Forward-time simulations using simuPOP, an in-depth course

Bo Peng, Ph.D.

Department of Epidemiology
UT MD Anderson Cancer Center
Houston, TX

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simuPOP workshop
School of Public Health, Department of Biostatistics
University of Alabama Birmingham

outline

Outline

1 Loading simuPOP

- simuPOP modules
- Random Number Generator
- Debug information
- Getting help

simuPOP modules

simuPOP provides six types of modules

1. Possible allele states:

short	$0 \sim 2^8 - 1$
long	$0 \sim 2^{16} - 1$
binary	0 and 1

2. Debug information and runtime validation

standard	with debug information and runtime validation
optimized	without debug information and runtime validation

Note: A MPI (Message Passing Interface) version of simuPOP is under development.

Loading appropriate module

1. Use `simuOpt.setOptions`

```
>>> from simuOpt import setOptions
>>> setOptions(alleleType='long', optimized=False)
>>> from simuPOP import *
simuPOP : Copyright (c) 2004-2006 Bo Peng
Developmental Version (Jun 12 2007) for Python 2.3.4
[GCC 3.4.6 20060404 (Red Hat 3.4.6-8)]
Random Number Generator is set to mt19937 with random seed 0x56338ac0e4025000
This is the standard long allele version with 65536 maximum allelic states.
For more information, please visit http://simupop.sourceforge.net,
or email simupop-list@lists.sourceforge.net (subscription required).
>>>
```

2. Set environment variables
   - `SIMUALLELETYPE = short/long/binary`
   - `SIMUOPTIMIZED` for optimized version
3. Command line argument of scripts using the `simuOpt` module (`--optimized`)

Standard modules

Perform strict runtime check. Produce proper debug information if anything goes wrong.

```
>>> pop = population(10, loci=[2])
>>> pop.locusPos(10)
Traceback (most recent call last):
  File "course.py", line 1, in ?
    #!/usr/bin/env python
IndexError: src/genoStru.h:428 absolute locus index (10) out of range of 0 - 1
>>> pop.individual(20).setAllele(1, 0)
Traceback (most recent call last):
  File "course.py", line 1, in ?
    #!/usr/bin/env python
IndexError: src/population.h:452 individual index (20) is out of range of 0 ~ 9
>>>
```

Optimized modules

No runtime check. Improper usages may crash simuPOP.

```
% setenv SIMUOPTIMIZED
% python
Python 2.3.4 (#1, Jan  9 2007, 16:40:09)
[GCC 3.4.6 20060404 (Red Hat 3.4.6-3)] on linux2
Type "help", "copyright", "credits" or "license" for more information.
>>> from simuPOP import *
simuPOP : Copyright (c) 2004-2006 Bo Peng
Developmental Version (May 21 2007) for Python 2.3.4
[GCC 3.4.6 20060404 (Red Hat 3.4.6-3)]
Random Number Generator is set to mt19937 with random seed 0x2f04b9dc5ca0fc00
This is the optimied short allele version with 256 maximum allelic states.
For more information, please visit http://simupop.sourceforge.net,
or email simupop-list@lists.sourceforge.net (subscription required).
>>> pop = population(10, loci=[2])
>>> pop.locusPos(10)
1.2731974748756028e-313
>>> pop.individual(20).setAllele(1, 0)
Segmentation fault
```

Random Number Generator

simuPOP uses RNG from the GNU Scientific Library

```
>>> rng().name()
'mt19937'
>>> rng().seed()
6211460872137756672
>>> r = ListAllRNG()
>>> print r[:5]
('gfsr4', 'mt19937', 'mt19937_1999', 'mt19937_1998', 'r250')
>>> SetRNG('taus2', 1234)
>>> rng().name()
'taus2'
>>> rng().seed()
1234
>>> rng().randUniform01()
0.8298943955011666
>>>
```

Note: simuPOP depends on system clock to set random seed under windows.

Debug information

Several ways to turn on/off debug information

- Set environment variable `SIMUDEBUG`
- Use function `TurnOnDebug, TurnOffDebug`
- Use operator `turnOnDebug, turnOffDebug` to turn on/off debug at specific generations

Debug information (cont.)


```
>>> TurnOnDebug(DBG_POPULATION)
>>> ind = population(10, loci=[5]).individual(1)
Constructor of population is called
Destructor of population is called
>>> # This line may crash simuPOP
>>> print ind.allele(2)
0
>>> # Show all debug code
>>> ListDebugCode()
Debug code                    On/Off
DBG_ALL                         0
DBG_GENERAL                     1
DBG_UTILITY                     0
DBG_OPERATOR                    0
DBG_SIMULATOR                   0
DBG_INDIVIDUAL                  0
DBG_OUTPUTER                    0
DBG_MUTATOR                     0
DBG_RECOMBINATOR                0
DBG_INITIALIZER                 0
DBG_POPULATION                  1
```

Getting help


```
>>> help(population.addInfoFields)
Help on method population_addInfoFields:

population_addInfoFields(...) unbound simuPOP_la.population method
    Description:

        add one or more information fields to a population

    Usage:

        x.addInfoFields(fields, init=0)

    Arguments:

        fields:         new information fields. If one or more of the
                        fields alreay exist, they will simply be re-
                        initialized.
        init:           initial value for the new fields.

>>>
```

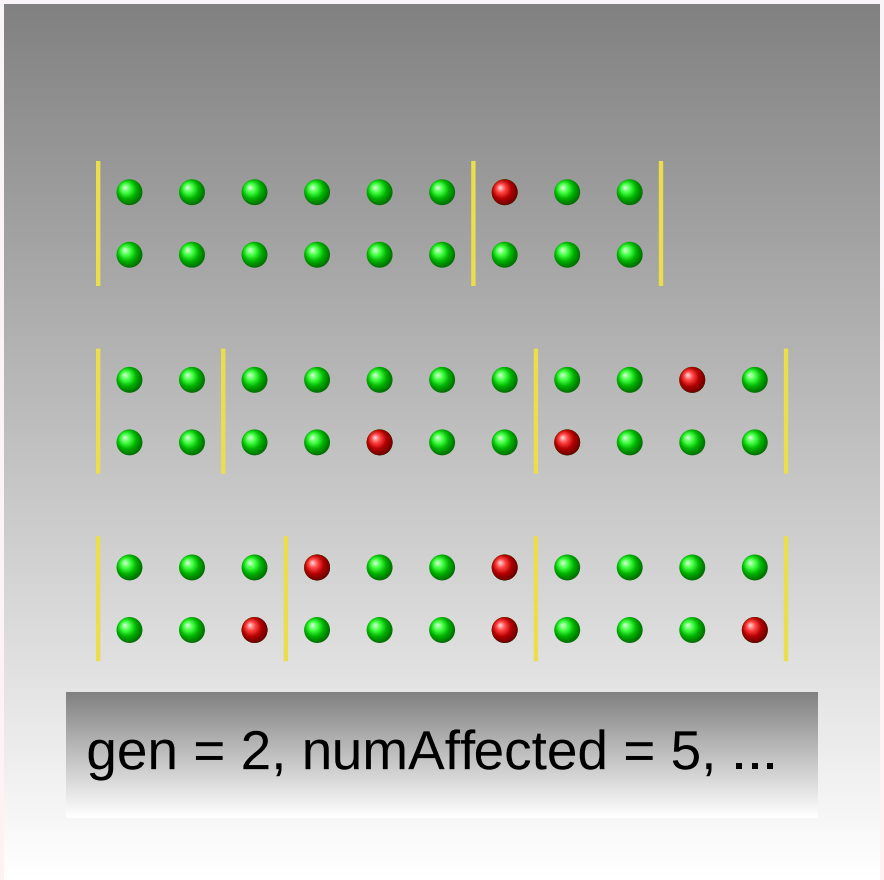
Outline

2 Population

- Structure of population
- Genotypic structure
- Population structure
- Population variables
- Manipulate population

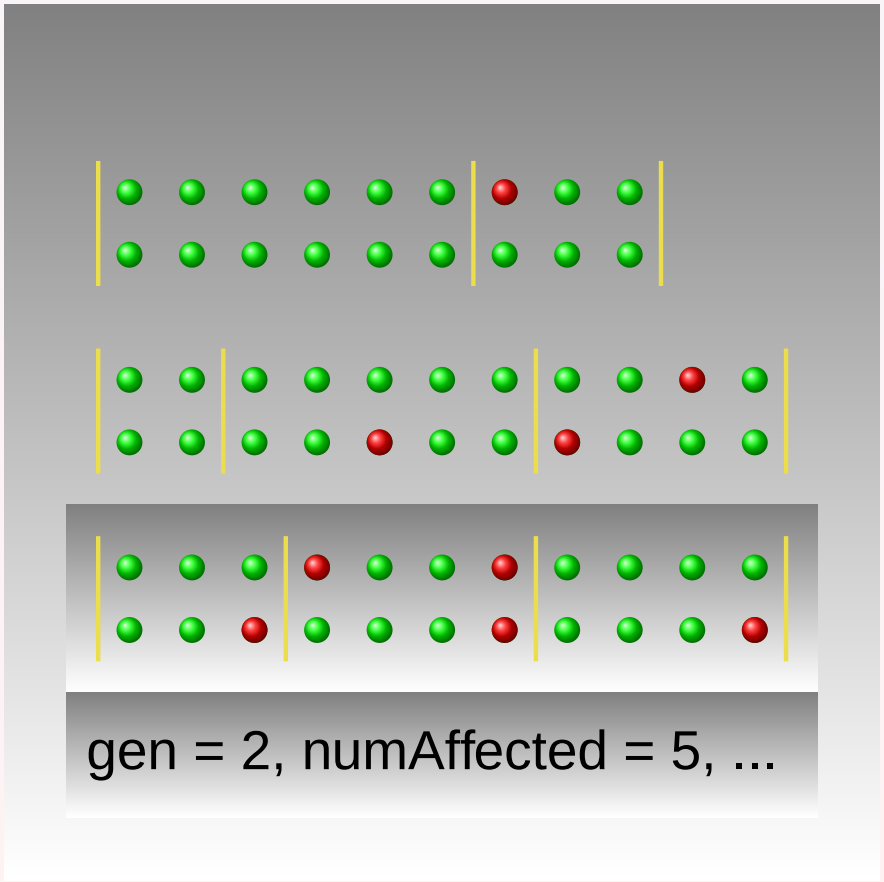
Structure of a population

- Unaffected
- Affected



Structure of a population

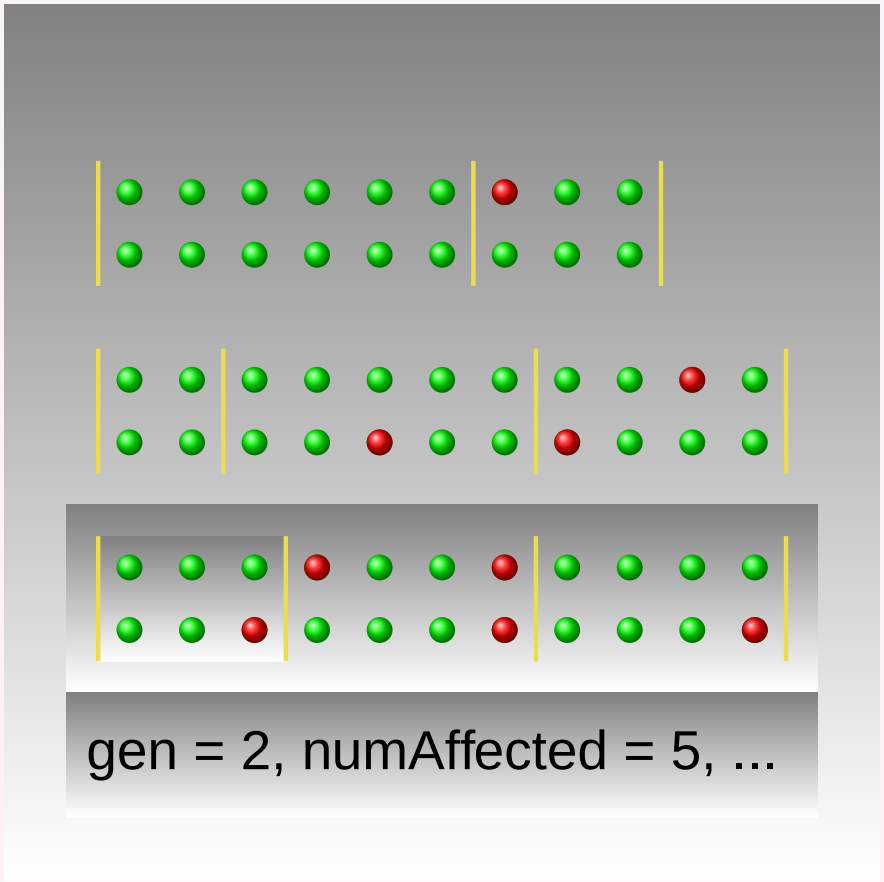
- Unaffected
- Affected



Current generation

Structure of a population

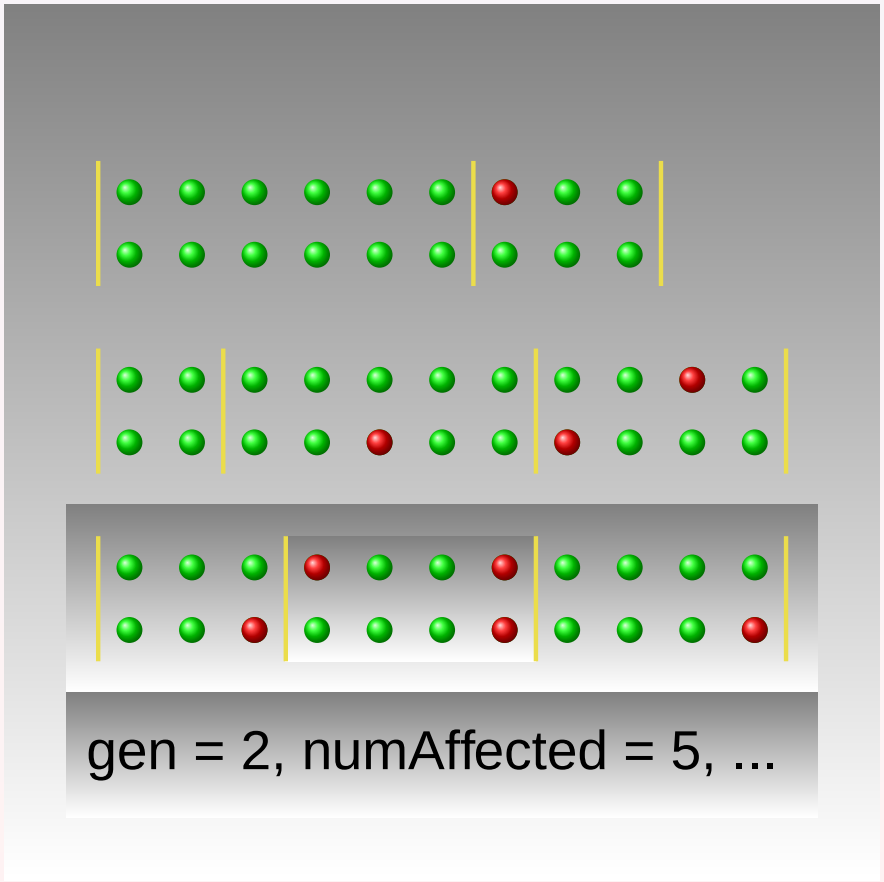
- Unaffected
- Affected



Current generation

Structure of a population

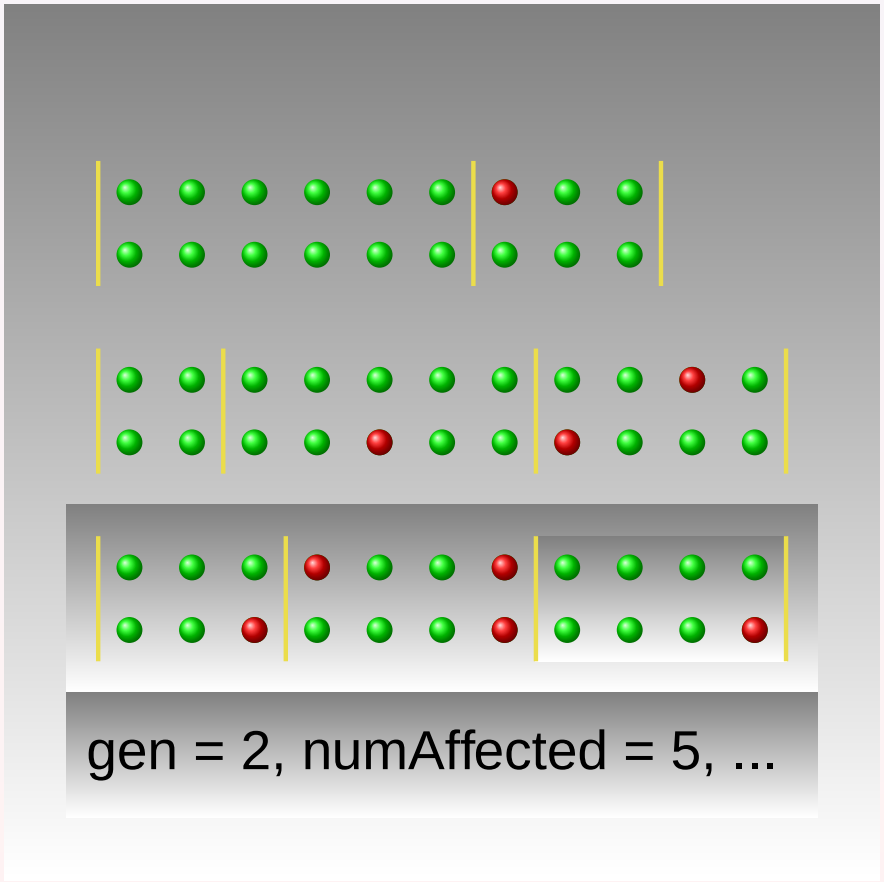
- Unaffected
- Affected



Current generation

Structure of a population

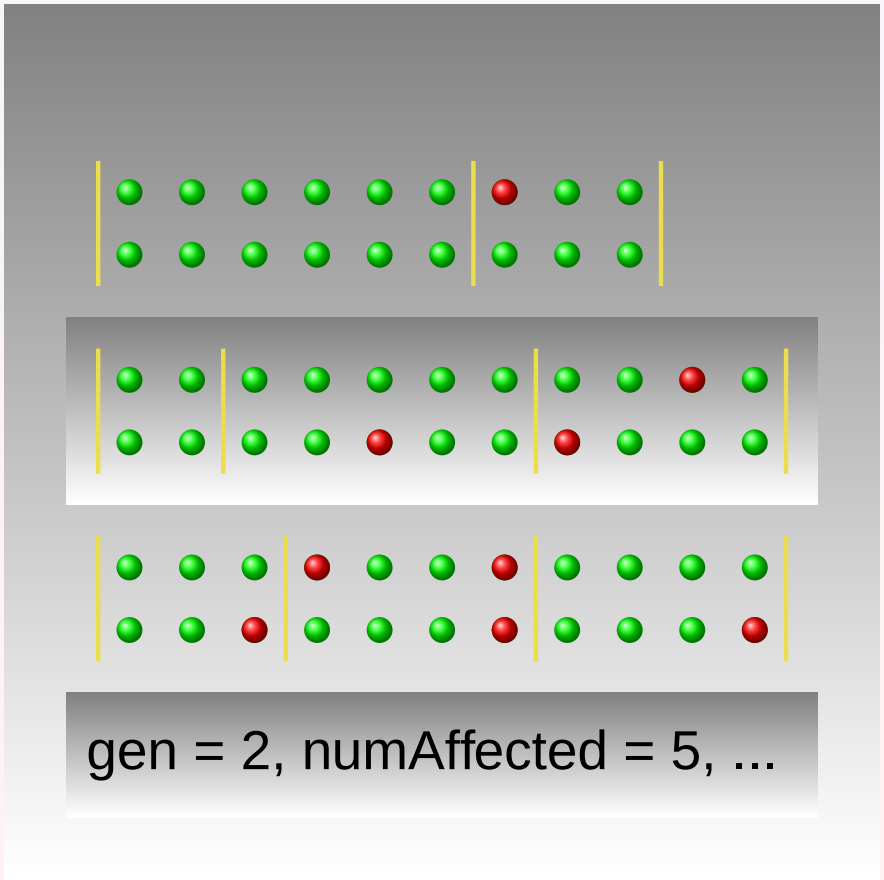
- Unaffected
- Affected



Current generation

Structure of a population

- Unaffected
- Affected

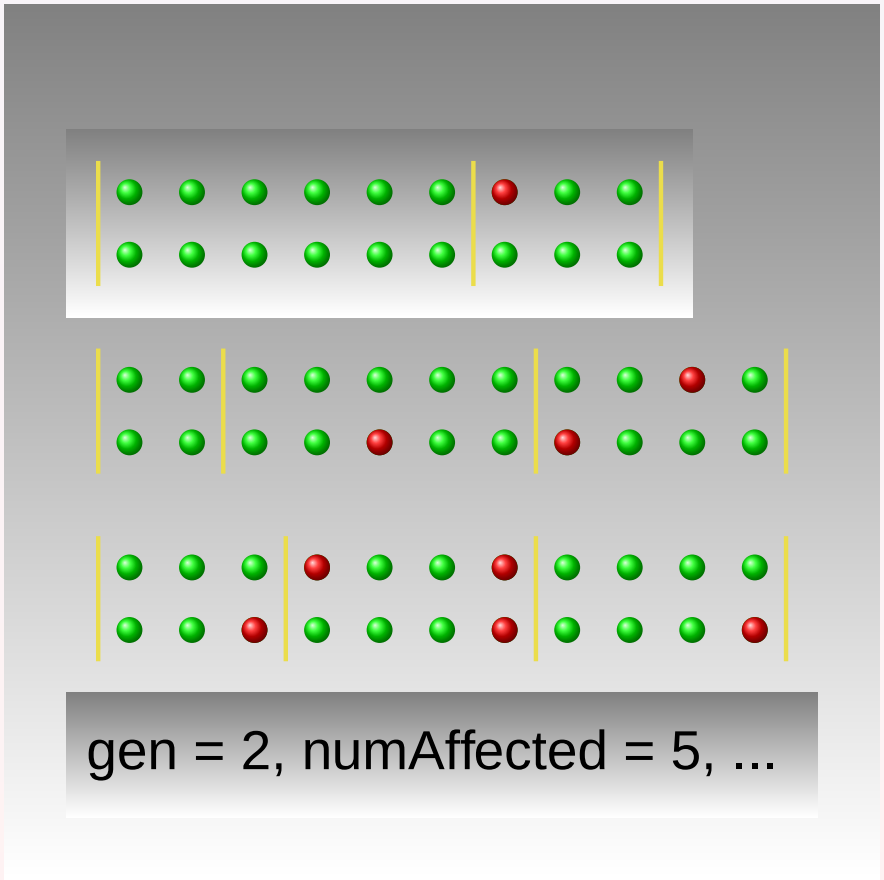


Ancestral generation 1

Current generation

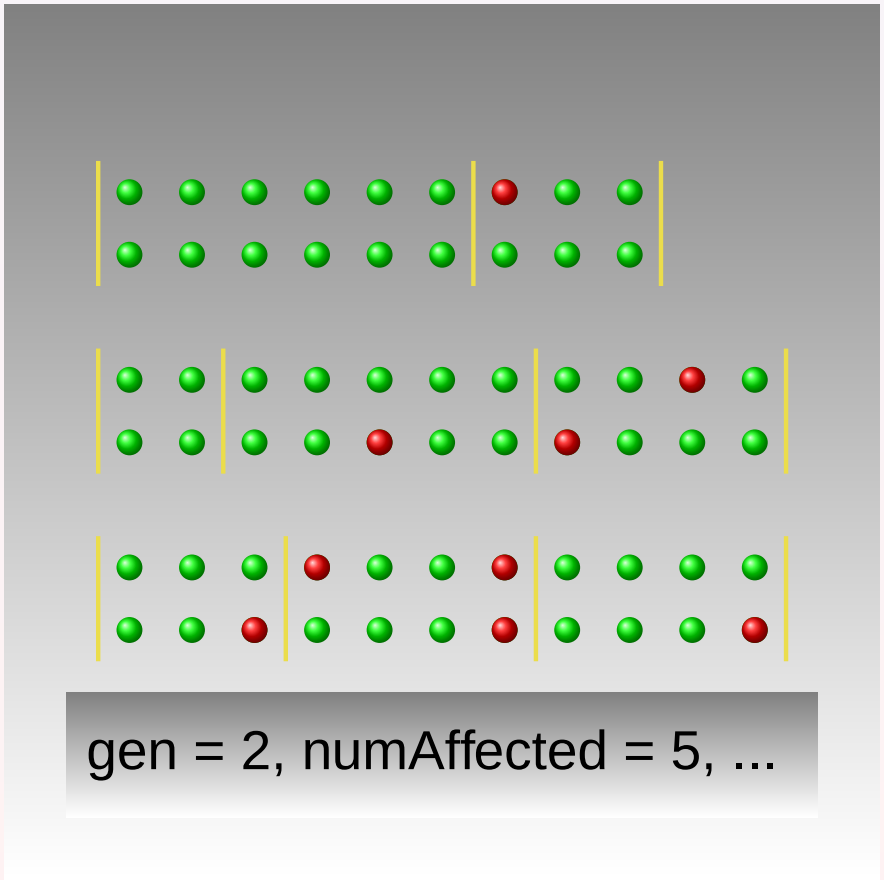
Structure of a population

- Unaffected
- Affected



Structure of a population

- Unaffected
- Affected



Ancestral generation 2

Ancestral generation 1

Current generation

Population variables

Genotypic Structure

All individuals have the same genotypic structure, which refers to

- Ploidy (diploid, haploid, triploid, ...)
- Number of chromosomes
- Number of loci on each chromosome
- Name and position of loci
- Name of information fields
- Allele names
- Existence of sex chromosome

Create a population


```
>>> pop = population(size=10, loci=[2, 3])
>>> Dump(pop)
Ploidy:                    2
Number of chrom:           2
Number of loci:            2 3
Maximum allele state:      65535
Loci positions:
                  1 2
                  1 2 3
Loci names:
                  loc1-1 loc1-2
                  loc2-1 loc2-2 loc2-3
population size:           10
Number of subPop:          1
Subpop sizes:              10
Number of ancestral populations:          0
individual info:
sub population 0:
   0: MU    0  0    0  0  0 |    0  0    0  0  0
   1: MU    0  0    0  0  0 |    0  0    0  0  0
   2: MU    0  0    0  0  0 |    0  0    0  0  0
   3: MU    0  0    0  0  0 |    0  0    0  0  0
```

Genotypic structure


```
>>> pop = population(subPop=[200, 300], loci=[3, 2],
...     maxAllele=3, ploidy=4,
...     lociPos=[[1, 3, 5], [2.5, 4]],
...     alleleNames=['A', 'C', 'T', 'G'])
>>> pop.numLoci(0)
3
>>> pop.totNumLoci()
5
>>> pop.locusPos(4)
4.0
>>> pop.subPopSize(1)
300
>>> pop.popSize()
500
>>> pop.ploidyName()
'tetraploid'
>>> pop.individual(1).allele(1, 2)
0
>>>
```

Have a look at the population (Dump)


```
>>> Dump(pop)
Ploidy:                  4
Number of chrom:         2
Number of loci:          3 2
Maximum allele state:    3
Loci positions:
                 1 3 5
                 2.5 4
Loci names:
                 loc1-1 loc1-2 loc1-3
                 loc2-1 loc2-2
population size:         500
Number of subPop:        2
Subpop sizes:            200 300
Number of ancestral populations:         0
individual info:
sub population 0:
   0: MU AAA AA | AAA AA | AAA AA | AAA AA
   1: MU AAA AA | AAA AA | AAA AA | AAA AA
   2: MU AAA AA | AAA AA | AAA AA | AAA AA
   3: MU AAA AA | AAA AA | AAA AA | AAA AA
   4: MU AAA AA | AAA AA | AAA AA | AAA AA
   5: MU AAA AA | AAA AA | AAA AA | AAA AA
   6: MU AAA AA | AAA AA | AAA AA | AAA AA
   7: MU AAA AA | AAA AA | AAA AA | AAA AA
   8: MU AAA AA | AAA AA | AAA AA | AAA AA
   9: MU AAA AA | AAA AA | AAA AA | AAA AA
  10: MU AAA AA | AAA AA | AAA AA | AAA AA
  11: MU AAA AA | AAA AA | AAA AA | AAA AA
  12: MU AAA AA | AAA AA | AAA AA | AAA AA
  13: MU AAA AA | AAA AA | AAA AA | AAA AA
```

Create a population with subpopulations


```
>>> pop = population(subPop=[2, 5, 6], loci=[2])
>>> print pop.popSize()
13
>>> print pop.subPopSizes()
(2, 5, 6)
>>> print pop.subPopSize(1)
5
>>> Dump(pop, infoOnly=True)
Ploidy:                    2
Number of chrom:           1
Number of loci:            2
Maximum allele state:   65535
Loci positions:
                  1 2
Loci names:
                  loc1-1 loc1-2
population size:           13
Number of subPop:          3
Subpop sizes:              2 5 6
Number of ancestral populations:        0
>>>
```

Mating is within subpopulation only


```
>>> pop = population(subPop=[5, 6], loci=[2])
>>> simu = simulator(pop, randomMating())
>>> simu.evolve(
...     preOps = [
...         initByFreq(alleleFreq=[0.2, 0.8], subPop=[0]),
...         initByFreq([0, 0, 0, 0.5, 0.5], subPop=[1])
...         ],
...     ops = [
...         dumper(alleleOnly=True, indRange=[[0, 3], [5, 7]]),
...         recombinator(rate=0.1) ],
...     end = 1
... )
```

Mating is within subpopulation only (cont.)


```
individual info:
sub population 0:
   0: MU   1  1 |   1  1
   1: FU   0  1 |   1  1
   2: FU   1  1 |   1  1
sub population 1:
   5: FU   4  4 |   4  3
   6: MU   4  4 |   4  4
End of individual info.


No ancenstral population recorded.
individual info:
sub population 0:
   0: FU   1  1 |   0  1
   1: FU   1  1 |   1  1
   2: MU   1  1 |   0  1
sub population 1:
   5: MU   4  4 |   4  3
   6: FU   4  4 |   4  3
End of individual info.
```

Population variables


```
>>> pop = population(subPop=[5, 10], loci=[5])
>>> InitByFreq(pop, [.6, .3, .1])
>>> Stat(pop, alleleFreq=[1], genoFreq=[2])
>>> print pop.dvars().alleleFreq[1][0]
0.7
>>> from simuUtil import ListVars
>>> ListVars(pop.dvars(), useWxPython=False)
 grp :  -1
 rep :  -1
 alleleNum :
   [1]
     [0]        21
     [1]        8
     [2]        1
 genoFreq :
   [2]
     [0]
       0 :      0.266666666667
       1 :      0.4
       2 :      0.266666666667
     [1]
       1 :      0.0666666666667
 genoNum :
   [2]
     [0]
       0 :      4.0
       1 :      6.0
       2 :      4.0
     [1]
       1 :      1.0
 alleleFreq :
```

Population variables (cont.)


```
subPop
  [0]
    alleleNum :
      [1]
        [0]    6
        [1]    3
        [2]    1
    genoNum :
      [2]
        [0]
          1 :  3.0
          2 :  2.0
    genoFreq :
      [2]
        [0]
          1 :  0.6
          2 :  0.4
    alleleFreq :
      [1]
        [0]    0.6
        [1]    0.3
        [2]    0.1
  [1]
    alleleNum :
      [1]
        [0]    15
```

Population manipulation


```
>>> # make a copy of pop
>>> pop = population(1000, loci=[2,3])
>>> pop1 = pop.clone()
>>> # remove loci 2, 3, 4
>>> pop.removeLoci(keep=[0, 1])
>>> # pop2 will have 3 chromosomes, with loci 2, 3, 2
>>> pop2 = MergePopulationsByLoci(pops=[pop, pop1])
>>> # randomly assign alleles using given allele frequencies
>>> InitByFreq(pop2, [0.8, .2])
>>> # assign affection status using a penetrance model
>>> MapPenetrance(pop2, locus=1,
...     penetrance={'0-0': 0.05, '0-1': 0.2, '1-1': 0.8})
>>> # draw case control sample
>>> (sample,) = CaseControlSample(pop2, cases=5, controls=5)
>>> # save sample in Merlin QTDT format
>>> from simuUtil import SaveQTDT
>>> SaveQTDT(sample, output='sample', affectionCode=['U', 'A'],
...     fields=['affection'])
>>> # have a look at the sample in Merlin-QTDT Format
>>> print open('sample.map').read()
CHROMOSOME MARKER POSITION
1       loc1-1  1.000000
```

Population manipulation (cont.)


```
1       loc1-2  2.000000
2       loc1-1_1        1.000000
2       loc1-2_1        2.000000
3       loc2-1  1.000000
3       loc2-2  2.000000
3       loc2-3  3.000000

>>> print open('sample.dat').read()
A       affection
M       loc1-1
M       loc1-2
M       loc1-1_1
M       loc1-2_1
M       loc2-1
M       loc2-2
M       loc2-3

>>> print open('sample.ped').read()
1 1 0 0 2 A 1 1 1 2 2 1 1 1 1 1 1 1 2 1
2 1 0 0 1 A 1 1 1 1 1 1 1 1 1 1 1 1 1 1
3 1 0 0 2 A 1 2 2 1 1 1 1 1 1 1 2 1 1 1
```

Population manipulation (cont.)


```
4 1 0 0 1 A 1 1 1 2 1 1 1 1 1 1 1 1 1 1
5 1 0 0 2 A 2 1 2 2 1 1 1 1 1 1 1 1 1 1
6 1 0 0 1 U 1 1 1 1 1 1 2 2 1 1 1 1 1 2
7 1 0 0 1 U 1 1 1 1 1 1 1 1 1 1 1 1 1 1
8 1 0 0 2 U 1 1 1 2 1 1 1 2 2 1 1 1 1 2
9 1 0 0 2 U 1 1 1 1 1 1 1 1 1 1 2 1 1 1
10 1 0 0 1 U 1 2 1 2 1 1 1 1 2 1 2 1 1 2

>>>
```

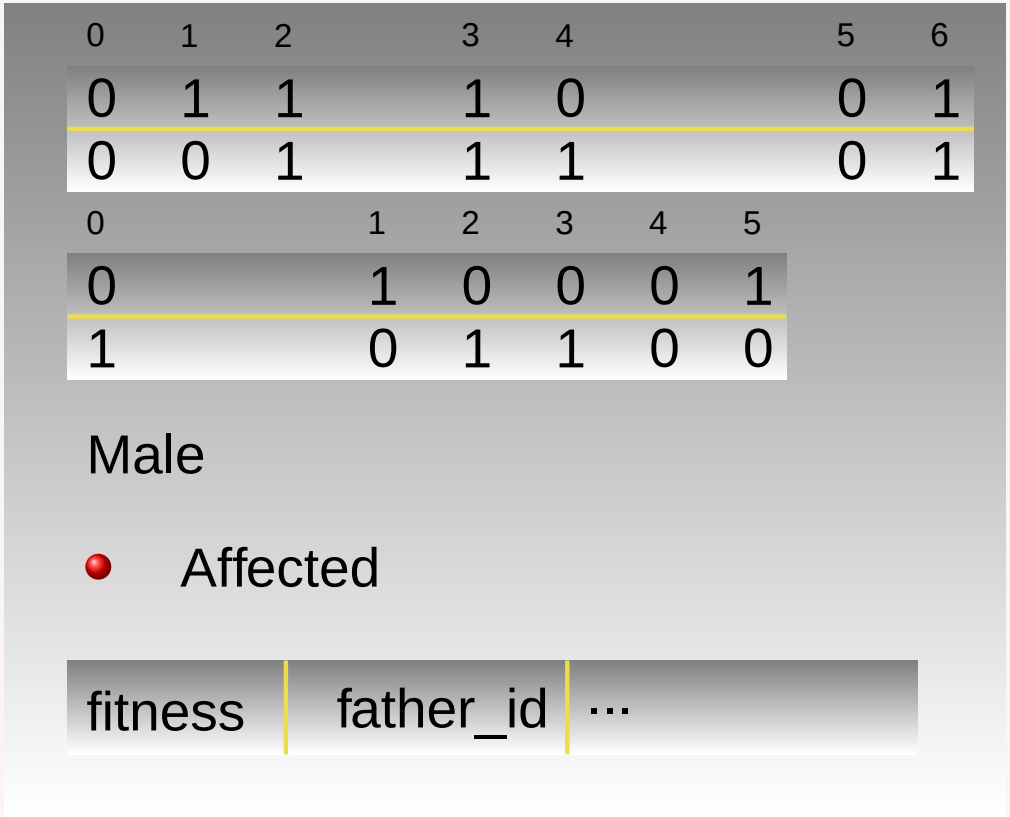
Outline

3 Individual

- Structure of individual
- Individual object
- Information fields

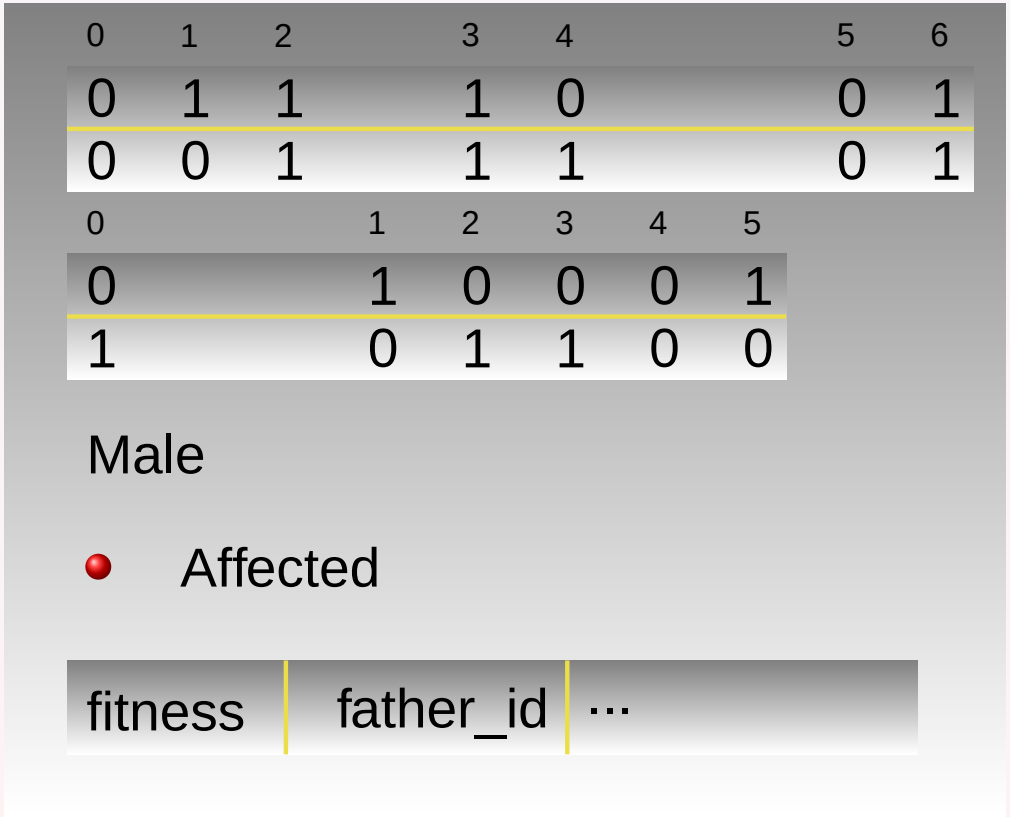
Structure of individual

Assume ploidy = 2, maxAllele = 1



Structure of individual

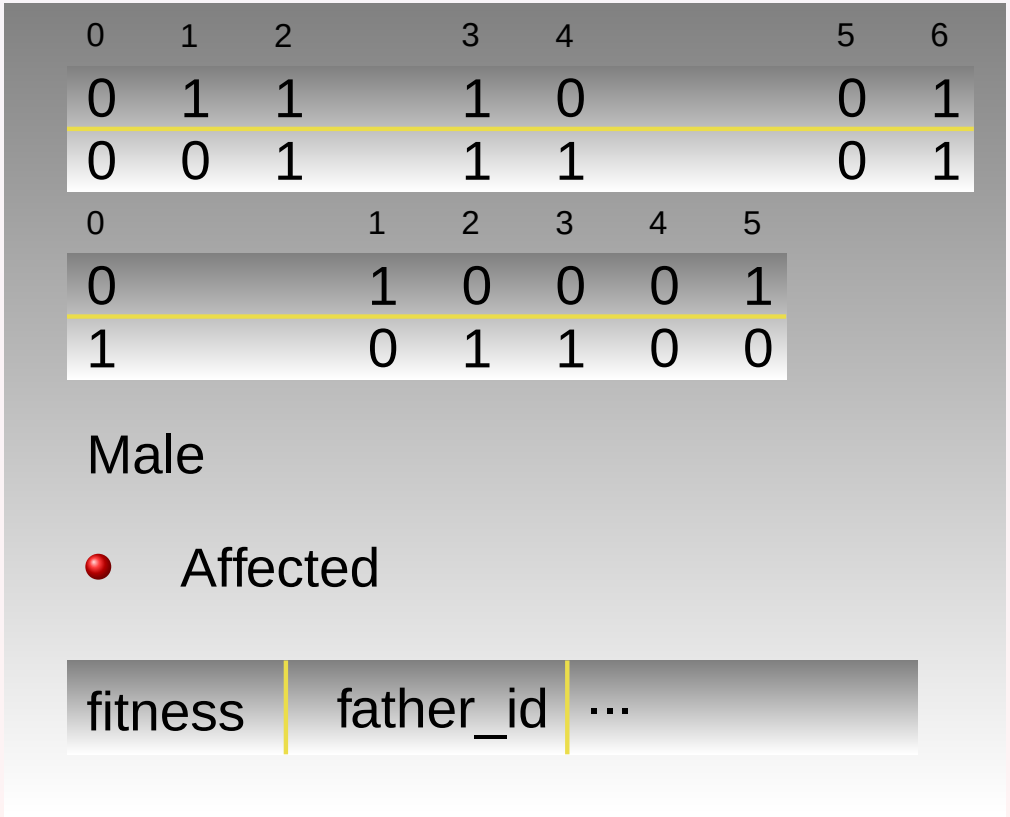
Assume ploidy = 2, maxAllele = 1



Chromosome 0

Structure of individual

Assume ploidy = 2, maxAllele = 1



Structure of individual

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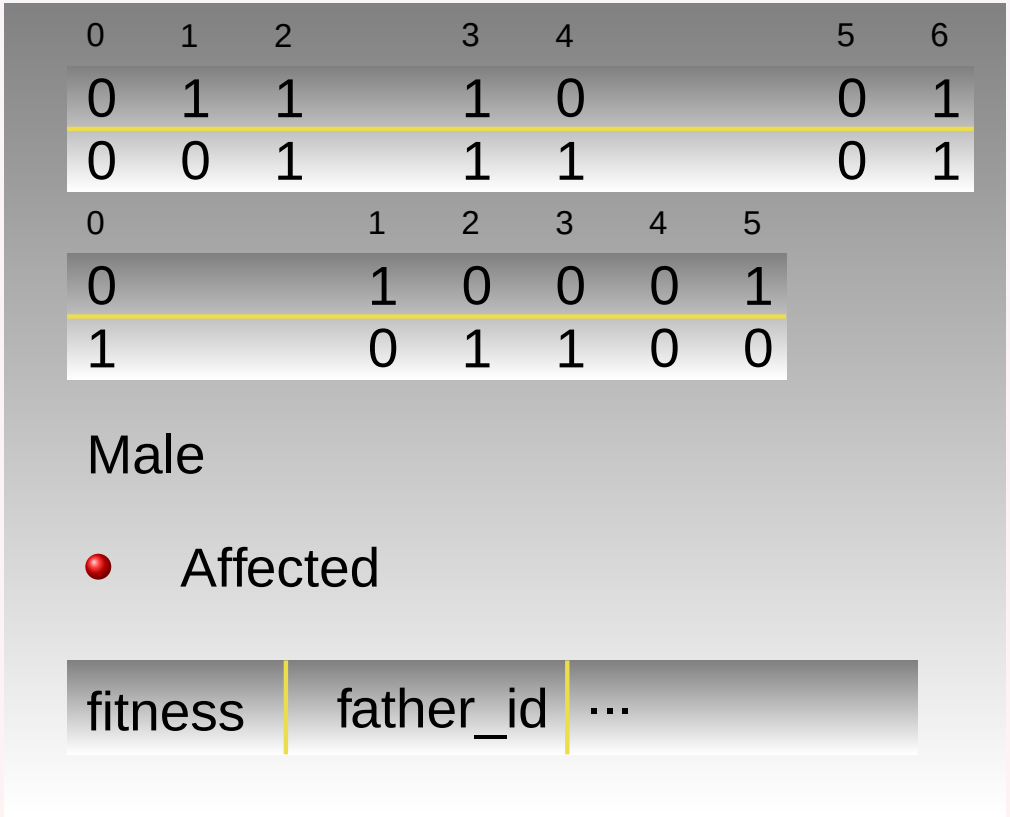
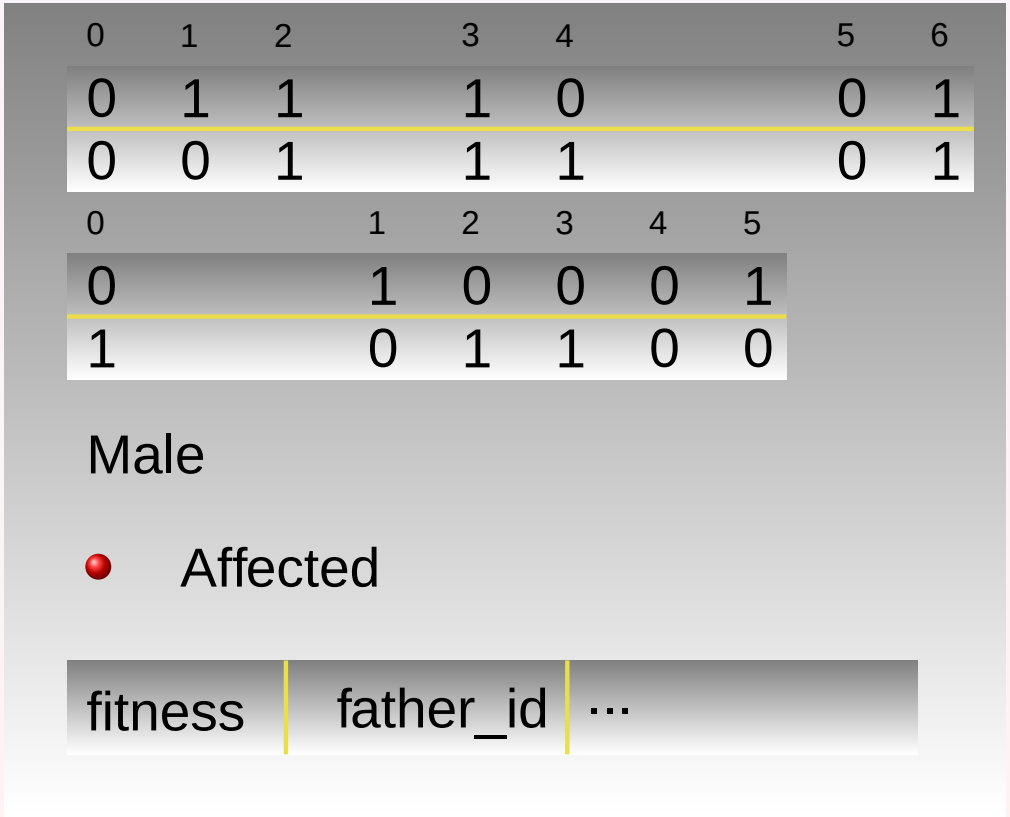


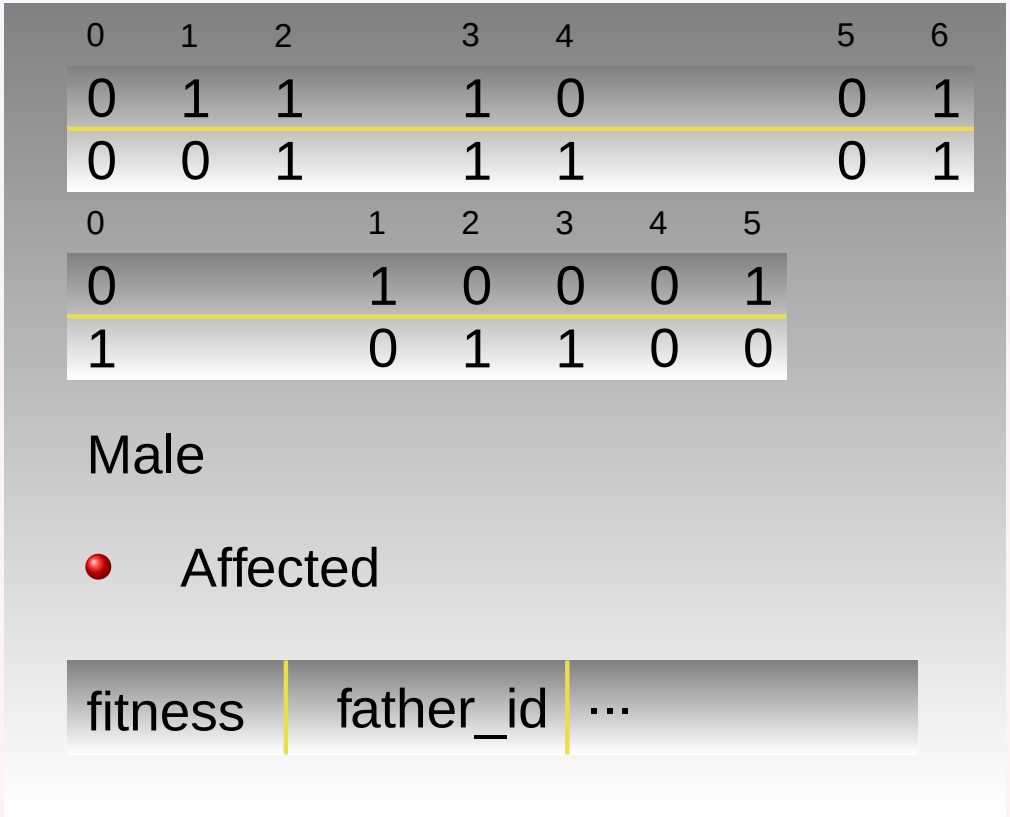
Structure of individual

Assume ploidy = 2, maxAllele = 1



Structure of individual

Assume ploidy = 2, maxAllele = 1



Individual


```
>>> pop =  population(subPop=[100, 200], loci=[2, 3])
>>> # the first individual
>>> ind1 = pop.individual(0)
>>> # the second individual in the second subpop
>>> ind2 = pop.individual(1, 1)
>>> # genotypic strcuture
>>> print ind1.numLoci(1)
3
>>> print ind1.numChrom()
2
>>> # an editable allele list
>>> alleles = ind1.arrGenotype(0)
>>> alleles[:] = range(ind1.totNumLoci())
>>> print ind1.arrGenotype(0)
[0, 1, 2, 3, 4]
>>> # ploidy 1, index 4
>>> ind1.setAllele(3, 4, 1)
>>> print ind1.allele(4, 1)
3
>>>
```

Information fields

Pieces of information that can be attached to each individual, e.g.

- `fitness:` fitness of each individual, calculated by selectors
- `father_idx, mother_idx`: index of parents in the parental generation
- `old_index:` index of an individual in the population where it is sampled

Or, self-defined

- birthday
- geographic location
- ...

Information fields


```
>>> pop = population(100, loci=[5, 8],
...     infoFields=['father_idx', 'mother_idx'])
>>> simu = simulator(pop, randomMating(numOffspring=2))
>>> simu.evolve(ops=[parentsTagger()], end=5)
True
>>> ind = simu.population(0).individual(0)
>>> ind1 = simu.population(0).individual(1)
>>> print ind.info('father_idx'), ind.info('mother_idx')
48.0 40.0
>>> print ind1.info('father_idx'), ind1.info('mother_idx')
48.0 40.0
>>>
>>>
```

Iterate through a population

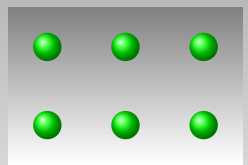

```
>>> pop = population(subPop=[5, 8], loci=[5],
...     infoFields=['penetrance'])
>>> InitByFreq(pop, [.6, .3, .1])
>>> MaPenetrance(pop, locus=2, penetrance=[0.05, 0.2, 0.5],
...     wildtype=[0], infoFields=['penetrance'])
>>> # iterate through all inviduals in subPop 1
>>> for ind in pop.individuals(1):
...     print 'Aff: %d Fit: %.3f Geno: %d %d' % \
...         (ind.affected(), ind.info('penetrance'), \
...         ind.allele(2, 0), ind.allele(2, 1))
...
Aff: 1 Fit: 0.200 Geno: 0 1
Aff: 0 Fit: 0.200 Geno: 0 2
Aff: 0 Fit: 0.200 Geno: 1 0
Aff: 0 Fit: 0.200 Geno: 1 0
Aff: 0 Fit: 0.200 Geno: 2 0
Aff: 0 Fit: 0.050 Geno: 0 0
Aff: 0 Fit: 0.050 Geno: 0 0
Aff: 0 Fit: 0.500 Geno: 1 1
>>>
```

Outline

4 Operator

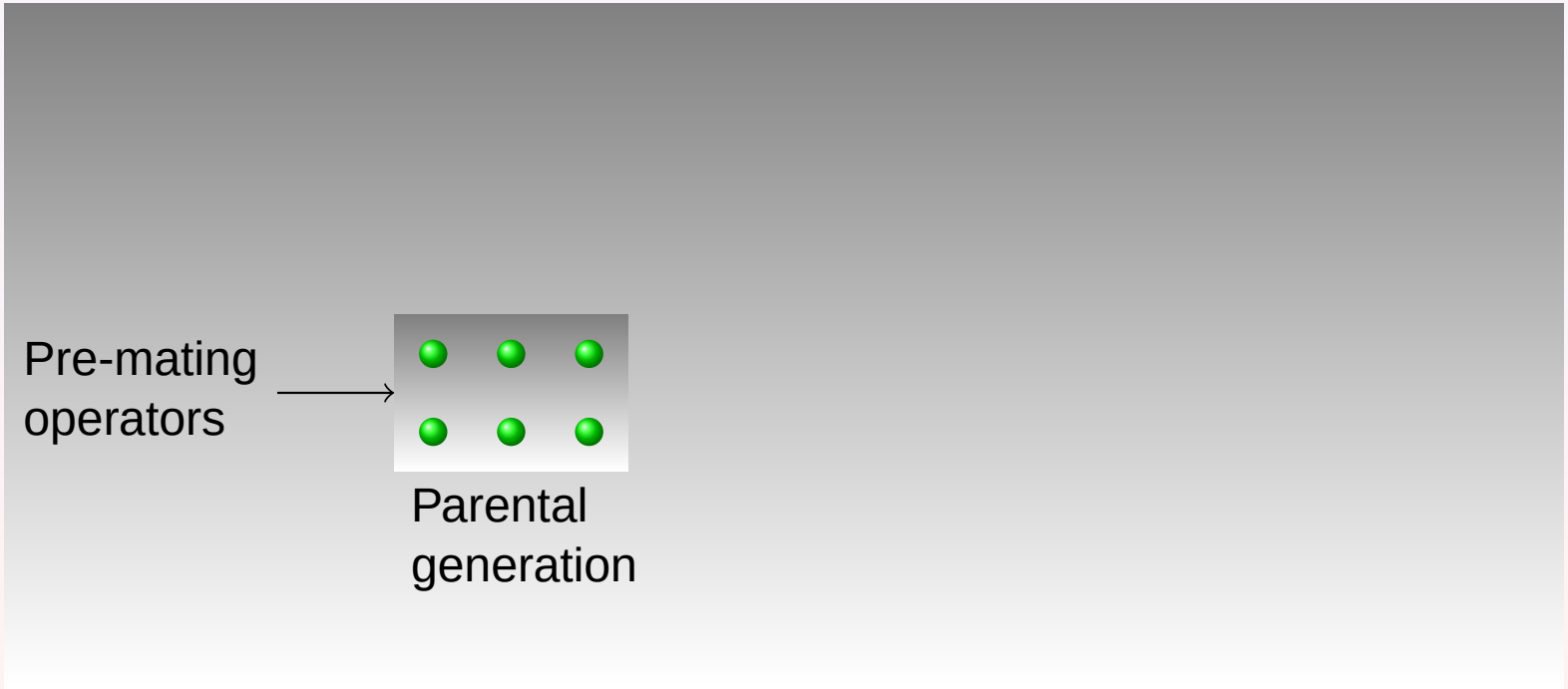
- Stage of an operator
- Applicable generations
- Replicate and replicate group
- Output
- Python Operators

Life cycle of a generation

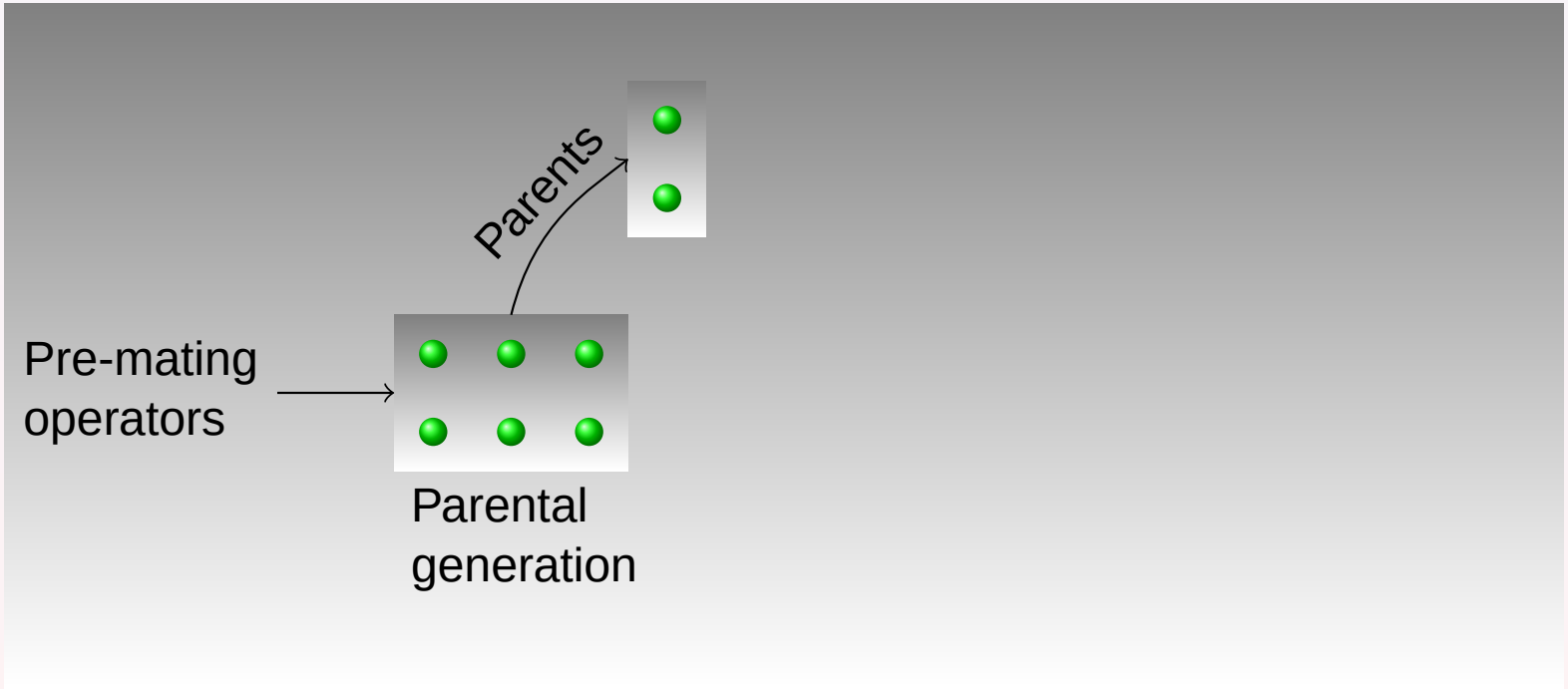


Parental generation

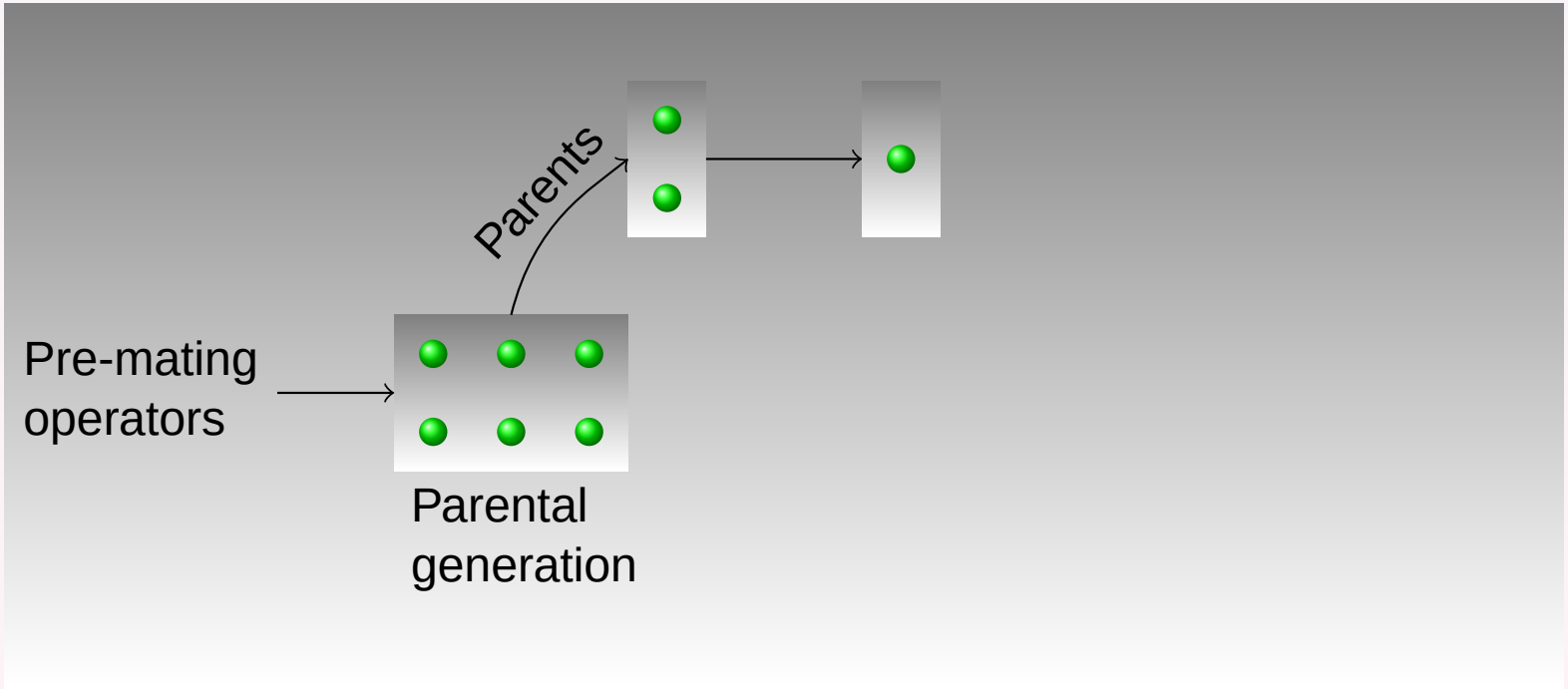
Life cycle of a generation



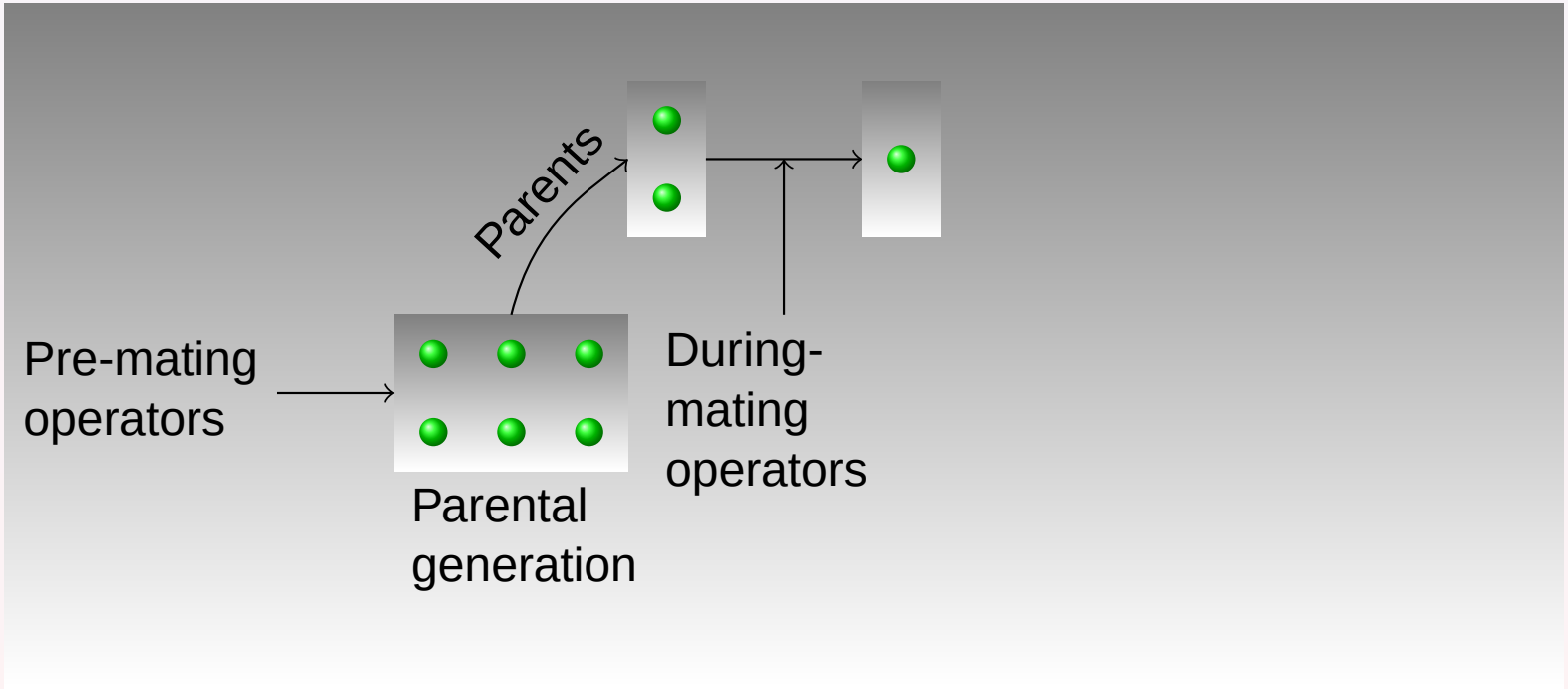
Life cycle of a generation



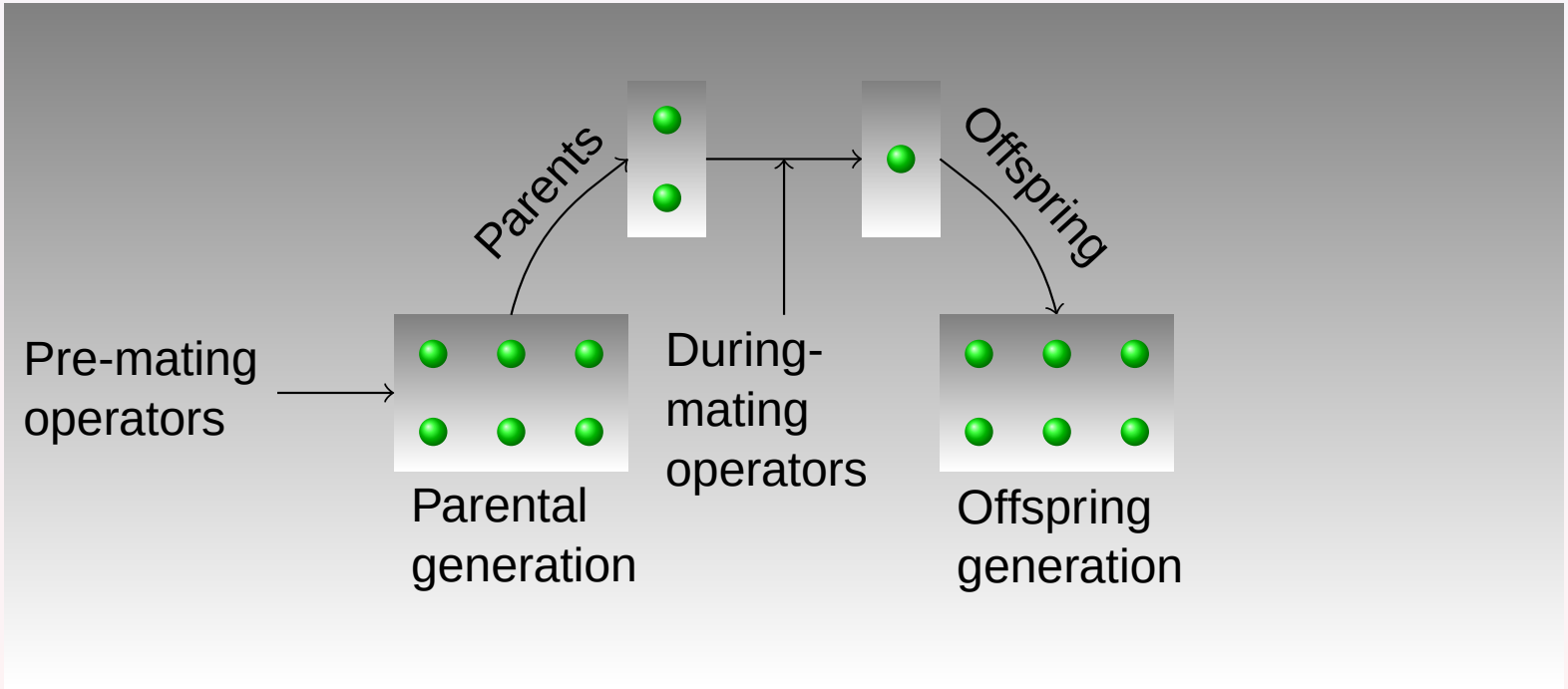
Life cycle of a generation



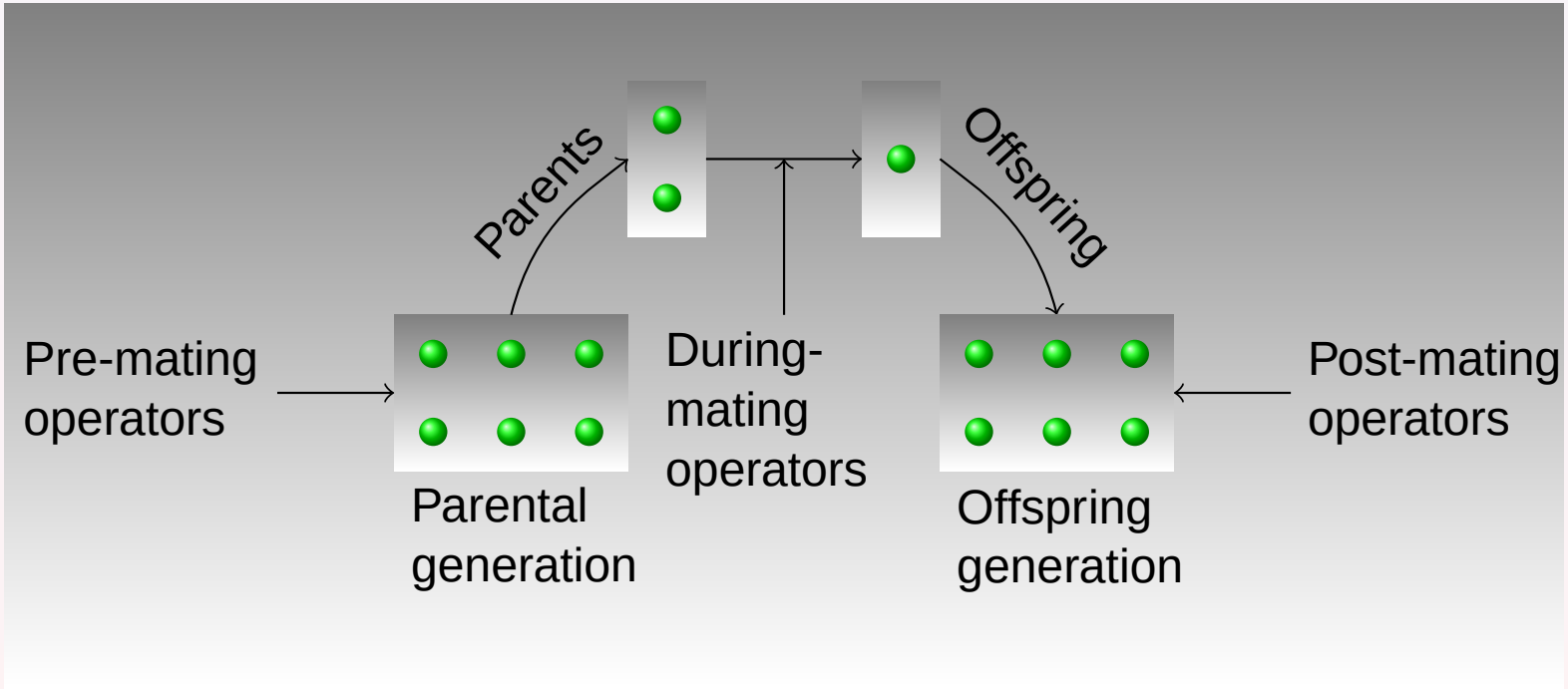
Life cycle of a generation



Life cycle of a generation



Life cycle of a generation



Pre-, During- and PostMating operators


```
>>> simu = simulator(
...     population(subPop=[20, 80], loci=[3]),
...     randomMating())
>>> simu.evolve(
...     preOps = [initByFreq([0.2, 0.8])],
...     ops = [
...         kamMutator(maxAllele=10, rate=0.00005, atLoci=[0,2]),
...         recombinator(rate=0.001),
...         dumper(stage=PrePostMating),
...         stat(alleleFreq=[1]),
...     ],
...     dryrun=True
... )
Dryrun mode: display calling sequence
Apply pre-evolution operators
  Replicate 0
      - <simuPOP::initByFreq> end at 1
Start evolution
  Replicate 0
    Pre-mating operators
      - <simuPOP::dumper> at all generations
    Start mating
      - <simuPOP::recombination> at all generations
    Apply post-mating operators
      - <simuPOP::k-allele model mutator K=10> at all generations
      - <simuPOP::dumper> at all generations
      - <simuPOP::statistics> at all generations
True
>>>
```

Applicable generations


```
>>> simu = simulator(
...     population(10000, loci=[3]),
...     randomMating())
>>> eval1 = r"'Gen: %3d  Freq: %f\n' % (gen, alleleFreq[1][0])"
>>> eval2 = r"'Last Gen: %3d  Freq: %s\n' % (gen, alleleFreq[1])"
>>> simu.evolve(
...     preOps = [initByFreq([0.3, 0.7])],
...     ops = [
...         recombinator(rate=0.01, begin=10, end=30),
...         stat(alleleFreq=[1], step=10),
...         pyEval(eval1, step=10),
...         pyEval(eval2, at=[-1])
...     ],
...     end = 50
... )
Gen:   0  Freq: 0.304200
Gen:  10  Freq: 0.290700
Gen:  20  Freq: 0.285300
Gen:  30  Freq: 0.288750
Gen:  40  Freq: 0.283750
Gen:  50  Freq: 0.284100
Last Gen:  50  Freq: [0.28410000000000002, 0.71589999999999998]
True
>>>
```

Applicable replicates


```
>>> simu = simulator(
...     population(100, loci=[3]),
...     randomMating(),
...     rep=5, grp=[1,1,2,2,2])
>>> simu.evolve(
...     preOps = [initByFreq([0.5, 0.5])],
...     ops = [
...         stat(alleleFreq=[1]),
...         recombinator(rate=0.01, grp=1),
...         recombinator(rate=0.01, grp=2),
...         pyEval(r"'%.2f ' % alleleFreq[1][0]", grp=1),
...         pyEval(r"'\n'", rep=REP_LAST),
...     ],
...     end=5
... )
0.47 0.52
0.49 0.56
0.51 0.60
0.52 0.62
0.56 0.60
0.52 0.62
True
>>>
```

Output


```
>>> simu = simulator(
...     population(100, loci=[3]),
...     randomMating(),
...     rep=5, grp=[1,1,2,2,2])
>>> simu.evolve(
...     preOps = [initByFreq([0.5, 0.5])],
...     ops = [
...         stat(alleleFreq=[1]),
...         pyEval(r"'%.2f ' % alleleFreq[1][0]",
...             output='>>out'),
...         pyEval(r"'\n'", rep=REP_LAST, output='>>out'),
...         pyEval(r"'%.2f ' % alleleFreq[1][0]",
...             outputExpr="'>>out%d' % grp"),
...     ],
...     end=2
... )
True
>>> print open('out').read()
0.56 0.55 0.46 0.47 0.54
0.56 0.55 0.42 0.55 0.57
0.58 0.56 0.40 0.57 0.56

>>> print open('out1').read()
0.56 0.55 0.56 0.55 0.58 0.56
>>> print open('out2').read()
0.46 0.47 0.54 0.42 0.55 0.57 0.40 0.57 0.56
>>>
```

Python operator

The most flexible operators that can perform any operation, but are less efficient.

The idea: user provide a function with specified input and output, simuPOP calls this function during evolution.

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

Python Individual operator

`func(ind [, genotype] [, param]), return True/False or an array`

- `ind`: individual
- `genotype`: if parameter loci is given, genotype at these loci are passed to the function
- `param`: if parameter param is given, param passed from simuPOP
- `return`: if parameter infoFields is given, assign return values to these information fields

Outline

5 Mating scheme

Mating schemes

Mating schemes

- Population offspring subpopulation from corresponding parental subpopulation
- Can change subpopulation size
- Select parents according to their `fitness` value (information field)
- Can produce more than one offspring

Demographic model


```
>>> def lin_inc(gen, oldsize=[]):
...     return [10+gen]*5
...
>>> simu = simulator(
...     population(subPop=lin_inc(1), loci=[1]),
...     randomMating(newSubPopSizeFunc=lin_inc)
... )
>>> simu.evolve(
...     ops = [
...         stat(popSize=True),
...         pyEval(r'"%d %d\n"%(gen, subPop[0]["popSize"])'),
...     ],
...     end=5
... )
0 10
1 11
2 12
3 13
4 14
5 15
True
>>>
```

Number of offspring


```
>>> simu = simulator(
...     population(size=10000, loci=[1]),
...     randomMating(),
... )
>>> simu.evolve(
...     preOps = [initByFreq([0.1, 0.9])],
...     ops = [ ], end=100
... )
True
>>> simu.setMatingScheme(randomMating(numOffspring=2))
>>> simu.addInfoFields(['father_idx', 'mother_idx'])
>>> simu.setAncestralDepth(1)
>>> simu.step(ops=[parentsTagger()])
True
>>> pop = simu.getPopulation(0)
>>> MaPenetrance(pop, locus=0, penetrance=[0.05, 0.1, 0.5])
>>> AffectedSibpairSample(pop, size=100)
[<simuPOP::population of size 200>]
>>>
```

Outline

6 Simulator

Simulator

A simulator manages

- Replicates of a population
- A mating scheme
- Many operators

and evolve the populations.