuals from China and Japan (Asia)
            ''',
        chooseOneOf = ['CEU', 'YRI', 'CHB+JPT'],
        validate = simuOpt.valueOneOf(['CEU', 'YRI', 'CHB+JPT']))
]
```

### 4.1.3 Get parameters (function `simuParam.getParam`)

A `simuParam` object can be created from a parameter specification list. A few member functions are immediately usable. For example, `simuParam.usage()` returns a detailed usage message about the script and all its parameters (although the usage message will be displayed automatically if command line option `-h` or `--help` is detected). The parameters become attributes of this object using `longarg` names so that you can access them easily (e.g. `par.rate`). Not surprisingly, all parameters now have the default value you assigned to them.

Function `simuParam.saveConfig(filename)` saves current values of parameters to a configuration file `filename`. Parameters that do not have a label are ignored. This configuration file can be loaded later using command line option `--config filename`, perhaps with option `--gui=False` to run the script in batch mode. A less noticed feature of this function is that it also writes a complete command that specifies the same parameters using command line options. This can be handy if you would like to use real parameter definitions instead of `--config filename` in a batch file.

The `params.simuParam` class provides a number of member functions that allow you to acquire user input in a number of ways. For example `simuParam.loadConfig` reads a configuration file, `simuParam.processArgs` checks commandline options, `simuParam.termGetParam` asks user input interactively, and `simuParam.guiGetParam` generates and uses a parameter input dialog. These functions can be used several times, on different sets of parameters. In addition, new options could be added programmatically using

function `simuParam.addOption` and allows further flexibility on how parameters are generated. Please refer to *the simuPOP reference manual* on how to use these functions.

#### Example 4.3: Get parameters using function `getParam`

```
>>> pars = simuOpt.simuParam(options, 'A demo simulation')
>>> print pars.usage()
A demo simulation

usage: runSampleCode.py [-opt [arg] | --opt [=arg]] ...

options:
  -h, --help            show this help message and exit
  --config ARG          load parameters from ARG
  --optimized           run the script using an optimized simuPOP module
  --gui ARG             which graphical toolkit to use
  -r ARG, --rate ARG    Recombination rate [default: [0.01] ]
                        Recombination rate for each replicate. If a single value
                        is given, it will be used for all replicates.
  --rep ARG            Number of replicates [default: 5 ]
                        Number of replicates to simulate.
  --pop ARG            Initial sim.population [default: CEU ]
                        Use one of the HapMap sim.populations as the initial
                        sim.population for this simulation. You can choose from:
                        YRI: 33 trios from the Yoruba people in Nigeria (Africa)
                        CEU: 30 trios from Utah with European ancestry
                        (European)
                        CHB+JPT: 90 unrelated individuals from China and Japan
                        (Asia)

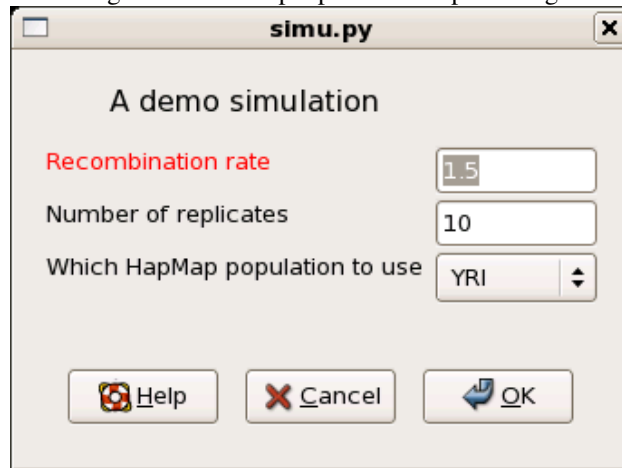
>>> # You can manually feed parameters...
>>> pars.processArgs(['--rep=10'])
True
>>> pars.rep
10
>>> if not pars.getParam():
...     sys.exit(1)
...
>>> pars.saveConfig('sample.cfg')
>>> # post-process parameters
```

Example 4.3 lists some methods to determine parameter values but the last function, `simuParam.getParam()`, will be used most of the time. This function processes each parameter in the following order:

- If a short or a long command line argument exists, use the command line argument.
- If a configuration file is specified from command line (`--config configFile`), look in this configuration file for a value.
- If `useDefault` is specified, assign a default value to this parameter.
- If `--gui=False` is specified, and the value of the parameter has not been determined, ask users interactively for a value. Otherwise, a parameter input dialog is displayed. A *Tkinter* dialog is usually used but a *wxPython* dialog will be used if *wxPython* is available (unless parameter `--gui=Tkinter` is set).

`simuParam.getParam` returns `False` if this process fails (e.g. users click cancel in the parameter input dialog). The parameter input dialog for Example 4.3 is shown in Figure 4.1. **Note:** If `simuParam.valueValidFile()` or `simuParam.valueValidDir()` is used to validate a parameter, **double click** the input textbox of this parameter will open a file or directory browse dialog.

Figure 4.1: A sample parameter input dialog



A parameter input dialog for a script that uses the same parameter specification list as Example 4.3. The command line is `simu.py --pop=YRI`. The first parameter is in red because its input is invalid.

#### 4.1.4 Access, manipulate and extract parameters

If `simuOpt.getParam` runs successfully, the `simuOpt` object should have valid value for each parameter. They can be retrieved as attributes (such as `par.rate`) and manipulated easily. Example 4.4 demonstrates how to extend parameter `par.rate` to have the same length as `par.rep`.

When there are a large number of parameters, passing this `simuParam` object, instead of tens of parameters, is a good way to provide clean interfaces. Alternatively, you can get a list or a dictionary of parameters using member functions `simuParam.asList()` and `simuParam.asDict()`.

Example 4.4: Use the `simuOpt` object

```
>>> pars.rate
[0.25]
>>> pars.rep
5
>>> pars.rate = pars.rate * pars.rep
>>> # extract parameters as a dictionary or a list
>>> pars.asDict()
{'rate': [0.25, 0.25, 0.25, 0.25, 0.25], 'rep': 5, 'pop': 'CEU'}
>>> pars.asList()
[[0.25, 0.25, 0.25, 0.25, 0.25], 5, 'CEU']
>>> # Default value of parameter rep is changed
>>> # additional attribute is added.
>>> par1 = simuOpt.simuParam(options, # all parameters with default values
...     rep=50,                    # default value of rep is changed
...     additional=10              # derived parameters are added
... )
>>> # print all parameters except for derived ones.
>>> print par1.asDict()
{'rate': [0.01], 'rep': 50, 'pop': 'CEU'}
>>> # All parameters are derived ...
>>> par2 = simuOpt.simuParam(rep=50, pop='CEU', rate=[0.5])
>>> print par2.asDict()
{}
>>> print par2.rep, par2.pop
50 CEU
```

It is easy to set **additional attributes** to a `simuParam` object, using either `par.name = value` statement or additional `name=value` pairs in the constructor of a `simuOpt` object. These attributes are not considered as parameters of an `simuOpt` object (e.g. they are not returned by function `simuParam.asDict()`) but could be used just like regular parameters. Note that the same operations for `simuOpt` parameters change the value of these parameters.

Additional attributes can be used to create a `simuOpt` object without user interaction. For example, objects `par1` and `par2` in Example 4.4 are created easily with needed attributes. They can be passed to functions where a `simuParam` object is needed, although some of the attributes are not real parameters (in the sense that they are not created by a parameter specification dictionary and will not be used to handle user input).

## 4.2 Module `simuPOP.utils`

The `simuPOP.utils` module provides a few utility functions and classes. They do not belong to the `simuPOP` core but are distributed with `simuPOP` because they are frequently used and play an important role in some specialized simulation techniques. Please refer to the `simuPOP` online cookbook (<http://simupop.sourceforge.net/cookbook>) for more utility modules and functions.

### 4.2.1 Trajectory simulation (classes `trajectory` and `trajectorySimulator`)

A forward-time simulation, by its nature, is directly influenced by random genetic drift. Starting from the same parental generation, allele frequencies in the offspring generation would vary from simulation to simulation, with perhaps a predictable mean frequency which is determined by factors such as parental allele frequency, natural selection, mutation and migration.

Genetic drift is unavoidable and is in many cases the target of theoretical and simulation studies. However, in certain types of studies, there is often a need to control the frequencies of certain alleles in the present generation. For example, if we are studying a particular penetrance model with pre-specified frequencies of disease predisposing alleles, the simulated populations would better have consistent allele frequencies at the disease predisposing loci, and consequently consistent disease prevalence.

`simuPOP` provides a special offspring generator `controlledOffspringGenerator` and an associated mating scheme called `controlledRandomMating` that can be used to generate offspring generations conditioning on frequencies of one or more alleles. This offspring generator essentially uses a reject-sampling algorithm to select (or reject) offspring according to their genotypes at specified loci. A detailed description of this algorithm is given in Peng et al. [2007].

The controlled random mating scheme accepts a user-defined trajectory function that tells the mating scheme the desired allele frequencies at each generation. Example 2.51 uses a manually defined function that raises the frequency of an allele steadily. However, given known demographic and genetic factors, **a trajectory should be simulated randomly so that it represents a random sample from all possible trajectories that match the allele frequency requirement**. If such a condition is met, the controlled evolutionary process can be considered as a random process conditioning on allele frequencies at the present generation. Please refer to Peng et al. [2007] for a detailed discussion about the theoretical requirements of a valid trajectory simulator.

The `simuUtil` module provides functions and classes that implement two trajectory simulation methods that can be used in different situations. The first class is `trajectorySimulator` which takes a demographic model and a selection model as its input and simulates allele frequency trajectories using a forward or backward algorithm. The demographic model is given by parameter `N`, which can be a constant (e.g. `N=1000`) for constant population size, a list of subpopulation sizes (e.g. `N=[1000, 2000]`) for a structured population with constant size, or a demographic function that returns population or subpopulation sizes at each generation. In the last case, subpopulations can be split or merged with the constraint that subpopulations can be merged into one, from split from one population.

A fitness model specifies the fitness of genotypes at one or more loci using parameter `fitness`. It can be a list of three numbers (e.g. `fitness=[1, 1.001, 1.003]`), representing the fitness of genotype `AA`, `Aa` and `aa` at one or more loci; or different fitness for genotypes at each locus (e.g. `fitness=[1, 1.001, 1.003, 1, 1,`

1.002]), or for each combination of genotype (interaction). In the last case,  $3^n$  values are needed for each genotype if there are  $n$  loci. This trajectory simulator also accepts generation-specific fitness values by accepting a function that returns fitness values at each generation.

The simulator then simulates trajectories of allele frequencies and return them as objects of class `trajectory`. This object can be used provide a trajectory function that can be used directly in a `controlledRandomMating` mating scheme (function `trajectory.func()`) or provide a list of `pointMutator` to introduce mutants at appropriate generations (function `trajectory.mutators()`). If a simulation failed after specified number of attempts, a `None` object will be returned.

### Forward-time trajectory simulations (function `ForwardTrajectory`)

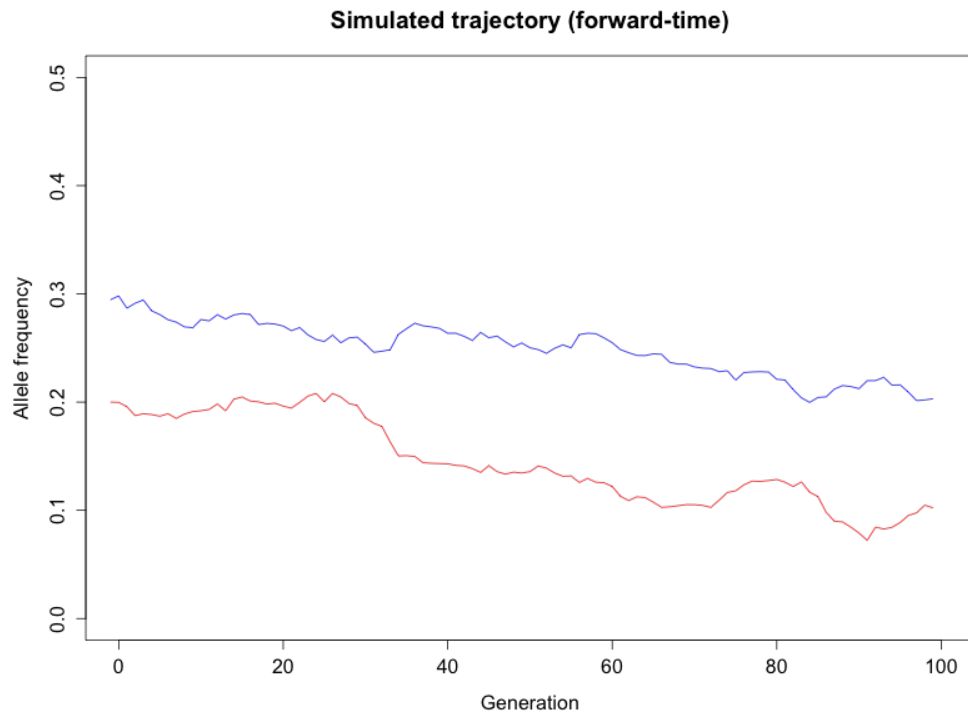
A forward simulation starts from a specified generation with specified allele frequencies at one or more loci. The simulator simulates allele frequencies forward-in-time, until it reaches a specified ending generation. A trajectory object will be returned if the simulated allele frequencies fall into specified ranges. Example 4.5 demonstrates how to use this simulation method to obtain and use a simulated trajectory, for two unlinked loci under different selection pressure.

Example 4.5: Simulation and use of forward-time simulated trajectories.

```
>>> import simuPOP as sim
>>> from simuPOP.utils import trajectory, ForwardTrajectory
>>>
>>> traj = ForwardTrajectory(N=[2000, 4000], fitness=[1, 0.99, 0.98],
...     beginGen=0, endGen=100, beginFreq=[0.2, 0.3],
...     endFreq=[[0.1, 0.11], [0.2, 0.21]])
>>> traj.plot('log/forwardTrajectory.png', plot_ylim=[0, 0.5], col_sp=['red', 'blue'],
...     plot_main='Simulated trajectory (forward-time)')
>>> simu = sim.simulator(
...     sim.population(size=[2000, 4000], loci=10, infoFields='fitness'),
...     sim.controlledRandomMating(
...         ops=[sim.recombinator(rates=0.01)],
...         loci=5, alleles=1, freqFunc=traj.func())
... )
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByFreq([0.8, 0.2], subPops=0),
...         sim.initByFreq([0.7, 0.3], subPops=1),
...         sim.pyOutput('Sp0: loc2\tloc5\tSp1: loc2\tloc5\n'),
...     ],
...     postOps = [
...         sim.stat(alleleFreq=[2, 5], vars=['alleleFreq_sp'], step=20),
...         sim.pyEval(r"'%.2f\t%.2f\t%.2f\t%.2f\n' % (subPop[0]['alleleFreq'][2][1],
...             "subPop[0]['alleleFreq'][5][1], subPop[1]['alleleFreq'][2][1],
...             "subPop[1]['alleleFreq'][5][1])", step=20)
...     ],
...     gen = 101
... )
Sp0: loc2      loc5      Sp1: loc2      loc5
0.21    0.20    0.29    0.29
0.19    0.20    0.28    0.27
0.14    0.14    0.33    0.27
0.13    0.13    0.35    0.26
0.14    0.13    0.35    0.23
0.08    0.10    0.37    0.20
(101,)
```

Figure 4.2 plots simulated trajectories of one locus in two subpopulations.

Figure 4.2: Simulated trajectories of one locus in two subpopulations



#### Backward-time trajectory simulations (function `BackwardTrajectory`).

A backward simulation starts from specified frequencies at the present generation. In the single-allele case, the simulation goes backward-in-time until an allele gets lost. The length of such a trajectory is random, which is usually a desired property because the age of a mutant in the present generation is usually unknown and is assumed to be random.

This trajectory simulation technique is usually used as follows:

1. Determine a demographic and a natural selection model using which a forward-time simulation will be performed.
2. Given current disease allele frequencies, simulate trajectories of allele frequencies at each DSL using a backward approach.
3. Evolve a population forward-in-time, using designed demographic and selection models. A `controlledRandomMating` scheme instead of the usual `randomMating` scheme should be used.

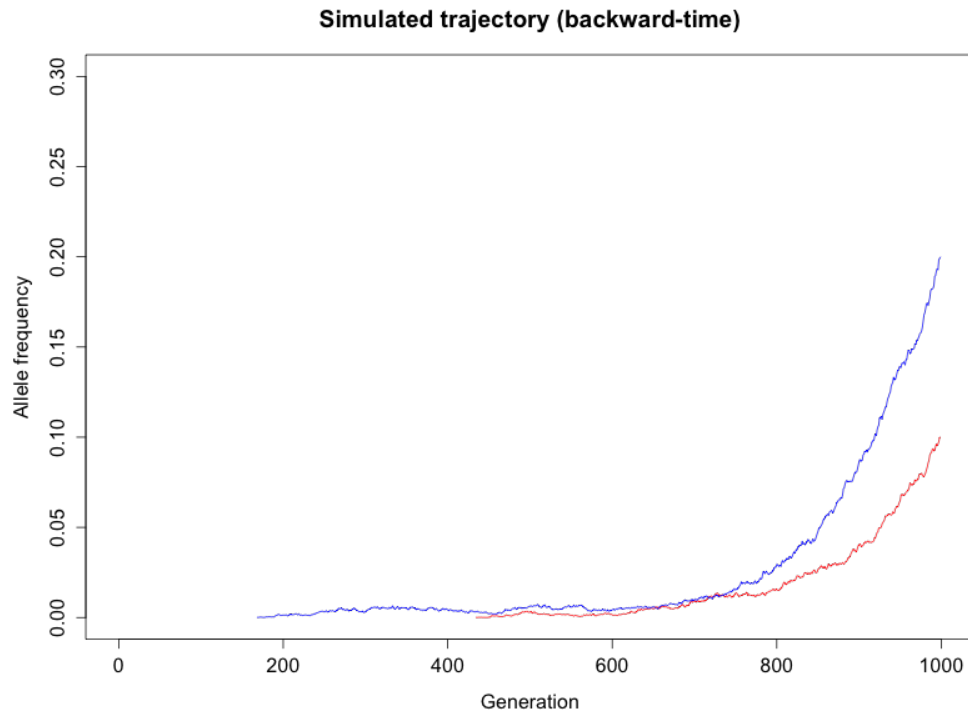
Figure 4.3 plots simulated trajectories of two unlinked loci.

The trajectory is used in a `controlledRandomMating` scheme in the following evolutionary scenario:

Example 4.6: Simulation and use of backward-time simulated trajectories.

```
>>> import simuPOP as sim
>>> from simuPOP.utils import trajectory, BackwardTrajectory
>>> from math import exp
>>> def Nt(gen, pop=None):
```

Figure 4.3: Simulated trajectories of two unlinked loci



```
...     'An exponential sim.population growth demographic model.'
...     return int((10**4) * exp(.00115 * gen))
...
>>> def fitness(gen, sp):
...     'sim.CONSTANT positive selection pressure.'
...     return [1, 1.01, 1.02]
...
>>> # simulate a trajectory backward in time, from generation 1000
>>> traj = BackwardTrajectory(N=Nt, fitness=fitness, nLoci=2,
...     endGen=1000, endFreq=[0.1, 0.2])
>>> traj.plot('log/backTrajectory.png', plot_ylim=[0, 0.3], plot_xlim=[0, 1000],
...     col_loc=['red', 'blue'], plot_main='Simulated trajectory (backward-time)')
>>> print 'Trajectory simulated with length %s ' % len(traj.traj)
Trajectory simulated with length 833
>>> pop = sim.population(size=Nt(0), loci=[1]*2)
>>> # save trajectory function in the sim.population's local namespace
>>> # so that the sim.pyEval operator can access it.
>>> pop.dvars().traj = traj.func()
>>> simu = sim.simulator(pop, sim.controlledRandomMating(loci=[0, 1], alleles=[1, 1],
...     subPopSize=Nt, freqFunc=traj.func()))
>>> simu.evolve(
...     initOps = [sim.initSex()],
...     preOps = traj.mutators(loci=[0, 1]),
...     postOps = [
...         sim.stat(alleleFreq=[0, 1], begin=500, step=100),
...         sim.pyEval(r"'%4d: %.3f (exp: %.3f), %.3f (exp: %.3f)\n' % (gen, alleleFreq[0][1],
...             "traj(gen)[0], alleleFreq[1][1], traj(gen)[1])",
...             begin=500, step=100)
...     ],

```

```

...     gen=1001 # evolve 1001 generations to reach the end of generation 1000
... )
500: 0.003 (exp: 0.003), 0.006 (exp: 0.006)
600: 0.002 (exp: 0.002), 0.004 (exp: 0.004)
700: 0.009 (exp: 0.009), 0.010 (exp: 0.010)
800: 0.016 (exp: 0.016), 0.028 (exp: 0.028)
900: 0.040 (exp: 0.040), 0.085 (exp: 0.084)
1000: 0.101 (exp: 0.100), 0.200 (exp: 0.200)
(1001,)

```

## 4.2.2 Progress bar

## 4.3 Module `simuPOP.plotter`

The `simuPOP.plotter` module defines a few utility functions and Python operators that help you plot variables and information fields during evolution. A number of operators are defined that

- Operator `plotter.varPlotter`: Plot a dynamically evaluated expression with its history. Each expression and its history form a line in the plot. Multiple lines will be plotted for multiple replicates and/or for each element of the expression (if the evaluated value of the expression is a sequence), with options to separate lines to different subplots.
- Operator `plotter.scatterPlotter`: Plot individuals in specified (virtual) subpopulations using values at two information fields as x and y axes. Individuals belonging to different (virtual) subpopulations will be plotted with different colors and shapes.
- Operator `plotter.infoPlotter`: Using a R function such as `hist` and `qqnorm` to plot one or more information fields of individuals in one or more (virtual) subpopulations. Two specialized operators `plotter.histPlotter` and `plotter.qqPlotter` are provided to plot the histograms and qq plots. Other functions could also be used, and it is even possible to draw a figure completely by your own (with stratified data provided to you by this operator).
- Operator `plotter.boxPlotter`: This operator uses R function `boxplot` to plot boxplots of data of one or more information fields of individuals in one or more (virtual) subpopulations. The whiskers could be grouped by information field or subpopulations.

These operators are derived from class `pyOperator` and call R plot functions when they are applied to a population. For example, operator `plotter.varPlotter` collects expression values and use functions `plot` and `lines` to plot the data, with help from other functions such as `par` (device property), `dev.print` (save figure to files) and `legend` (add legend). Some functions are called multiple times for different replicate, subpopulation or information fields.

### 4.3.1 Derived keyword arguments \*

One of the most interesting feature of this module is its use of derived keyword parameters to send arbitrary parameters to the underlying R functions, which usually accept a large number of parameters to customize every aspect of a figure. A **derived keyword argument** is an argument that is prefixed with a function name and/or suffixed by an iterator name. The former specifies to which underlying R function this parameter will be passed to; the latter allows the users to specify a list of values that will be passed, for example, to lines representing different replicates. For example, parameter `par_mar=[1]*4` will pass `mar=[1]*4` to R function `par`, and `lty_rep=[1, 2, 3]` will pass `lty=1`, `lty=2` and `lty=3` to different replicates. A class usually has one or two default functions (such as `plot`, `lines`) to which keyword arguments without function prefix will be sent.



In addition, the values of these keyword arguments could vary during evolution. More specifically, if the value is a string with a leading exclamation mark (!), the remaining string will be considered as an expression. This expression will be evaluated against the current population during evolution and the return value will become the value of the parameter at that generation. For example, keyword parameter `main="!'Allele frequency at generation %d' % gen"` will become `main='Allele frequency at generation 10' at generation 10`.

### 4.3.2 Plot of expressions and their histories (operator `plotter.varPlotter`)

Class `plotter.varPlotter` plots the current and historical values of a Python expression (`expr`), which are evaluated (against each population's local namespace) and saved during evolution. The return value of the expression can be a number or a sequence, but should have the same type and length across all replicates and generations. Histories of each value (or each item in the returned sequence) of each replicate form a line, with generation numbers as its x-axis. Number of lines will be the number of replicates multiplied by dimension of the expression. Although complete histories are usually saved, you can use parameter `win` to save histories only within the last `win` generations.

Except for the first generation where no line could be drawn, a figure will be drawn after this operator is applied to the last specified replicate (parameter `reps` could be used to specify a subset of replicates). For example, although linkage disequilibrium values between the first two loci are evaluated and saved at the end of generations 0, 5, 10, ..., (step=5) figures are only drawn at generations 40 and 80 (`update=40`) in Example 4.7. This example also demonstrates the use of parameters `saveAs` and `legend`. By given a filename `rpy.png` to parameter `saveAs`, this operator will save figures (named `rpy_40.png` and `rpy_80.png`) after they are drawn.

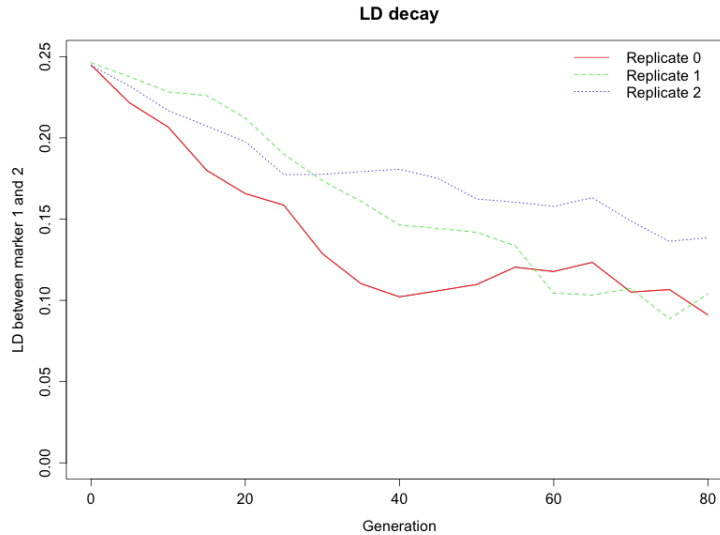
Example 4.7: Use `rpy` to plot an expression

```
>>> import simuPOP as sim
>>> import simuPOP as sim
>>> from simuPOP.plotter import varPlotter
>>> pop = sim.population(size=1000, loci=2)
>>> simu = sim.simulator(pop, sim.randomMating(ops=sim.recombinator(rates=0.01)), rep=3)
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         sim.initByValue([1, 2, 2, 1])
...     ],
...     postOps = [
...         sim.stat(LD=[0, 1]),
...         varPlotter('LD[0][1]', step=5, update=40, saveAs='log/rpy.png',
...             legend=['Replicate %d' % x for x in range(3)],
...             ylab='LD between marker 1 and 2',
...             ylim=[0, 0.25], main='LD decay', lty_rep=[1, 2, 3],
...         ),
...     ],
...     gen=100
... )
(100, 100, 100)
```

Parameters after `legend(xlab, ylab, ylim, main, ...)` deserve more attention here. These parameters are derived keyword arguments because they are not defined by `varPlotter`. Parameters without prefix are passed directly to the R functions `plot` and `line`. They could be used to customize line type (`lty`), color (`col`), title (`main`), limits of x and y axes (`xlim` and `ylim`) and many other graphical features (see R manual for details). If multiple lines are drawn, a list of values could be applied to these lines if you add `_rep` (for each replicate) or `_dim` (for each item of a sequence) after the name of the parameter. For example, `lty_rep=[1, 2, 3]` is used in Example 4.7 to pass parameters `lty=1`, `lty=2` and `lty=3` to lines for three replicates. Suffix `_repdim` can also be used to specify values for every replication and dimension. Figure 4.4 displayed `rpy_80.png` that is saved at generation 80 for this example.

If the expression is multidimensional, the number of lines can be large and it is often desired to separate these lines

Figure 4.4: rpy\_80.png saved at generation 80 for Example 4.7



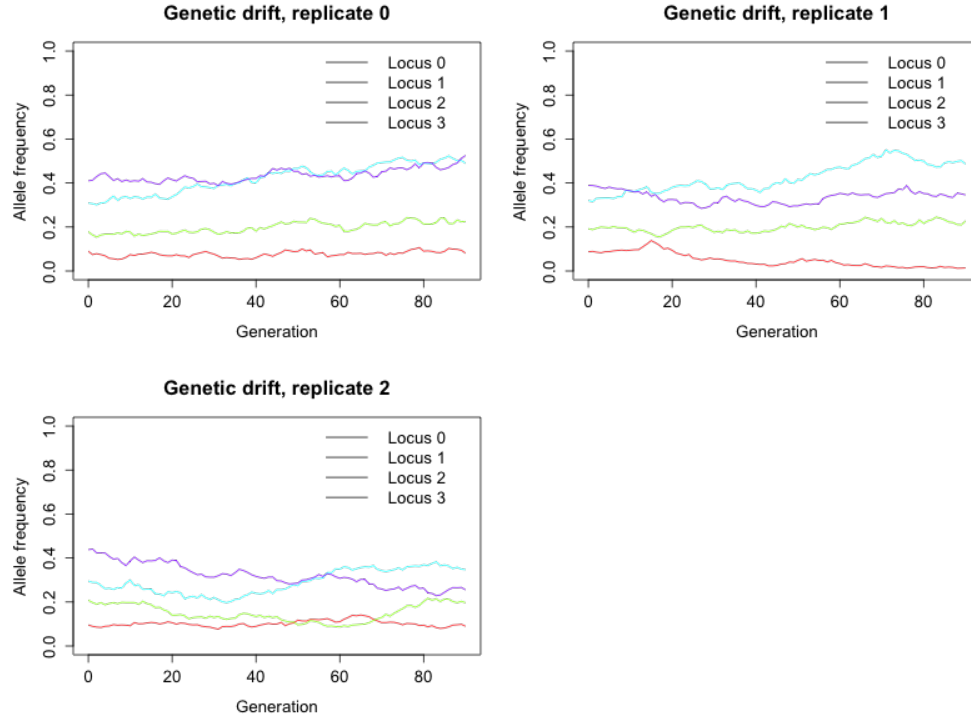
into subplots. This can be done by parameters `byRep` or `byDim`. The former plots lines replicate by replicate and the latter does it dimension by dimension. For example, Example 4.8 and 4.9 both have three replicates and the expression has allele frequency for four loci. The total number of lines is therefore 12. In Example 4.8, these lines are separated to three subplots, replicate by replicate, with different titles (parameter `main_rep`). In each subplot, allele frequency trajectories (histories) for different loci are plotted in different color (parameter `col_dim`). The last saved figure (`rpy_byRep_90.png`) is displayed in Figure 4.5. In Example 4.9, these lines are separated to four subplots, locus by locus, with different titles (parameter `main_dim`). In each subplot, allele frequency trajectories (histories) for different loci are plotted in different color (parameter `col_rep`) and line type (parameter `lty_rep`). The last saved figure (`rpy_byDim_90.png`) is displayed in Figure 4.6.

Example 4.8: Separate figures by replicate

```
>>> import simuPOP as sim
>>> import simuPOP as sim
>>> from simuPOP.plotter import varPlotter
>>> pop = sim.population(size=1000, loci=1*4)
>>> simu = sim.simulator(pop, sim.randomMating(), rep=3)
>>> simu.evolve(
...     initOps = [sim.initSex()] +
...     [sim.initByFreq([0.1*(x+1), 1-0.1*(x+1)], loci=x) for x in range(4)],
...     postOps = [
...         sim.stat(alleleFreq=range(4)),
...         varPlotter('[alleleFreq[x][0] for x in range(4)]', byRep=True,
...             update=10, saveAs='log/rpy_byRep.png',
...             legend=['Locus %d' % x for x in range(4)],
...             ylab='Allele frequency',
...             ylim=[0, 1],
...             main_rep=['Genetic drift, replicate %d' % x for x in range(3)],
...         ),
...     ],
...     gen=100
... )
(100, 100, 100)
```

Example 4.9 also demonstrates some advanced features of this plotter that allow further customization of the figures. More specifically,

Figure 4.5: Allele frequency trajectories separated by replicates



- Function-specific parameters can be passed to the underlying R function by prefixing function names to parameter names. For example, `plot_axis=False` is used to pass `axis=False` to the `r.plot` function (and not to function `lines` which does not accept this parameter).
- Several hook function can be defined and passed to parameters `preHook`, `postHook` and `plotHook`, which will be called, respectively, before a figure is drawn, after a figure is drawn, and after each `r.plot` call. Example 4.9 uses a `plotHook` function to draw axes of the plots and call `mtext` to add texts to the margins.

Example 4.9: Separate figures by Dimension

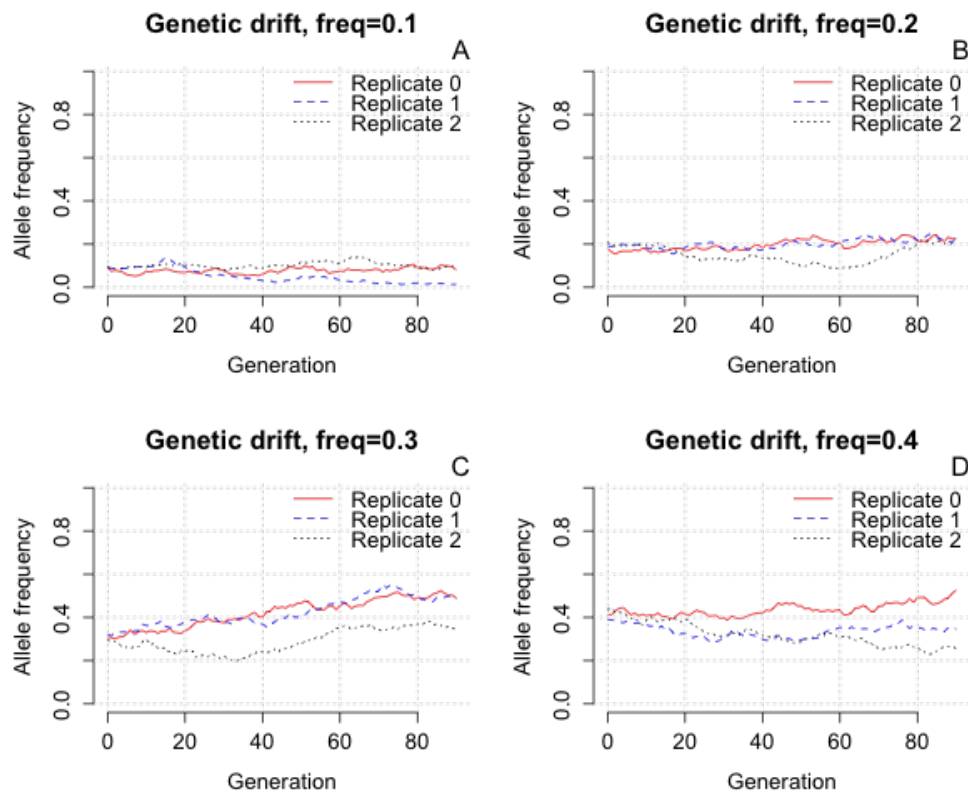
```
>>> import simuPOP as sim
>>> import simuPOP as sim
>>> from simuPOP.plotter import varPlotter
>>> pop = sim.population(size=1000, loci=1*4)
>>> simu = sim.simulator(pop, sim.randomMating(), rep=3)
>>> def drawFrame(r, dim=None, **kwargs):
...     '''Draw a frame around subplot dim. Parameter r is defined in the rpy
...     module and is used for calling R functions. Parameter dim is the dimension
...     index. Other parameters are ignored.
...     '''
...     r.axis(1)
...     r.axis(2)
...     r.grid()
...     r.mtext({0:'A', 1:'B', 2:'C', 3:'D'}[dim], adj=1)
...
>>> simu.evolve(
...     initOps = [sim.initSex()+
...                 [sim.initByFreq([0.1*(x+1), 1-0.1*(x+1)], loci=x) for x in range(4)],
...     postOps = [
...         sim.stat(alleleFreq=range(4)),
```

```

...     varPlotter('[alleleFreq[x][0] for x in range(4)]', byDim=True,
...               update=10, saveAs='log/rpy_byDim.png',
...               legend=['Replicate %d' % x for x in range(3)],
...               ylab='Allele frequency',
...               ylim=[0, 1],
...               main_dim=['Genetic drift, freq=%1f' % ((x+1)*0.10) for x in range(4)],
...               col_rep=['red', 'blue', 'black'],
...               lty_rep=[1, 2, 3],
...               # the default png dimension is 800x600
...               dev_print_width=600, dev_print_height=500,
...               # do not draw axes in r.plot, leaving the job to drawFrame
...               plot_axes=False,
...               # plot frame, grid etc after each r.plot call
...               plotHook = drawFrame,
...               ),
...     ],
...     gen=100
... )
(100, 100, 100)

```

Figure 4.6: Allele frequency trajectories separated by loci



### 4.3.3 Scatter plots (operator `plotter.scatterPlotter`)

Operator `plotter.scatterPlotter` plots individuals in all or selected (virtual) subpopulations in a 2-D plot, using values at two information fields as their x- and y-axis. In the most simplified form,

```
infoPlotter(infoFields=['x', 'y'])
```

will plot all individuals according their values of information fields  $x$  and  $y$ . Additional parameters such as `pch`, `col`, and `cex` can be used to control the shape, color and size of the points.

What makes this operator useful is its ability to differentiate points (individuals) by (virtual) subpopulations (VSPs). If a list of VSPs are given, points representing individuals from these VSPs will be plotted with different colors and shapes. Because simulations that keep track of multiple information fields are usually complicated, let us simulate something interesting and examine Example 4.10 in details.

At the beginning of this example, all individuals are scattered randomly with  $x$  and  $y$  being their physical locations. We use `anc` to record individual ancestry and assign 0 and 1 each to half of the population. During evolution,

- Offspring ancestry values are the average of their parents.
- Offspring with higher ancestry value tend to move to the right. More specifically, locations of an offspring will be

$$\frac{(x_1 + x_2)}{2} + N\left(\frac{a_1 + a_2}{2} - 0.5, 0.1\right), \frac{(y_1 + y_2)}{2} + N(0, 0.1)$$

where  $(x_1, y_1)$  and  $(x_2, y_2)$  are locations of parents,  $a_1$  and  $a_2$  are ancestry values of the parents, and  $N(a, b)$  are a random number with normal distribution.

An `scatterPlotter` is used to plot the physical location of all individuals. Individual ancestries are divided into five regions (0, 0.2, 0.4, 0.6, 0.8, 1) indicated by small to larger points. MALE and female individuals are plotted by different symbol. This scripts uses the following techniques:

- Set individual information fields randomly using `setIndInfo`.
- Define virtual subpopulations using a `infoSplitter`.
- Use `pyTagger` to calculate offspring information fields from parental fields.
- Mark individuals in different VSPs using parameters `col_sp` and `cex_sp`.
- Use `plot_axes=False` and `par_mar=[0, 0, 2, 0]` to pass parameters `axes=False` and `mar=[0, 0, 2, 0]` to functions `plot` and `par` respectively.

VSPs 0 and 4 appear at the beginning of generation 0, VSP 2 appears at the end of generation 0, and VSP 1 and 3 appear at the end of generation 1. Figure 4.7 displays a figure at the begging of generation 2.

Example 4.10: Use `scatterPlotter` to plot ancestry of individuals with geographic information.

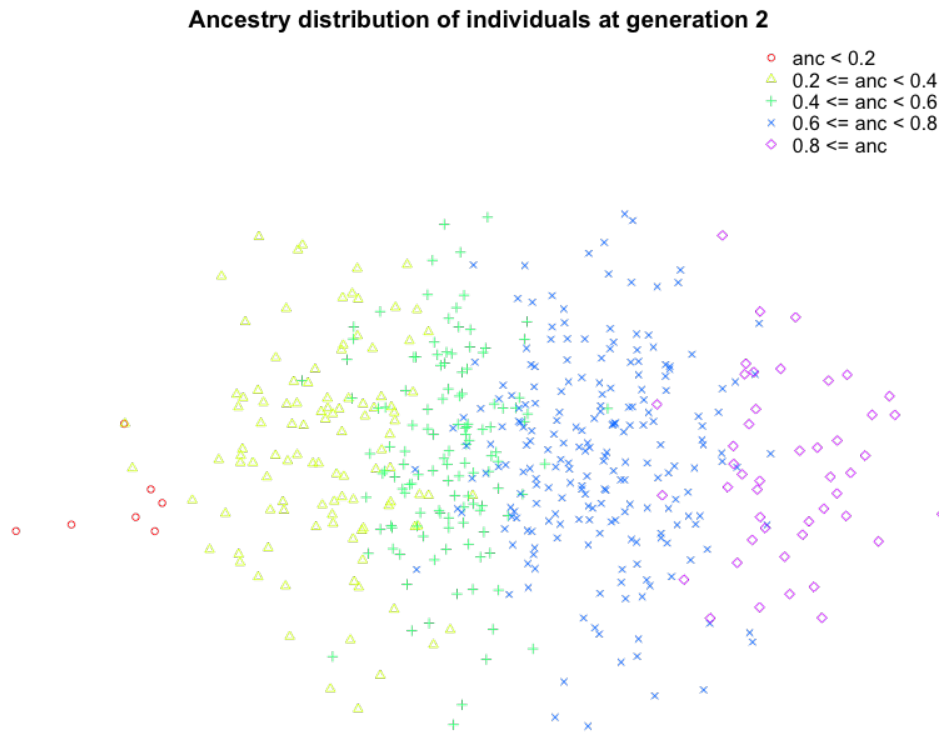
```
>>> import simuPOP as sim
>>> import simuPOP as sim
>>> from simuPOP.plotter import scatterPlotter
>>> import random
>>> pop = sim.population([500], infoFields=['x', 'y', 'anc'])
>>> # Defines VSP 0, 1, 2, 3, 4 by anc.
>>> pop.setVirtualSplitter(sim.infoSplitter('anc', cutoff=[0.2, 0.4, 0.6, 0.8]))
>>> #
>>> def passInfo(fields):
...     'Parental fields will be passed as x1, y1, anc1, x2, y2, anc2'
...     x1, y1, anc1, x2, y2, anc2 = fields
...     anc = (anc1 + anc2)/2.
...     x = (x1 + x2)/2 + random.normalvariate(anc - 0.5, 0.1)
...     y = (y1 + y2)/2 + random.normalvariate(0, 0.1)
...     return x, y, anc
...
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = [
```

```

...     sim.initSex(),
...     # random geographic location
...     sim.initInfo(random.random, infoFields=['x', 'y']),
...     # anc is 0 or 1
...     sim.initInfo(lambda : random.randint(0, 1), infoFields='anc')
... ],
... postOps = [
...     scatterPlotter(['x', 'y'],
...         saveAs = 'log/scatterPlotter.png',
...         subPops = [(0, 0), (0, 1), (0, 2), (0, 3), (0, 4)],
...         ylim = [0, 1.2],
...         main = "!'Ancestry distribution of individuals at generation %d' % gen",
...         legend = ['anc < 0.2', '0.2 <= anc < 0.4', '0.4 <= anc < 0.6',
...             '0.6 <= anc < 0.8', '0.8 <= anc'],
...         plot_axes = False,
...         par_mar = [0, 0, 2, 0],
...     ),
... ],
... ],
... duringOps = sim.pyTagger(passInfo, infoFields=['x', 'y', 'anc']),
... gen = 5,
... )
(5,)

```

Figure 4.7: Plot of individuals with ancestry marked by different colors



#### 4.3.4 Histograms, QQ plots and boxplots (operator `plotter.infoPlotter`, `plotter.histPlotter`, `plotter.qqPlotter`).

Class `plotter.infoPlotter` can be used to draw figures for information fields of individuals in one or more subpopulations. `plotter.histPlotter` and `plotter.qqPlotter` are two special cases of this class that

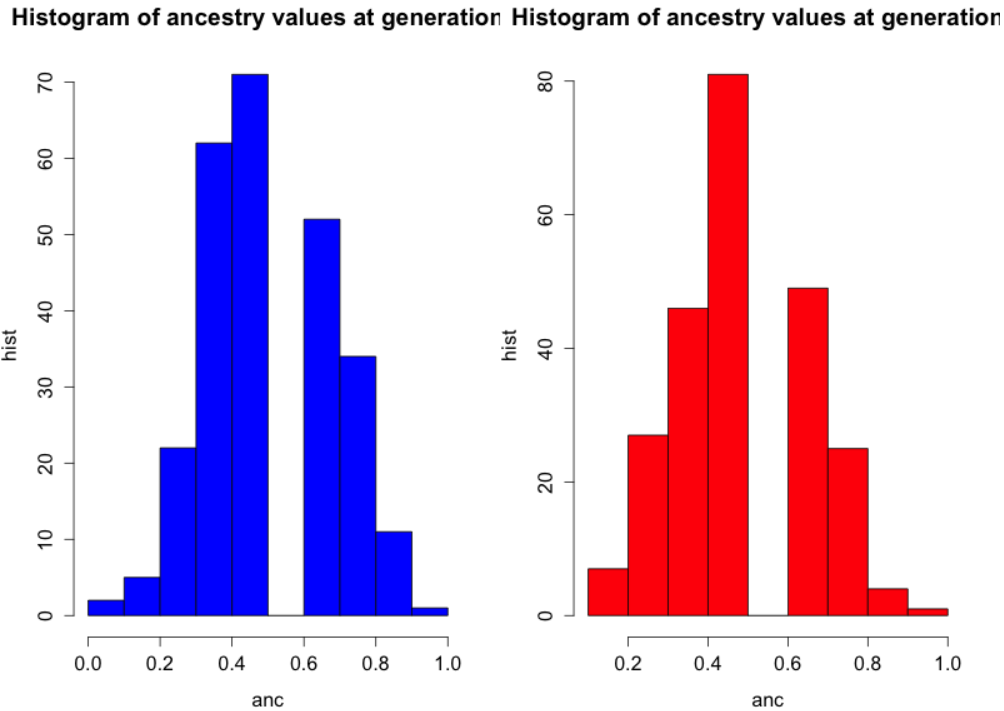
uses functions `hist` and `qqnorm` respectively. Although an `infoPlotter` using a `boxplot` function could be used, a specialized `plotter.boxPlotter` is defined so that multiple boxplot whiskers could be drawn in the same plot.

Using the same evolutionary process as Example 4.10, Example 4.11 uses a `histPlotter` to plot the histograms (Figure 4.8), a `qqPlotter` to plot QQ plot (Figure 4.9), and a `boxPlotter` to plot the boxplots (Figure 4.10) of individual ancestry values. By defining two virtual subpopulations by sex, the `histPlotter` and `qqPlotter` plots two histograms and two QQ plots, one for males and one for females. Different colors are used for these figures. Note that these plots use the special expression value for parameter `main` so that generation number can appear in the titles. The same technique is used in the `dev_print_file` parameter of the `boxPlotter`, which overrides the default filename derived from parameter `saveAs`.

Example 4.11: Use `histPlotter` to plot the histogram of individual ancestries.

```
>>> import simuPOP as sim
>>> import simuPOP as sim
>>> from simuPOP.plotter import histPlotter, qqPlotter, boxPlotter
>>> import random
>>> pop = sim.population([500], infoFields=['x', 'y', 'anc'])
>>> # Defines VSP 0, 1, 2, 3, 4 by anc.
>>> pop.setVirtualSplitter(sim.sexSplitter())
>>> def passInfo(fields):
...     'Parental fields will be passed as x1, y1, anc1, x2, y2, anc2'
...     x1, y1, anc1, x2, y2, anc2 = fields
...     anc = (anc1 + anc2)/2.
...     x = (x1 + x2)/2 + random.normalvariate(anc - 0.5, 0.1)
...     y = (y1 + y2)/2 + random.normalvariate(0, 0.1)
...     return x, y, anc
...
>>> simu = sim.simulator(pop, sim.randomMating())
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         # random geographic location
...         sim.initInfo(random.random, infoFields=['x', 'y']),
...         # anc is 0 or 1
...         sim.initInfo(lambda : random.randint(0, 1), infoFields='anc')
...     ],
...     postOps = [
...         histPlotter(infoFields='anc',
...             subPops=[(0,0), (0,1)], col_sp=['blue', 'red'],
...             saveAs='log/histPlotter.png',
...             main="!'Histogram of ancestry values at generation %d' % gen",
...         ),
...         qqPlotter(infoFields='anc',
...             subPops=[(0,0), (0,1)], col_sp=['blue', 'red'],
...             saveAs='log/qqPlotter.png',
...             main="!'QQ plot of ancestry values at generation %d' % gen",
...         ),
...         boxPlotter(infoFields='anc',
...             subPops=[(0,0), (0,1)],
...             saveAs='whatever',
...             dev_print_file='!log/Gen%d.png' % gen,
...             main="!'Boxplots of ancestry values at generation %d' % gen",
...         ),
...     ],
...     duringOps = sim.pyTagger(passInfo, infoFields=['x', 'y', 'anc']),
...     gen = 5,
... )
(5,)
```

Figure 4.8: Histogram of individual ancestry values



## 4.4 Module `simuPOP.sampling`

### 4.4.1 Introduction

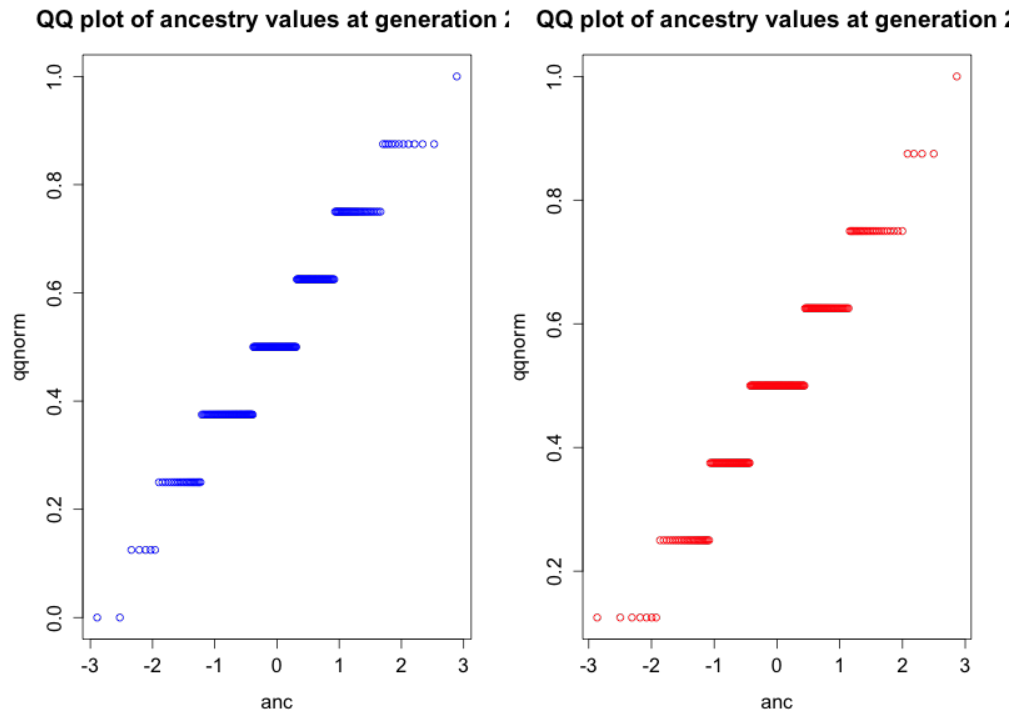
Sampling, in `simuPOP` term, is the action of extracting individuals from a large, potentially multi-generational, population according to certain criteria. the `simuPOP.sampling` module provides several classes and functions and allows you to define more complicated sampling schemes by deriving from its these class. For example, you can use `DrawRandomSample(pop, size=100)` to select 100 random individuals from a population, or use `DrawAffectedSibpairSample(pop, families=100)` to select 100 pairs of affected individuals with their parents from a multi-generational population, or a age-structured population with parents and offspring in the same generation.

The `simuPOP.sampling` module currently support random, case control, affected sibpair, nuclear family and three-generation family sampling types, and a combined sampling type that allows you to draw different types of samples. For each sampling type X, a sampler class and two functions `DrawXSample` and `DrawXSamples` are provided. The first function returns a population with all sampled individuals and the second function returns a list of sample populations.

If you would like to define your own sampling type, you can derive your sampler from one of the existing sampler classes. These sampler classes provide member functions `prepareSample`, `drawSample` and `drawSamples` and you typically only need to extend `prepareSample` of an appropriate base class.



Figure 4.9: QQ plot of individual ancestry values



#### 4.4.2 Sampling individuals randomly (class `randomSampler`, functions `DrawRandomSample` and `DrawRandomSamples`)

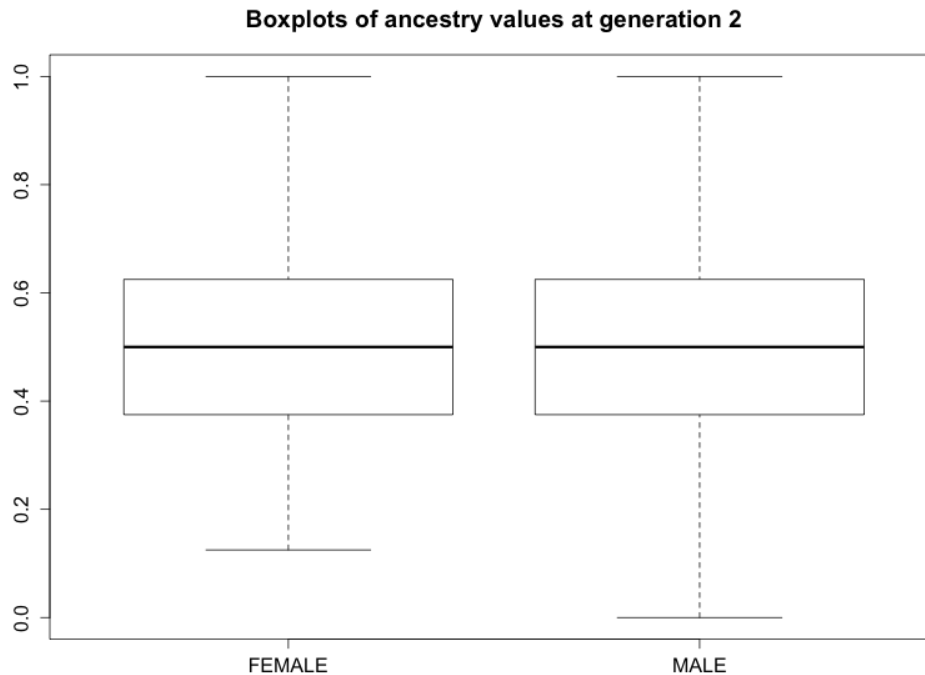
Functions `DrawRandomSample` and `DrawRandomSamples` draw random individuals from a given population. If a simple number is given to parameter `size`, population structure will be ignored so individuals will be drawn from all subpopulations. If a list of numbers are given, this function will draw specified numbers of individuals from each subpopulation. This function does not need parental information. If your population does not have an ID field, you will not be able to locate extracted individuals in the original population.

Example 4.12 demonstrates how to draw a random sample from the whole population, and from each subpopulation. Because sample populations keep the population structure of the source population (this might change when parameter `subPops` is used, see a later section for details), we can use `sample.subPopSizes()` to check how many individuals are sampled from each subpopulation.

Example 4.12: Draw random samples from a structured population

```
>>> import simuPOP as sim
>>> from simuPOP.sampling import DrawRandomSample
>>> pop = sim.population([2000]*5, loci=1)
>>> # sample from the whole population
>>> sample = DrawRandomSample(pop, sizes=500)
>>> print sample.subPopSizes()
(85, 100, 101, 113, 101)
>>> # sample from each subpopulation
>>> sample = DrawRandomSample(pop, sizes=[100]*5)
>>> print sample.subPopSizes()
(100, 100, 100, 100, 100)
```

Figure 4.10: Boxplot of individual ancestry values



#### 4.4.3 Sampling cases and controls (class `caseControlSampler`, functions `CaseControlSample` and `CaseControlSamples`)

Functions `DrawCaseControlSample` and `DrawCaseControlSamples` draw cases (affected individuals) and controls (unaffected individuals) from a given population. If a simple number is given to parameter `cases` and `controls`, population structure will be ignored so individuals will be drawn from all subpopulations. If a list of numbers are given, this function will draw specified number of cases and controls from each subpopulation.

Example 4.13 demonstrates how to draw multiple case-control samples from a population, and perform case-control association tests using the `Stat` function.

Example 4.13: Draw case control samples from a population and perform association test

```
>>> import simuPOP as sim
>>> from simuPOP.sampling import DrawCaseControlSamples
>>> pop = sim.population([10000], loci=5)
>>> sim.InitByFreq(pop, [0.2, 0.8])
>>> sim.MaPenetrance(pop, loci=2, penetrance=[0.11, 0.15, 0.20])
>>> # draw multiple case control sample
>>> samples = DrawCaseControlSamples(pop, cases=500, controls=500, numofSamples=5)
>>> for sample in samples:
...     sim.Stat(sample, association=range(5))
...     print ', '.join(['%.6f' % sample.dvars().Allele_ChiSq_p[x] for x in range(5)])
...
1.000000, 0.737316, 0.011017, 0.694196, 0.956408
0.317883, 0.154192, 0.012317, 0.221325, 0.621548
0.288627, 0.163181, 0.000413, 0.619078, 0.544861
0.368372, 0.869744, 0.002297, 0.295641, 0.623939
0.955378, 0.644326, 0.017138, 0.359830, 0.065325
```

#### 4.4.4 Sampling pedigrees (functions `IndexToID` and `PlotPedigree`)

If your sampling scheme involves parental information, you need to prepare your population so that it has

- an ID field (usually `'ind_id'`) that stores a unique ID for each individual.
- two information fields (usually `'father_id'`, and `'mother_id'`) that stores the ID of parents of each individual. Although `simuPOP` supports one-parent pedigrees, this feature will not be discussed in this guide.

The preferred method to prepare such a population is to add information fields `ind_id`, `father_id` and `mother_id` to a population and track ID based pedigrees during evolution. More specifically, you can use operators `idTagger` and `pedigreeTagger` to assign IDs and record parental IDs of each offspring during mating. This method supports age-structured population when parents and offspring can be stored in the same generation.

You can also use information fields `father_idx` and `mother_idx` and operator `parentsTagger` to track indexes of parents in the parental generations. Before sampling, you can use function `sampling.IndexToID` to add needed information fields and convert index based parental relationship to ID based relationship. Because parents have to stay in ancestral generations, this method does not support age-structured population.

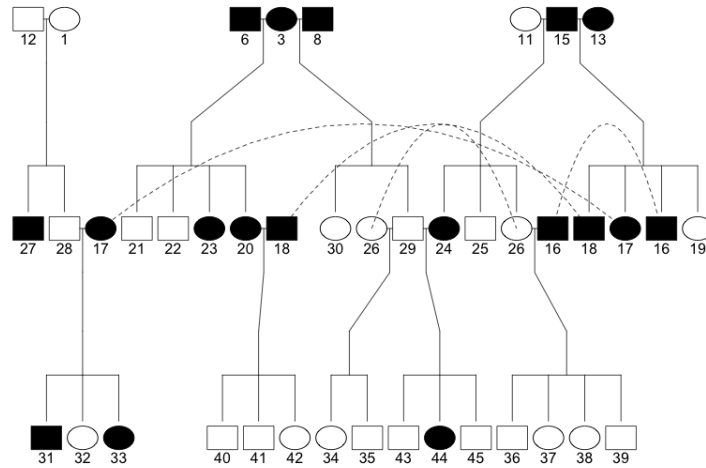
If you have R and `rpy` installed on your system, you can install the `kinship` library of R and use it to analyze pedigree. The `simuPOP.sampling` module provides a function `PlotPedigree` to use this library to plot pedigrees. Example 4.14 demonstrates how to use function `sampling.IndexToID` to prepare a pedigree and how to use `sampling.DrawPedigree` to plot it.

Example 4.14: Prepare and plot pedigrees

```
>>> import simuPOP as sim
>>> from simuPOP.sampling import IndexToID, PlotPedigree
>>> pop = sim.population(size=15, loci=5, infoFields=['father_idx', 'mother_idx'], ancGen=2)
>>> simu = sim.simulator(pop, sim.randomMating(numOffspring=(sim.UNIFORM_DISTRIBUTION, 2, 4)))
>>> simu.evolve(
...     preOps = [
...         sim.initSex(),
...         sim.initByFreq([0.7, 0.3]),
...     ],
...     duringOps = sim.parentsTagger(),
...     postOps = sim.maPenetrance(loci=3, penetrance=(0.1, 0.4, 0.7)),
...     gen = 5
... )
(5,)
>>> pop = simu.extract(0)
>>> IndexToID(pop, reset=True)
>>> # three information fields were added
>>> print pop.infoFields()
('father_idx', 'mother_idx', 'ind_id', 'father_id', 'mother_id')
>>> # save this population for future use
>>> pop.save('log/pedigree.pop')
>>> # draw pedigree
>>> PlotPedigree(pop, filename='log/pedigree.png')
Loading required package: survival
Loading required package: splines
Loading required package: nlme
Loading required package: lattice
[1] "kinship is loaded"
Did not plot the following people: 2 4 5 7 9 10 14
```

Figure 4.11 plots a small three-generational population with 15 individuals at each generation. It is pretty clear that random mating produces bad pedigree structure because it is common that one parent would have multiple spouses.

Figure 4.11: Structure of a small complete pedigree



#### 4.4.5 Sampling affected sibpairs (class `affectedSibpairSampler`, functions `DrawAffectedSibpairSample(s)`)

An affected sibpair family consists of two parents and their affected offspring. Such families are useful in linkage analysis because of high likelihood of shared disease predisposing alleles between siblings. `simuPOP.sampling` module provides functions `DrawAffectedSibpairSample` and `DrawAffectedSibpairSamples` to draw such families from a population. Example 4.15 draws two affected sibpair from the pedigree created in Example 4.14, with samples plotted in Figure 4.12.

Example 4.15: Draw affected sibpairs from a population

```
>>> import simuPOP as sim
>>> from simuPOP.sampling import DrawAffectedSibpairSample, PlotPedigree
>>> pop = sim.LoadPopulation('log/pedigree.pop')
>>> sample = DrawAffectedSibpairSample(pop, families=2)
>>> PlotPedigree(sample, filename='log/affectedSibpair.png')
```

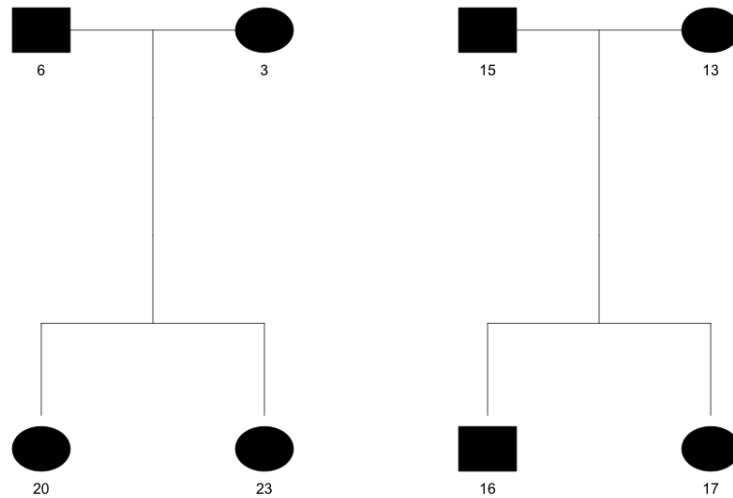
#### 4.4.6 Sampling nuclear families (class `nuclearFamilySampler`, functions `DrawNuclearFamilySample` and `DrawNuclearFamilySamples`)

A nuclear family consists of two parents and their offspring. Functions `DrawNuclearFamilySample` and `DrawNuclearFamilySamples` to draw such families from a population, with restrictions on number of offspring, number of affected parents and number of affected offspring. Although fixed numbers could be given, a range with minimal and maximal acceptable numbers are usually provided. Example 4.16 draws two nuclear families from the pedigree created in Example 4.14. The samples are plotted in Figure 4.13.

Example 4.16: Draw nuclear families from a population

```
>>> import simuPOP as sim
>>> from simuPOP.sampling import DrawNuclearFamilySample, PlotPedigree
>>> pop = sim.LoadPopulation('log/pedigree.pop')
>>> sample = DrawNuclearFamilySample(pop, families=2, numOffspring=(2,4),
...     affectedParents=(1,2), affectedOffspring=(1, 3))
>>> PlotPedigree(sample, filename='log/nuclearFamily.png')
```

Figure 4.12: Affected sibpairs drawn from a small pedigree



#### 4.4.7 Sampling three-generation families (class `threeGenFamilySampler`, functions `DrawThreeGenFamilySample` and `DrawThreeGenFamilySamples`)

A three-generation family consists of two parents, their common offspring, offspring's spouses, and their common offspring (grandchildren). Individuals in sampled families have either no or two parents. Functions `DrawThreeGenFamilySample` and `DrawThreeGenFamilySamples` to draw such families from a population, with restrictions on number of offspring, total number of individuals and number of affected individuals in the pedigree. These parameters (`numOffspring`, `pedSize` and `numAffected`) could be a fixed number of a range with minimal and maximal acceptable numbers. Example 4.16 draws two three generation families from the pedigree created in Example 4.14. The samples are plotted in Figure 4.13.

Example 4.17: Draw three-generation families from a population

```

>>> import simuPOP as sim
>>> from simuPOP.sampling import DrawThreeGenFamilySample, PlotPedigree
>>> pop = sim.LoadPopulation('log/pedigree.pop')
>>> sample = DrawThreeGenFamilySample(pop, families=2, numOffspring=(1, 3),
...     pedSize=(8, 15), numOfAffected=(2, 5))
>>> PlotPedigree(sample, filename='log/threeGenFamily.png')
  
```

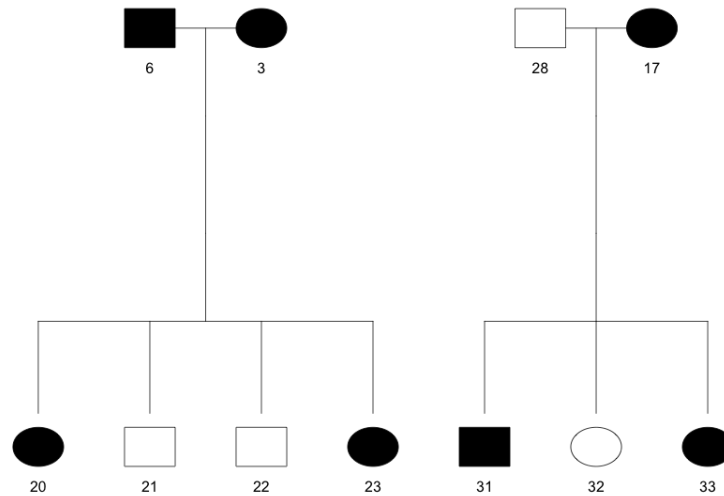
#### 4.4.8 Sampling different types of samples (class `combinedSampler`, functions `DrawCombinedSample` and `DrawCombinedSamples`)

Samples in real world studies sometimes do not have uniform types so it is useful to draw samples of different types from the same population. Although it is possible to draw samples using different functions and combine them, handling of overlapping individuals, namely individuals who are chosen by multiple samplers, can be a headache. The combined sampler of `simuPOP.sampling` is designed to overcome this problem. This sampler takes a list of sampler objects and apply them to a population sequentially. The extracted sample will not have overlapping individuals.

Example 4.18 draws an affected sibpair family and a nuclear family from the pedigree created in Example 4.14. The samples are plotted in Figure 4.18.

Example 4.18: Draw different types of samples from a population

Figure 4.13: Nuclear families drawn from a small pedigree



```
>>> import simuPOP as sim
>>> from simuPOP.sampling import DrawCombinedSample, affectedSibpairSampler, nuclearFamilySampler,
>>> pop = sim.LoadPopulation('log/pedigree.pop')
>>> sample = DrawCombinedSample(pop, samplers = [
...     affectedSibpairSampler(families=1),
...     nuclearFamilySampler(families=1, numOffspring=(2,4), affectedParents=(1,2), affectedOffspring=(1,2)),
... ])
>>> PlotPedigree(sample, filename='log/combinedSampling.png')
```

#### 4.4.9 Sampling from subpopulations and virtual subpopulations \*

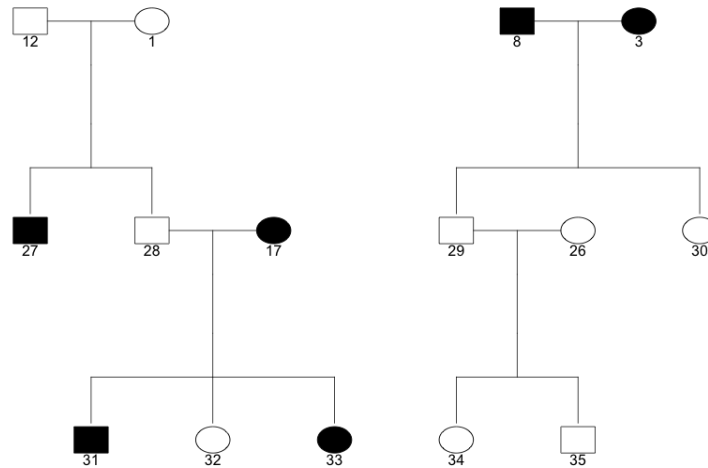
Virtual subpopulations (VSPs) could be specified in the `subPops` parameter of sampling classes and functions. This can be used to limit your samples to individuals with certain properties. For example, you may want to match the age of cases and controls in a case-control association study by selecting your samples from a certain age group. For examples, Example 4.19 draws 500 cases and 500 controls from two a VSP with individual ages between 40 and 60.

Example 4.19: Draw samples from a virtual subpopulation.

```
>>> import simuPOP as sim
>>> # create an age-structured population with a disease
>>> import random
>>> pop = sim.population(10000, loci=10, infoFields='age')
>>> sim.InitByFreq(pop, [0.3, 0.7])
>>> sim.InitInfo(pop, lambda: random.randint(0, 70), infoFields='age')
>>> pop.setVirtualSplitter(sim.infoSplitter(cutoff=(40, 60), field='age'))
>>> sim.MaPenetrance(pop, loci=5, penetrance=(0.1, 0.2, 0.3))
>>> #
>>> from simuPOP.sampling import DrawCaseControlSample
>>> sample = DrawCaseControlSample(pop, cases=500, controls=500, subPops=[(0,1)])
>>> ageInSample = sample.indInfo('age')
>>> print min(ageInSample), max(ageInSample)
40.0 59.0
```

If a list of sample sizes is given, specified number of samples will be drawn from each subpopulation. For example, if you have an age-structured population when individuals with different ages have different risk to a disease,

Figure 4.14: Three generation families drawn from a small pedigree



you might want to draw affected individuals from different age groups and perform association analyses. Function `DrawCaseControlSample` cannot be used because both groups are affected, but you can `DrawRandomSample` from two VSPs defined by age. Example 4.20 demonstrates how to use this method.

Example 4.20: Sampling separately from different virtual subpopulations

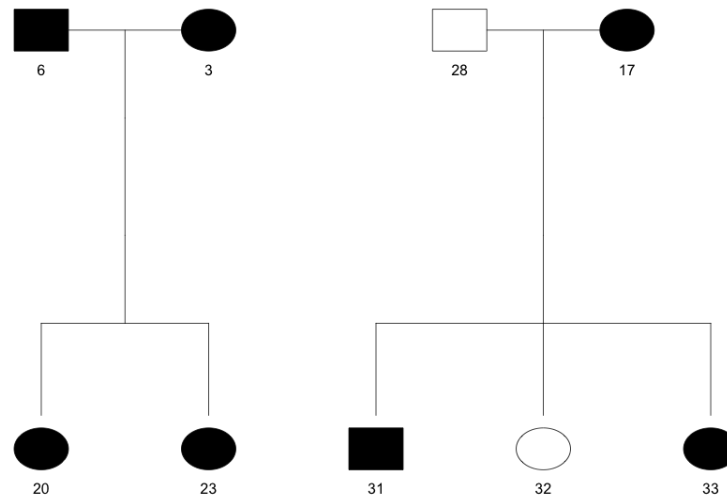
```
>>> import simuPOP as sim
>>> # create an age-structured population with a disease
>>> import random
>>> pop = sim.population(10000, loci=10, infoFields='age')
>>> sim.InitByFreq(pop, [0.3, 0.7])
>>> sim.InitInfo(pop, lambda: random.randint(0, 70), infoFields='age')
>>> pop.setVirtualSplitter(sim.infoSplitter(cutoff=(20, 40), field='age'))
>>> # different age group has different penetrance
>>> sim.MaPenetrance(pop, loci=5, penetrance=(0.1, 0.2, 0.3), subPops=[(0,1)])
>>> sim.MaPenetrance(pop, loci=5, penetrance=(0.2, 0.4, 0.6), subPops=[(0,2)])
>>> # count the number of affected individuals in each group
>>> sim.Stat(pop, numOfAffected=True, subPops=[(0,1), (0,2)], vars='numOfAffected_sp')
>>> print pop.dvars((0,1)).numOfAffected, pop.dvars((0,2)).numOfAffected
678 2169
>>> #
>>> from simuPOP.sampling import DrawRandomSample
>>> sample = DrawRandomSample(pop, sizes=[500, 500], subPops=[(0,1), (0,2)])
>>> # virtual subpopulations are rearranged to different subpopulations.
>>> print sample.subPopSizes()
(500, 500)
```

## 4.5 Module `simuPOP.gsl`

`simuPOP` makes use of many functions from the GUN Scientific Library. These functions are used to generate random number and perform statistical tests within `simuPOP`. Although these functions are not part of `simuPOP`, they can be useful to users of `simuPOP` from time to time and it makes sense to expose these functions directly to users.

Module `simuPOP.gsl` contains a number of GSL functions. Because only a small proportion of GSL functions are

Figure 4.15: An affected sibpair and a nuclear family drawn from a small pedigree



used in simuPOP, this module is by no means a comprehensive wrapper of GSL. Please refer to the simuPOP reference manual for a list of functions included in this module, and the GSL manual for more details.



## Chapter 5

# A real world example

Previous chapters use a lot of examples to demonstrate individual simuPOP features. However, it might not be clear how to integrate these features in longer scripts that address real world problems, which may involve larger populations, more complex genetic and demographic models and may run thousands of replicates with different parameters. This chapter will show you, step by step, how to write a complete simuPOP script that has been used in a real-world research topic.

### 5.1 Simulation scenario

Reich and Lander [2001] proposed a population genetics framework to model the evolution of allelic spectra (the number and population frequency of alleles at a locus). The model is based on the fact that human population grew quickly from around 10,000 to 6 billion in 18,000 -150,000 years. His analysis showed that at the founder population, both common and rare diseases have simple spectra. After the sudden expansion of population size, the allelic spectra of simple diseases become complex; while those of complex diseases remained simple.

This example is a simplified version of the `simuCDCV.py` script that simulates this evolution process and observe the allelic spectra of both types of diseases. The complete script is available at [the simuPOP online cookbook](#). The results are published in Peng and Kimmel [2007], which has much more detailed discussion about the simulations, and the parameters used.

### 5.2 Demographic model

Reich and Lander [2001] used a very simple instant population growth model. Under the model assumption, a population with an initial population size  $N_0$  would evolve  $G_0$  generations, instantly expand its population size to  $N_1$  and evolve another  $G_1$  generations. Such a model can be easily implemented as follows:

```
def ins_expansion(gen, oldsize=[]):
    'An instant population growth model'
    if gen < G0:
        return N0
    else:
        return N1
```

Other demographic models could be implemented similarly. For example, an exponential population growth model that expand the population size from  $N_0$  to  $N_1$  in  $G_1$  generations could be defined as

```
def exp_expansion(gen, oldsize=[]):
    'An exponential population growth model'
```

```

if gen < G0:
    return N0
else:
    rate = (math.log(N1) - math.log(N0))/G1
    return int(N0 * math.exp((gen - G0) * rate))

```

That is to say, we first solve  $r$  from  $N_1 = N_0 \exp(rG_1)$  and then calculate  $N_t = N_0 \exp(rG)$  for a given generation.

There is a problem here: the above definitions treat  $N_0$ ,  $G_0$ ,  $N_1$  and  $G_1$  as global variables. This is OK for small scripts but is certainly not a good idea for larger scripts especially when different parameters will be used. A better way is to wrap these functions by another function that accept  $N_0$ ,  $G_0$ ,  $N_1$  and  $G_1$  as parameters. That is demonstrated in Example 5.1 where a function `demo_model` is defined to return either an instant or an exponential population growth demographic function.

Example 5.1: A demographic function producer

```

>>> import simuPOP as sim
>>> import math
>>> def demo_model(model, N0=1000, N1=100000, G0=500, G1=500):
...     '''Return a demographic function
...     model: linear or exponential
...     N0:    Initial sim.population size.
...     N1:    Ending sim.population size.
...     G0:    Length of burn-in stage.
...     G1:    Length of sim.population expansion stage.
...     '''
...     def ins_expansion(gen, oldsize=[]):
...         if gen < G0:
...             return N0
...         else:
...             return N1
...         rate = (math.log(N1) - math.log(N0))/G1
...     def exp_expansion(gen, oldsize=[]):
...         if gen < G0:
...             return N0
...         else:
...             return int(N0 * math.exp((gen - G0) * rate))
...     if model == 'instant':
...         return ins_expansion
...     elif model == 'exponential':
...         return exp_expansion
...
>>> # when needed, create a demographic function as follows
>>> demo_func = demo_model('exponential', 1000, 100000, 500, 500)
>>> # sim.population size at generation 700
>>> print demo_func(700)
6309

```

**Note:** The defined demographic functions return the total population size (a number) at each generation because no subpopulation is considered. A list of subpopulation sizes should be returned if there are more than one subpopulations.

## 5.3 Mutation and selection models

The theoretical model employs an infinite allele model where there is a single wild type allele and an infinite number of disease alleles. Each mutation would introduce a new disease allele and there is no back mutation (mutation from disease allele to wild type allele).

This mutation model can be mimicked by a  $k$ -allele model with reasonably large  $k$ . We initialize all alleles to 0 which is the wild type ( $A$ ) and all other alleles are considered as disease alleles ( $a$ ). Because an allele in a  $k$ -allele mutation model can mutate to any other allele with equal probability,  $P(A \rightarrow a) \gg P(a \rightarrow A)$  since there are many more disease alleles than the wild type allele. If we choose a smaller  $k$  (e.g.  $k = 20$ ), recurrent and back mutations can no longer be ignored but it would be interesting to simulate such cases because they are more realistic than the infinite allele model in some cases.

A  $k$ -allele model can be simulated using the `kamMutator` operator which accepts a mutation rate and a maximum allelic state as parameters.

```
kamMutator(rate=mu, maxAllele=k)
```

Because there are many possible disease alleles, a multi-allelic selector (`maSelector`) could be used to select against the disease alleles. This operator accepts a single or a list of wild type alleles (`[0]` in this case) and treats all other alleles as disease alleles. A penetrance table is needed which specifies the fitness of each individual when they have 0, 1 or 2 disease alleles respectively. In this example, we assume a recessive model in which only genotype  $aa$  causes genetic disadvantages. If we assume a selection pressure parameter  $s$ , the operator to use is

```
maSelector(loci=0, wildtype=0, penetrance=[1, 1, 1-s])
```

Note that the use of this selector requires a population information field `fitness`.

This example uses a single-locus selection model but the complete script allows the use of different kinds of multi-locus selection model. If we assume a multiplicative multi-locus selection model where fitness values at different loci are combined (multiplied), a multi-locus selection model (`mlSelector`) could be used as follows:

```
mlSelector([
    maSelector(locus=loc1, fitness=[1,1,1-s1], wildtype=[0]),
    maSelector(locus=loc2, fitness=[1,1,1-s2], wildtype=[0])],
    mode=MULTIPLICATIVE
)
```

These multi-locus models treat disease alleles at different loci more or less independently. If more complex multi-locus models (e.g. models involve gene - gene and/or gene - interaction) are involved, a multi-locus selector that uses a multi-locus penetrance table could be used.

## 5.4 Output statistics

We first want to output total disease allele frequency of each locus. This is easy because `stat()` operator can calculate allele frequency for us. What we need to do is use a `stat()` operator to calculate allele frequency and get the result from population variable `alleleFreq`. Because allele frequencies add up to one, we can get the total disease allele frequency using the allele frequency of the wild type allele 0 ( $\sum_{i=1}^{\infty} f_i = 1 - f_0$ ). The actual code would look more or less like this:

```
stat(alleleFreq=[0,1]),
pyEval(r' "%.2f" % (1-alleleFreq[0][0])')
```

We are also interested in the effective number of alleles [Reich and Lander, 2001] at a locus. Because `simuPOP` does not provide an operator or function to calculate this statistic, we will have to calculate it manually. Fortunately, this is not difficult because effective number of alleles can be calculated from existing allele frequencies, using formula

$$n_e = \left( \sum_{i=1}^{\infty} \left( \frac{f_i}{1 - f_0} \right)^2 \right)^{-1}$$

where  $f_i$  is the allele frequency of disease allele  $i$ .

A quick-and-dirty way to output  $n_e$  at a locus (e.g. locus 0) can be:

```
pyEval('1./sum([(alleleFreq[0][x]/(1-alleleFreq[0][0]))**2 for x in alleleFreq[0].keys() if x != 0])
```

but this expression looks complicated and does not handle the case when  $f_0 = 1$ . A more robust method would involve the `stmts` parameter of `pyEval`, which will be evaluated before parameter `expr`:

```
pyEval(stmts='''if alleleFreq[0][0] == 1:
    ne = 0
else:
    freq = [freq[0][x] for x in alleleFreq[0].keys() if x != 0]
    ne = 1./sum([(f/(1-alleleFreq[0][0]))**2 for x in freq])
''', expr=r'("%.3f" % ne)')
```

However, this piece of code does not look nice with the multi-line string, and the operator is not really reusable (only valid for locus 0). It makes sense to define a function to calculate  $n_e$  generally:

```
def ne(pop, loci):
    ' calculate effective number of alleles at given loci'
    Stat(pop, alleleFreq=loci)
    ne = {}
    for loc in loci:
        freq = [y for x,y in pop.dvars().alleleFreq[loc].iteritems() if x != 0]
        sumFreq = 1 - pop.dvars().alleleFreq[loc][0]
        if sumFreq == 0:
            ne[loc] = 0
        else:
            ne[loc] = 1. / sum([(x/sumFreq)**2 for x in freq])
    # save the result to the population.
    pop.dvars().ne = ne
    return True
```

When it is needed to calculate effective number of alleles, a Python operator that uses this function can be used. For example, operator

```
pyOperator(func=ne, param=[0], step=5)
pyEval(r'("%.3f" % ne[0])', step=5)
```

would calculate effective number of alleles at locus 0 and output it.

The biggest difference between `pyEval` and `pyOperator` is that `pyOperator` is no longer evaluated in the population's local namespace. You will have to get the variables explicitly using the `pop.dvars()` function, and the results have to be explicitly saved to the population's local namespace.

The final implementation, as a way to demonstrate how to define a new statistics that hides all the details, defines a new operator by inheriting a class from `pyOperator`. The resulting operator could be used as a regular operator (e.g., `ne(loci=[0])`). A function `Ne` is also defined as the function form of this operator. The code is listed in Example 5.2

Example 5.2: A customized operator to calculate effective number of alleles

```
>>> import simuPOP as sim
>>> class ne(sim.pyOperator):
...     '''Define an operator that calculates effective number of
...     alleles at given loci. The result is saved in a sim.population
...     variable ne.
...     '''
...     def __init__(self, loci, *args, **kwargs):
...         self.loci = loci
...         sim.pyOperator.__init__(self, func=self.calcNe, *args, **kwargs)
...     #
...     def calcNe(self, pop):
...         sim.Stat(pop, alleleFreq=self.loci)
```

```

...     ne = {}
...     for loc in self.loci:
...         freq = pop.dvars().alleleFreq[loc]
...         sumFreq = 1 - pop.dvars().alleleFreq[loc][0]
...         if sumFreq == 0:
...             ne[loc] = 0
...         else:
...             ne[loc] = 1. / sum([(freq[x]/sumFreq)**2 for x in freq.keys() if x != 0])
...         # save the result to the sim.population.
...         pop.dvars().ne = ne
...     return True
...
>>> def Ne(pop, loci):
...     '''Function form of operator ne'''
...     ne(loci).apply(pop)
...     return pop.dvars().ne
...
>>> pop = sim.population(100, loci=[10])
>>> sim.InitByFreq(pop, [.2] * 5)
>>> print Ne(pop, loci=[2, 4])
{2: 3.9544814641013608, 4: 3.8032493907392362}

```

## 5.5 Initialize and evolve the population

With appropriate operators to perform mutation, selection and output statistics, it is relatively easy to write a simulator to perform a simulation. This simulator would create a population, initialize alleles with an initial allelic spectrum, and then evolve it according to specified demographic model. During the evolution, mutation and selection will be applied, statistics will be calculated and outputed.

Example 5.3: Evolve a population subject to mutation and selection

```

>>> import simuPOP as sim
>>>
>>>
>>> def simulate(model, N0, N1, G0, G1, spec, s, mu, k):
...     '''Evolve a sim.population using given demographic model
...     and observe the evolution of its allelic spectrum.
...     model: type of demographic model.
...     N0, N1, G0, G1: parameters of demographic model.
...     spec: initial allelic spectrum, should be a list of allele
...           frequencies for each allele.
...     s: selection pressure.
...     mu: mutation rate.
...     k: k for the k-allele model
...     '''
...     demo_func = demo_model(model, N0, N1, G0, G1)
...     simu = sim.simulator(
...         sim.population(size=demo_func(0), loci=1, infoFields='fitness'),
...         sim.randomMating(subPopSize=demo_func)
...     )
...     simu.evolve(
...         initOps = [
...             sim.initSex(),
...             sim.initByFreq(loci=0, alleleFreq=spec)
...         ],
...         postOps = [
...             sim.kamMutator(k=k, rates=mu),

```

```

...         sim.maSelector(loci=0, fitness=[1, 1, 1 - s], wildtype=0),
...         ne(loci=[0], step=100),
...         sim.pyEval(r'%d: %.2f\t%.2f\n' % (gen, 1 - alleleFreq[0][0], ne[0])),
...         step=100),
...     ],
...     gen = G0 + G1
... )
...
>>> simulate('instant', 1000, 10000, 500, 500, [0.9]+[0.02]*5, 0.01, 1e-4, 200)
0: 0.09 4.91
100: 0.12      2.63
200: 0.10      1.36
300: 0.08      1.00
400: 0.05      1.02
500: 0.04      1.02
600: 0.06      1.79
700: 0.09      2.51
800: 0.09      2.46
900: 0.08      3.63

```

## 5.6 Option handling

Everything seems to be perfect until you need to

1. Run more simulations with different parameters such as initial population size and mutation rate. This requires the script to get its parameters from command line (or a configuration file) and executes in batch mode, perhaps on a cluster system.
2. Allow users who are not familiar with the script to run it. This would better be achieved by a graphical user interface.
3. Allow other Python scripts to import your script and run the simulation function directly.

Although a number of Python modules such as `getopt` are available, the `simuPOP` `simuOpt` module is especially designed to allow a `simuPOP` script to be run both in batch and in GUI mode, in standard and optimized mode. Example 5.4 makes use of this module.

Example 5.4: A complete simulation script

```

#!/usr/bin/env python
#
# Author: Bo Peng
# Purpose: A real world example for simuPOP user's guide.
#
'''
Simulation the evolution of allelic spectra (number and frequencies
of alleles at a locus), under the influence of sim.population expansion,
mutation, and natural selection.
'''
import simuOpt
simuOpt.setOptions(quiet=True, alleleType='long')
import simuPOP as sim
import sys, types, os, math
options = [
    {'longarg': 'demo=',
     'default': 'instant',
     'label': 'Population growth model',

```

```

    'description': 'How does a sim.population grow from N0 to N1.',
    'chooseOneOf': ['instant', 'exponential'],
},
{'longarg': 'N0=',
 'default': 10000,
 'label': 'Initial sim.population size',
 'allowedTypes': [types.IntType, types.LongType],
 'description': '''Initial sim.population size. This size will be maintained
                    till the end of burnin stage''',
 'validate': simuOpt.valueGT(0)
},
{'longarg': 'N1=',
 'default': 100000,
 'label': 'Final sim.population size',
 'allowedTypes': [types.IntType, types.LongType],
 'description': 'Ending sim.population size (after sim.population expansion)',
 'validate': simuOpt.valueGT(0)
},
{'longarg': 'G0=',
 'default': 500,
 'label': 'Length of burn-in stage',
 'allowedTypes': [types.IntType],
 'description': 'Number of generations of the burn in stage.',
 'validate': simuOpt.valueGT(0)
},
{'longarg': 'G1=',
 'default': 1000,
 'label': 'Length of expansion stage',
 'allowedTypes': [types.IntType],
 'description': 'Number of geneartions of the sim.population expansion stage',
 'validate': simuOpt.valueGT(0)
},
{'longarg': 'spec=',
 'default': [0.9] + [0.02]*5,
 'label': 'Initial allelic spectrum',
 'allowedTypes': [types.TupleType, types.ListType],
 'description': '''Initial allelic spectrum, should be a list of allele
                    frequencies, for allele 0, 1, 2, ... respectively.'''',
 'validate': simuOpt.valueListOf(simuOpt.valueBetween(0, 1)),
},
{'longarg': 's=',
 'default': 0.01,
 'label': 'Selection pressure',
 'allowedTypes': [types.IntType, types.FloatType],
 'description': '''Selection coefficient for homozygtes (aa) genotype.
                    A recessive selection model is used so the fitness values of
                    genotypes AA, Aa and aa are 1, 1 and 1-s respectively.'''',
 'validate': simuOpt.valueGT(-1),
},
{'longarg': 'mu=',
 'default': 1e-4,
 'label': 'Mutation rate',
 'allowedTypes': [types.IntType, types.FloatType],
 'description': 'Mutation rate of a k-allele mutation model',
 'validate': simuOpt.valueBetween(0, 1),
},
{'longarg': 'k=',
 'default': 200,
 'label': 'sim.MAXIMUM allelic sim.state',

```

```

        'allowedTypes': [types.IntType],
        'description': 'sim.MAXIMUM allelic sim.state for a k-allele mutation model',
        'validate': simuOpt.valueGT(1),
    },
]

def demo_model(type, N0=1000, N1=100000, G0=500, G1=500):
    '''Return a demographic function
    type: linear or exponential
    N0: Initial sim.population size.
    N1: Ending sim.population size.
    G0: Length of burn-in stage.
    G1: Length of sim.population expansion stage.
    '''
    rate = (math.log(N1) - math.log(N0))/G1
    def ins_expansion(gen, pop=None):
        if gen < G0:
            return N0
        else:
            return N1

    def exp_expansion(gen, pop=None):
        if gen < G0:
            return N0
        else:
            return int(N0 * math.exp((gen - G0) * rate))

    if type == 'instant':
        return ins_expansion
    elif type == 'exponential':
        return exp_expansion

class ne(sim.pyOperator):
    '''Define an operator that calculates effective number of
    alleles at given loci. The result is saved in a sim.population
    variable ne.
    '''
    def __init__(self, loci, *args, **kwargs):
        self.loci = loci
        sim.pyOperator.__init__(self, func=self.calcNe, *args, **kwargs)

    def calcNe(self, pop):
        sim.Stat(pop, alleleFreq=self.loci)
        ne = {}
        for loc in self.loci:
            freq = pop.dvars().alleleFreq[loc][1:]
            sumFreq = 1 - pop.dvars().alleleFreq[loc][0]
            if sumFreq == 0:
                ne[loc] = 0
            else:
                ne[loc] = 1. / sum([(x/sumFreq)**2 for x in freq])
        # save the result to the sim.population.
        pop.dvars().ne = ne
        return True

def simuCDCV(model, N0, N1, G0, G1, spec, s, mu, k):
    '''Evolve a sim.population using given demographic model
    and observe the evolution of its allelic spectrum.
    model: type of demographic model.

```



```

N0, N1, G0, G1: parameters of demographic model.
spec: initial allelic spectrum, should be a list of allele
      frequencies for each allele.
s: selection pressure.
mu: mutation rate.
k: maximum allele for the k-allele model
'''
demo_func = demo_model(model, N0, N1, G0, G1)
print demo_func(0)
simu = sim.simulator(
    sim.population(size=demo_func(0), loci=1, infoFields='fitness'),
    sim.randomMating(subPopSize=demo_func(
)
simu.evolve(
    initOps = [
        sim.initSex(),
        sim.initByFreq(loci=0, alleleFreq=spec)
    ],
    postOps = [
        sim.kamMutator(rate=mu, maxAllele=k),
        sim.maSelector(loci=0, fitness=[1, 1, 1 - s], wildtype=0),
        ne(loci=0, step=100),
        sim.pyEval(r'"%d: %.2f\t%.2f\n" % (gen, 1 - alleleFreq[0][0], ne[0])',
                    step=100),
    ],
    gen = G0 + G1
)
return simu.extract(0)

if __name__ == '__main__':
    # get parameters
    par = simuOpt.simuParam(options, __doc__)
    if not par.getParam():
        sys.exit(1)

    if not sum(par.spec) == 1:
        print 'Initial allelic spectrum should add up to 1.'
        sys.exit(1)
    # save user input to a configuration file
    par.saveConfig('simuCDCV.cfg')
    #
    simuCDCV(*par.asList())

```

Example 5.4 uses a programming style that is used by almost all simuPOP scripts. I highly recommend this style because it makes your script self-documentary and work well under a variety of environments. A script written in this style follows the following order:

1. First comment block

The first line of the script should always be

```
#!/usr/bin/env python
```

This line tells a Unix shell which program should be used to process this script if the script is to be executable. This line is ignored under windows. It is customary to put author and date information at the top of a script as Python comments.

2. Module doc string

The first string in a script is the module docstring, which can be referred by variable `__doc__` in the script. It is a good idea to describe what this script does in detail here. As you will see later, this docstring will be used in the `simuOpt.getParam()` function and be outputted in the usage information of the script.

### 3. Loading simuPOP and other Python modules

`simuPOP` and other modules are usually imported after module docstring. This is where you specify which `simuPOP` module to use. Although a number of parameters could be used, usually only `alleleType` is specified because other parameters such as `gui` and `optimized` should better be controlled from command line.

### 4. Parameter description list

A list of parameter description dictionaries are given here. This list specifies what parameters will be used in this script and describes the type, default value, name of command line option, label of the parameter in the parameter input dialog in detail. Although some dictionary items can be ignored, it is a good practice to give detailed information about each parameter here.

### 5. Helper functions and classes

Helper functions and classes are given before the main simulation function.

### 6. Main simulation function

The main simulation function preforms the main functionality of the whole script. It is written as a function so that it can be imported and executed by another script. The parameter processing part of the script would be ignored in this case.

### 7. Script execution part conditioned by `__name__ == '__main__'`

The execution part of a script should always be inside of a `if __name__ == '__main__':` block so that the script will not be executed when it is imported by another script. The first few lines of this execution block are almost always

```
par = simuOpt.simuOpt(options, __doc__)
if not par.getParam():
    sys.exit(1)
```

which creates a `simuOpt` object and tries to get parameters from command line option, a configuration file, a parameter input dialog or interactive user input, depending on how this script is executed. Optionally, you can use

```
par.saveConfig('file.cfg')
```

to save the current configuration to a file so that the same parameters could be retrieved later using parameter `--config file.cfg`.

After simply parameter validation, the main simulation function can be called. This example uses `simuCDCV(*par.asList())` because the parameter list in the `par` object match the parameter list of function `simuCDCV` exactly. If there are a large number of parameters, it may be better to pass the `simuOpt` object directly in the main simulation function.

The script written in this style could be executed in a number of ways.

1. If a user executes the script directly, a Tkinter or wxPython dialog will be displayed for users to input parameters. This parameter is shown in Figure 5.1.
2. The help message of this script could be displayed using the Help button of the parameter input dialog, or using command `simuCDCV.py -h`. The help message is displayed in Example 5.5.

Figure 5.1: Parameter input dialog of the simuCDCV script

Example 5.5: Help information for the simuCDCV script

```
Simulation the evolution of allelic spectra (number and frequencies
of alleles at a locus), under the influence of sim.population expansion,
mutation, and natural selection.

usage: simuCDCV.py [-opt [arg] | --opt [=arg]] ...

options:
  -h, --help                show this help message and exit
  --config ARG              load parameters from ARG
  --optimized               run the script using an optimized simuPOP module
                             which graphical toolkit to use
  --demo ARG                Population growth model [default: instant ]
                             How does a sim.population grow from N0 to N1.
  --N0 ARG                  Initial sim.population size [default: 10000 ]
                             Initial sim.population size. This size will be
                             maintained till the end of burnin stage
  --N1 ARG                  Final sim.population size [default: 100000 ]
                             Ending sim.population size (after sim.population
                             expansion)
  --G0 ARG                  Length of burn-in stage [default: 500 ]
                             Number of generations of the burn in stage.
  --G1 ARG                  Length of expansion stage [default: 1000 ]
                             Number of geneartions of the sim.population expansion
                             stage
```

<code>--spec ARG</code>	Initial allelic spectrum [default: [0.9, 0.02, 0.02, 0.02, 0.02, 0.02]] Initial allelic spectrum, should be a list of allele frequencies, <b>for</b> allele 0, 1, 2, ... respectively.
<code>--s ARG</code>	Selection pressure [default: 0.01 ] Selection coefficient <b>for</b> homozygtes (aa) genotype. A recessive selection model <b>is</b> used so the fitness values of genotypes AA, Aa <b>and</b> aa are 1, 1 <b>and</b> 1-s respectively.
<code>--mu ARG</code>	Mutation rate [default: 0.0001 ] Mutation rate of a k-allele mutation model
<code>--k ARG</code>	sim.MAXIMUM allelic sim.state [default: 200 ] sim.MAXIMUM allelic sim.state <b>for</b> a k-allele mutation model

3. Using parameter `--gui=False`, the script will be run in batch mode. You can specify parameters using

```
simuCDCV.py --gui=False --config file.cfg
```

if a parameter file is available, or use command line options such as

```
simuCDCV.py --gui=False --demo='instant' --N0=10000 --N1=100000 \  
  --G0=500 --G1=500 --spec='[0.9]+[0.02]*5' --s=0.01 \  
  --mu='1e-4' --k=200
```

Note that parameters with `useDefault` set to `True` can be ignored if the default parameter is used. In addition, parameter `--optimized` could be used to load the optimized version of a `simuPOP` module. For this particular configuration, the optimized module is 30% faster (62s vs. 40s) than the standard module.

4. The simulation function could be imported to another script as follows

```
from simuCDCV import simuCDCV  
simuCDCV(model='instant', N0=10000, N1=10000, G0=500, G1=500,  
  spec=[0.9]+[0.02]*5, s=0.01, mu=1e-4, k=200)
```

## Chapter 6

# Advanced topics \*

### 6.1 Age structured populations with overlapping generations \*

Age is an important factor in many applications because it is related to many genetic (most obviously mating) and environmental factors that influence the evolution of a population. The evolution of age structured populations will lead to overlapping generations because parents can co-exist with their offspring in such a population. Although simuPOP is based on a discrete generation model, it can be used to simulate age structured populations.

To evolve an age structured population, you will need to

- Define an information field `age` and use it to store age of all individuals. Age is usually assigned randomly at the beginning of a simulation.
- Define a virtual splitter that splits the parental population into several virtual subpopulation. The most important VSP consists of mating individuals (e.g. individuals with age between 20 and 40). Advanced features of virtual splitters can be used to define complex VSPs such as males between age 20 - 40 and females between age 15-30 (use a `productSplitter` to split subpopulations by sex and age, and then a `combinedSplitter` to join several smaller VSPs together).
- Use a heterogeneous mating scheme that clones most individuals to the next generation (year) and produce offspring from the mating VSP.

Example 6.1 gives an example of the evolution of age-structured population.

Example 6.1: Example of the evolution of age-structured population.

```
>>> import simuPOP as sim
>>> import random
>>> N = 10000
>>> pop = sim.population(10000, loci=1, infoFields='age')
>>> pop.setVirtualSplitter(sim.infoSplitter(field='age', cutoff=[20, 50, 75]))
>>> def demoModel(gen, pop):
...     '''A demographic model that keep a constant supply of new individuals'''
...     # number of individuals that will die
...     sim.Stat(pop, popSize=True, subPops=[(0,3)])
...     # individuals that will be kept, plus some new guys.
...     return pop.popSize() - pop.dvars().popSize + N / 75
...
>>> def pene(geno, age, gen):
...     'Define an age-dependent penetrance function'
...     # the probability of getting disease increases with age
...     return (0., 0.01*age[0], 0.01*age[0])[sum(geno)]
```

```

...
>>> def outputStat(pop):
...     'Calculate and output statistics'
...     sim.Stat(pop, popSize=True, numOfAffected=True,
...             subPops=[(0,0), (0,1), (0,2), (0,3)],
...             vars=['popSize_sp', 'propOfAffected_sp'])
...     for sp in range(3):
...         print '%s: %.3f%% (size %d)' % (pop.subPopName((0,sp)),
...             pop.dvars((0,sp)).propOfAffected * 100.,
...             pop.dvars((0,sp)).popSize),
...     print
...     return True
...
>>> simu = sim.simulator(pop,
...     sim.heteroMating([
...         # all individuals with age < 75 will be kept. Note that
...         # cloneMating will keep individual sex, affection status and all
...         # information fields (by default).
...         sim.cloneMating(subPops=[(0,0), (0,1), (0,2)], weight=-1),
...         # only individuals with age between 20 and 50 will mate and produce
...         # offspring. The age of offspring will be zero.
...         sim.randomMating(subPops=[(0,1)]),
...     ], subPopSize=demoModel)
... )
>>>
>>> simu.evolve(
...     initOps = [
...         sim.initSex(),
...         # random assign age
...         sim.initInfo(lambda: random.randint(0, 75), infoFields='age'),
...         # random genotype
...         sim.initByFreq([0.5, 0.5]),
...         sim.pyOutput('Prevalence of disease in each age group:\n'),
...     ],
...     # increase the age of everyone by 1 before mating.
...     preOps = sim.infoExec('age += 1'),
...     # number of individuals?
...     postOps = [
...         sim.pyPenetrance(func=pene, loci=0, paramFields='age'),
...         sim.pyOperator(func=outputStat)
...     ],
...     gen = 10
... )
Prevalence of disease in each age group:
age < 20: 6.589% (size 2671) 20 <= age < 50: 26.087% (size 3933) 50 <= age < 75: 46.379% (size 3314)
age < 20: 7.687% (size 2680) 20 <= age < 50: 24.681% (size 3918) 50 <= age < 75: 45.567% (size 3316)
age < 20: 7.463% (size 2680) 20 <= age < 50: 24.385% (size 3904) 50 <= age < 75: 45.126% (size 3324)
age < 20: 6.493% (size 2680) 20 <= age < 50: 25.006% (size 3903) 50 <= age < 75: 46.867% (size 3335)
age < 20: 7.351% (size 2680) 20 <= age < 50: 25.826% (size 3903) 50 <= age < 75: 45.719% (size 3340)
age < 20: 6.667% (size 2670) 20 <= age < 50: 24.522% (size 3919) 50 <= age < 75: 45.672% (size 3350)
age < 20: 7.183% (size 2687) 20 <= age < 50: 26.064% (size 3925) 50 <= age < 75: 46.145% (size 3346)
age < 20: 7.401% (size 2689) 20 <= age < 50: 25.622% (size 3938) 50 <= age < 75: 45.561% (size 3334)
age < 20: 6.872% (size 2663) 20 <= age < 50: 24.416% (size 3981) 50 <= age < 75: 45.952% (size 3310)
age < 20: 7.016% (size 2651) 20 <= age < 50: 25.698% (size 3977) 50 <= age < 75: 45.367% (size 3324)
(10,)

```

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