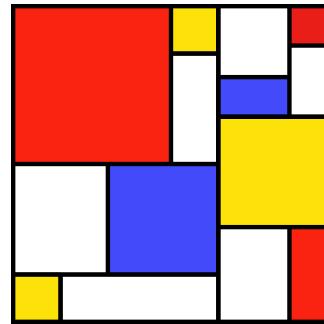


SLiM

Workshop Series



#1: Introduction to SLiM

SLiM Contributors



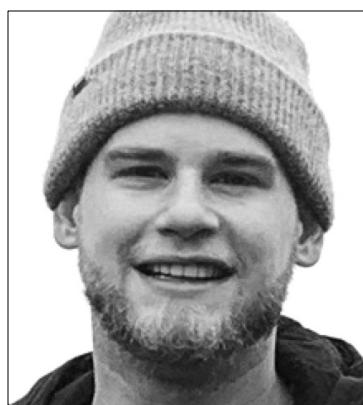
Benjamin C. Haller



Philipp W. Messer



Peter Ralph



Jared Galloway



Jerome Kelleher

SLiM Users

i.e., you!

Forward genetic simulation

• Simulate a population forward in time

• Create a pedigree tree

• Add mutations to the genome

• Calculate recombination rates

• Calculate mutation rates

• Calculate selection rates

• Calculate migration rates

• Calculate mutation rates

• Calculate recombination rates

• Calculate selection rates

• Calculate migration rates

• Calculate mutation rates

• Calculate recombination rates

• Calculate selection rates

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Forward genetic simulation

- “Forward”:
 - runs forward from an initial state
(vs. coalescent methods)

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 - explicit loci on a chromosome
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Forward genetic simulation

- “Forward”:
 - runs forward from an initial state
(vs. coalescent methods)
- “Genetic”:
 - explicit loci on a chromosome
(vs. phenotypic simulations)
- “Simulation”:
 - individual-based modeling
(vs. analytical modeling)

Why do simulations?

Why do simulations?

- Fitting **empirical** population genomic data
 - analyzing past evolutionary forces
 - predicting future evolution

Why do simulations?

- Fitting **empirical** population genomic data
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 - predicting future evolution
- Analyzing **theoretical** evolutionary models
 - predicting the consequences of a new theory
 - comparing multiple theories

Why do simulations?

- Fitting **empirical** population genomic data
 - analyzing past evolutionary forces
 - predicting future evolution
- Analyzing **theoretical** evolutionary models
 - predicting the consequences of a new theory
 - comparing multiple theories
- Developing **statistical** methods
 - testing a method's accuracy, bias, or power
 - generating datasets for machine learning

Why do *forward* simulations?

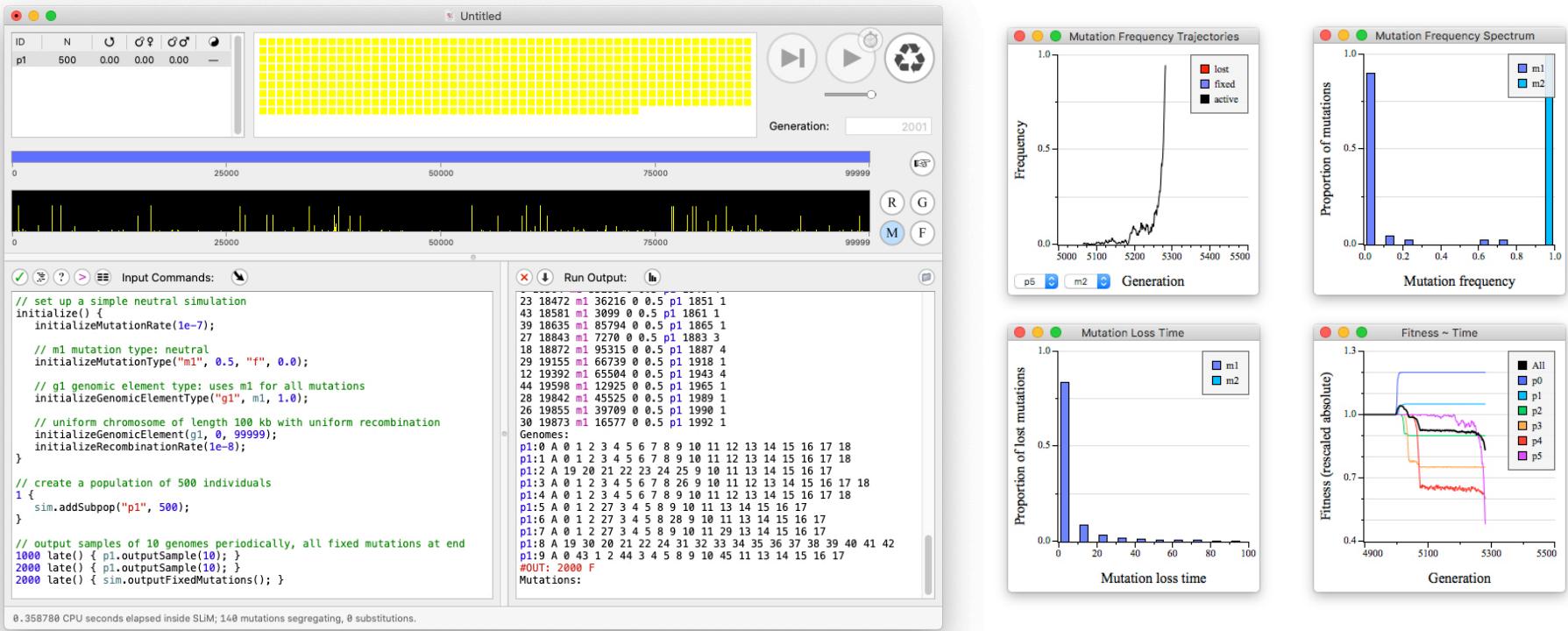
Why do *forward* simulations?

- **Evolution is complex:**
 - complex demography and population structure
 - non-random mating and complex mating systems
 - spatial structure and non-random dispersal
 - spatial and temporal variation in selection
 - frequency-dependent selection, kin selection, etc.
 - realistic genetic/chromosomal structure
 - epistasis, polygenic traits, pleiotropy
 - multiple loci under selection
 - variable recombination / mutation rate

Why use SLiM?

Why use SLiM?

- Interactive and graphical
 - easy to visualize / debug / explore



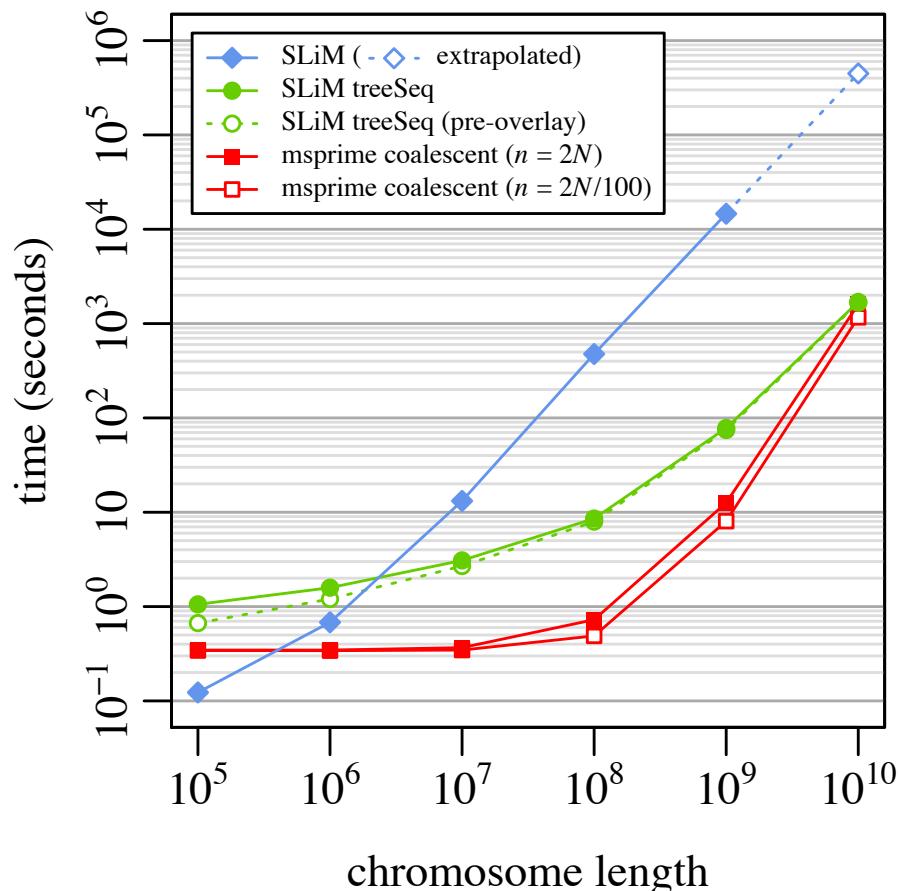
Why use SLiM?

- Flexible and customizable with Eidos
 - scriptability means there are (almost) no limits
 - similar to R in its syntax and function names
 - ends statements with semicolons; zero-based!

```
x = 0;  
for (i in 1:10)  
    x = x + i;  
print(x);
```

Why use SLiM?

- Very fast: SLiM is highly optimized



Why use SLiM?

- Open source on GitHub, GPL license
 - free, reusable, shareable, debugged, easy!



Free as in Freedom

How to use SLiM?

How to use SLiM?

- Do **initial modeling** in SLiMgui
 - interactive model development & visual debugging
 - syntax coloring, online docs, code completion

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 - trivial to build and run on a computing cluster
 - do many replicate runs simultaneously, one per core

How to use SLiM?

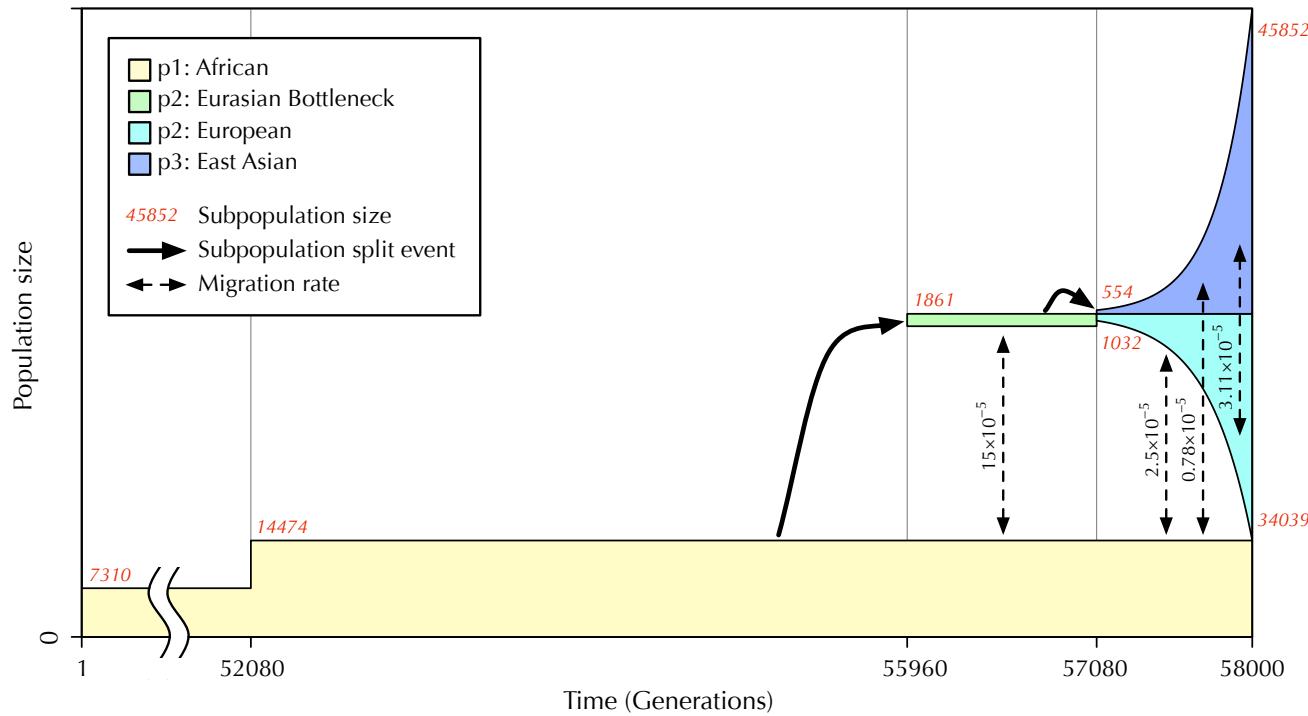
- Do **initial modeling** in SLiMgui
 - interactive model development & visual debugging
 - syntax coloring, online docs, code completion
- Do **production runs** on the cluster
 - trivial to build and run on a computing cluster
 - do many replicate runs simultaneously, one per core
- Do **post-run analysis** in Eidos, Python, or R
 - a lot of analysis can be done in-script in Eidos
 - .trees output can be read in Python with `pyslim`

SLiM Recipes



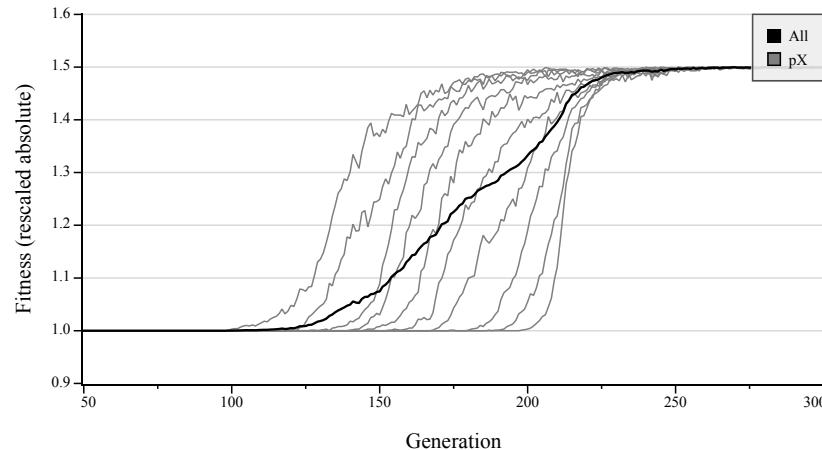
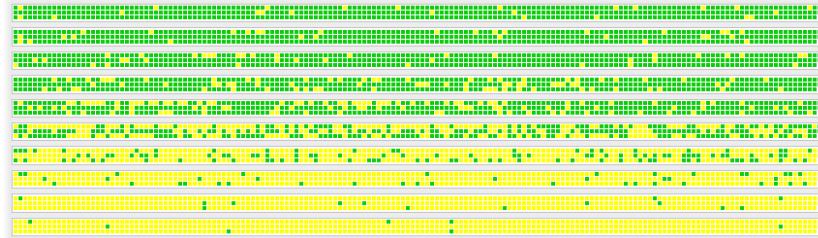
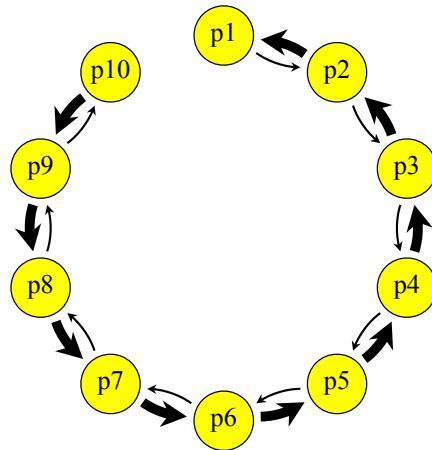
The Gravel model (5.4)

- Simulating human evolutionary history
- Demographic events, exponential growth



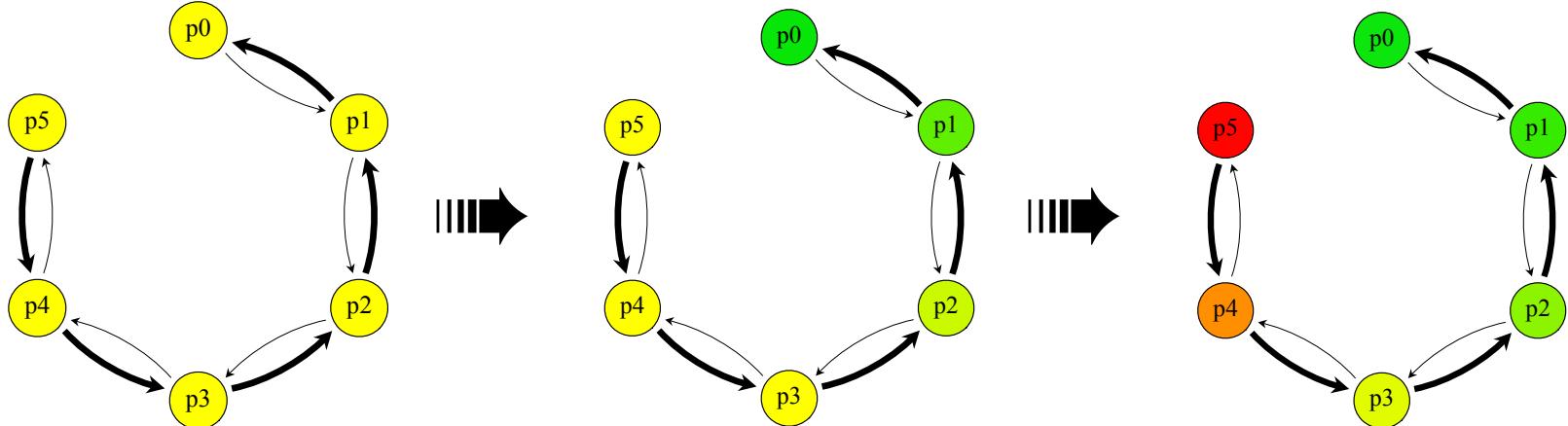
Introgression & sweeps (9.7)

- Introgression of a single introduced mutation
- Ten subpopulations connected by migration



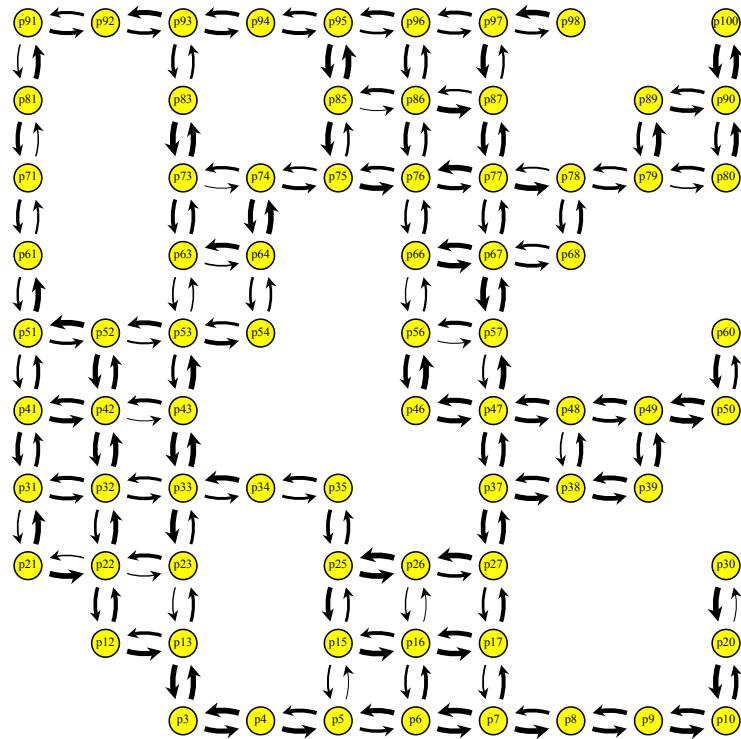
Gene drives (12.3)

- Simulating CRISPR gene drive
- Fixes despite negative fitness effects
- Fixes despite going against migration



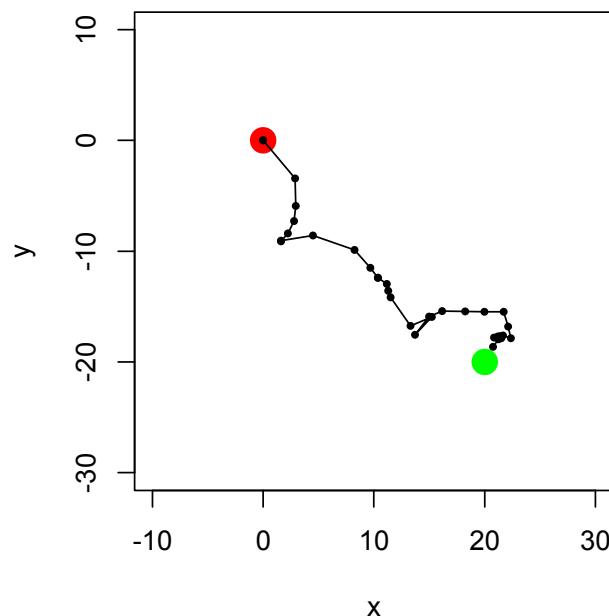
Metapopulations (5.3.4)

- Many subpopulations connected by migration
- The connection pattern can be spatial, or not



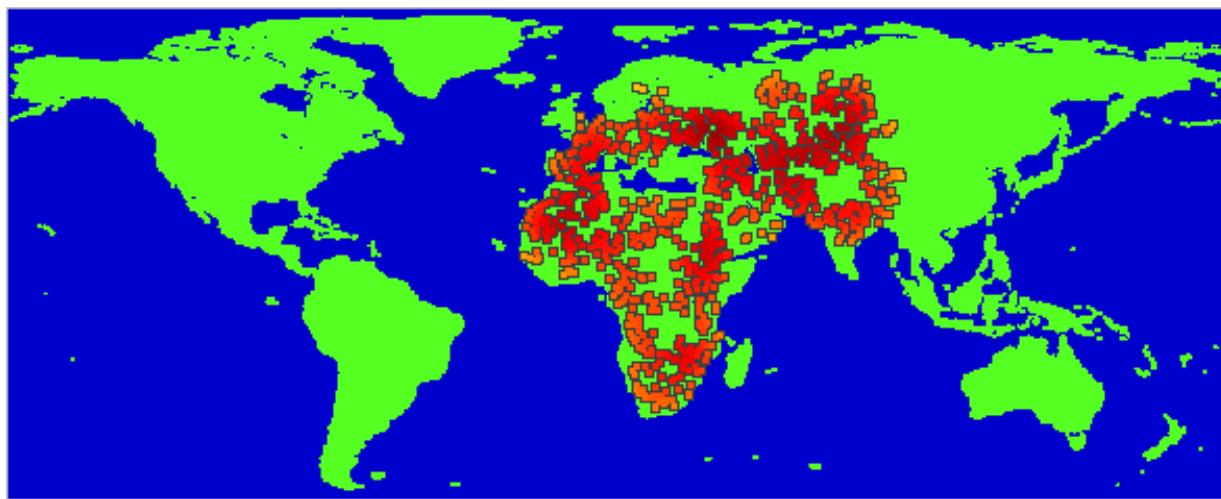
Adaptive walks (14.8)

- A QTL-based model with pleiotropy (M-matrix)
- Two phenotypic traits defined by additive QTLs
- Live plotting in R using `system()`



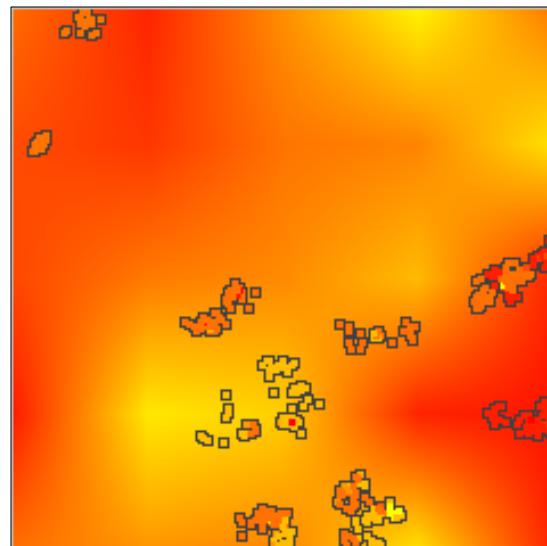
Continuous space (15.10)

- Individuals live in a continuous 2-D space
- A landscape map of the world is used
- Population expansion out of Africa



Local adaptation (15.11)

- Individuals live in a continuous 2-D space
- A map defines a heterogeneous environment
- Adaptation to the local environment results



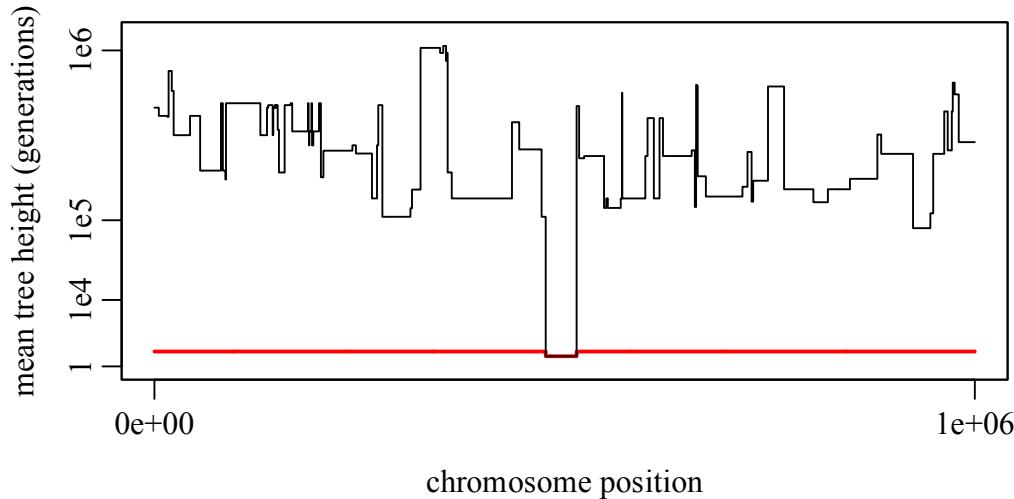
Nucleotide-based models (18.1)

- Track the nucleotide sequence of every genome
- Mutations have an associated nucleotide
- Mutation rates are sequence-dependent
- Realistic gene conversion, including gBGC

GAATGTCGGTTAGAGCAACCTAGCTTCTCAGATCGCAATA
GAATGTC~~C~~GTTAGAGCAACCTAGCTTCTCAGATGGCTATA
GAATGTC~~C~~GTTAGAGCAACCTAGCTTCTCAGATGCCATA
GAATGTCGGTTAGAGCATCCTAGCTTCTCAGATCGCAATA
GAATGTCGGTTAGAGCAACCTAGCTTCTCAGATCGCAATA
GAATGTC~~C~~GTTAGAGCAACCTAGCTTCTCAGATGGCAATA
GAATGTCGGTTAGAGCATCCTAGC~~C~~TCTCAGATGGCAATA
GAATGTCGGTTAGAGCA~~T~~CCTAGCTTCTCAGATCGCAATA

Tree sequences & ancestry (17.10)

- Tracking the ancestry tree at every position
- Mean tree height is a proxy for diversity at a site
- After a sweep, diversity is lowest near the sweep
- Recapitation constructs neutral burn-in history



Workshop Plan

- Introductory models:
 - Introduction
 - Chromosome hierarchy
 - Population hierarchy
 - Eidos overview
 - Demography
 - Recombination

Workshop Plan

- Intermediate models:
 - Selective sweeps
 - Callbacks I: `fitness()`
 - Callbacks II: `mateChoice()`
 - Callbacks III: `modifyChild()`
 - Quantitative traits
 - Live plotting in R

Workshop Plan

- Advanced models:
 - non-Wright–Fisher models
 - Modeling haploidy
 - Continuous space I
 - Continuous space II
 - Nucleotide-based models
 - Tree-sequence recording

Workshop Plan

- Format:
 - short lecture, then exercise
- Extras:
 - informal explorations
 - self-guided modeling time
 - possibly presentations by you
 - if you have developed your own SLiM model
 - if you want to research a particular SLiM topic

Resources

messerlab.org/slim/



SLIM 3: Forward Genetic Simulations Beyond the Wright–Fisher Model

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Associate editor: Ryan Hernandez

Abstract

With the desire to model population genetic processes under increasingly realistic scenarios, forward genetic simulations have become a critical part of the toolbox of modern evolutionary biology. The SLIM forward genetic simulation framework has been used to model a wide variety of scenarios in plants and animals. However, its focus is on the Wright–Fisher model, and it has been found to pose an obstacle to implementing many types of models; it is difficult to adapt the Wright–Fisher model, with its many assumptions, to modeling ecologically realistic scenarios such as explicit space, overlapping generations, individual variation in reproduction, density-dependent population regulation, individual variation in dispersal or migration, local extinction and recolonization, mating between subpopulations, age structure, fitness-based survival and hard selection, emergent sex ratios, and so forth. In response to this need, we here introduce SLIM 3, which contains two key innovations. First, it is designed at establishing these limitations. Second, the new non-Wright–Fisher model is highly modular, making it much more flexible and amenable to the implementation of all the above scenarios and many more. Second, SLIM 3 adds support for continuous space, including spatial interactions and spatial maps of environmental variables. We provide a conceptual overview of these new features, and present several example models to illustrate their use.

Key words: eco-evolutionary dynamics, whole-population modeling, tree sequence recording, spatial population dynamics, landscape modeling, genealogy simulation.

Introduction

Forward genetic simulations are playing an increasingly important role in evolutionary biology. They are used to model a wide range of population genetic mechanisms and include a high level of ecological detail in the simulated scenario (Carvalho-Rodriguez 2010; Yuan et al. 2012; Bank et al. 2014; Hoban 2014; Thornton 2014; Haller and Messer 2017). Haller et al. (2017) have developed a graphical user interface for SLIM (Haller 2013; Haller and Messer 2016), which has proved to be a powerful tool for this purpose, and constitutes one of the most widely used computational frameworks for implementing such simulations at the present time.

The National Cancer Institute's Genome Simulation Resource (CSR) was the predecessor of the comprehensive database of genetic simulation software tools (NCI 2018). At the time of writing, the CSR listed 42 packages supporting forward simulation; this includes many tools that are specialized for a particular type of model, as well as tools that support a wide range of evolutionary scenarios. SLIM's popularity among these tools is likely to be due to its ease of use. First, it is highly scriptable, allowing the mechanics of the SLIM framework to be fundamentally modified and extended in many ways. At the same time, even fairly sophisticated evolutionary models can often be expressed in a page of code or less, since all of the core simulation code is provided by SLIM, yielding tremendous benefits compared with writing

simulations from scratch in a language such as C++.

Second, SLIM includes a full-featured graphical modeling environment, SLIMgui, that makes interactive model development, visualization, and hands-on exploration easy, with large benefits throughout the modeling process (Grimm 2002).

And third, a great deal of work has been devoted to making SLIM easy to learn and use. In addition to a wide variety of simulation scenarios, these great benefits are inherited for free by any model running within SLIM. The CSR does not provide performance comparisons, so users with performance concerns should run their own tests before settling upon a particular package; for comparing the features available in different packages, however, the GSR can be a very helpful resource.

In our contact with users of SLIM over the past years, one category of questions has predominated: how can SLIM simulations be constructed that go beyond the standard Wright–Fisher or “WF” model (Wright 1931)? This model, which has provided the conceptual foundation for all previous versions of SLIM (Messer 2010; Haller and Messer 2017), is defined by a number of simplifying assumptions. For example, the model assumes that generations are nonoverlapping and discrete, without any age structure or age-based differentiation among individuals. Another critical assumption of the model lies in the rules governing the generation of offspring from the parental populations in the

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RESOURCE ARTICLE

WILEY MOLECULAR ECOLOGY RESOURCES

Tree-sequence recording in SLIM opens new horizons for forward-time simulation of whole genomes

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1 | INTRODUCTION

Forward simulations are increasingly important in population genetics and evolutionary biology. For example, they can be useful for modeling the expected evolutionary dynamics of real-world systems

(*Joint senior authors)

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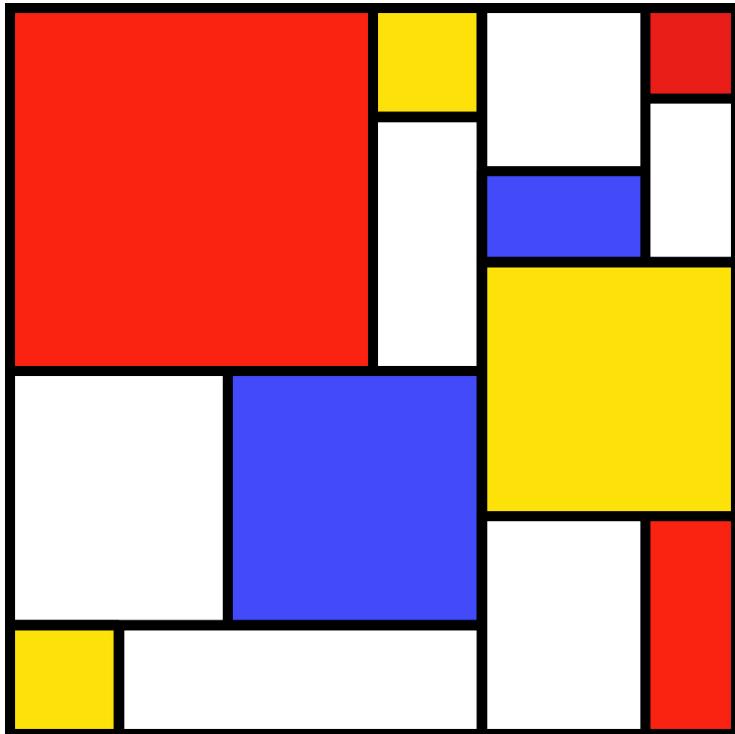
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SLiM Workshop Exercise #1