How to Study Evolution Using Scientific Python

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PyCon Israel 2016

Encyclopædia Britannica Online

Who I am

- PhD in **Evolutionary Theory** at TAU
- Using Python since 2002
- Using **Scientific Python** since 2011
- Teaching Python since 2011
- Python training for engineers & scientists

Why Scientific Python

(why not MATLAB?)

Python is…

- **Free as in beer**
- **Free as in speech**
- **General purpose**
- **Large, diverse, active community**
- Beautiful design
- Portable
- Easy to learn, fast to develop
- Fast enough
- Many libraries

I used Matlab. Now I use Python. by Steve Tjoa

Why use Python for scientific computing?

Introduction to Python for MATLAB users

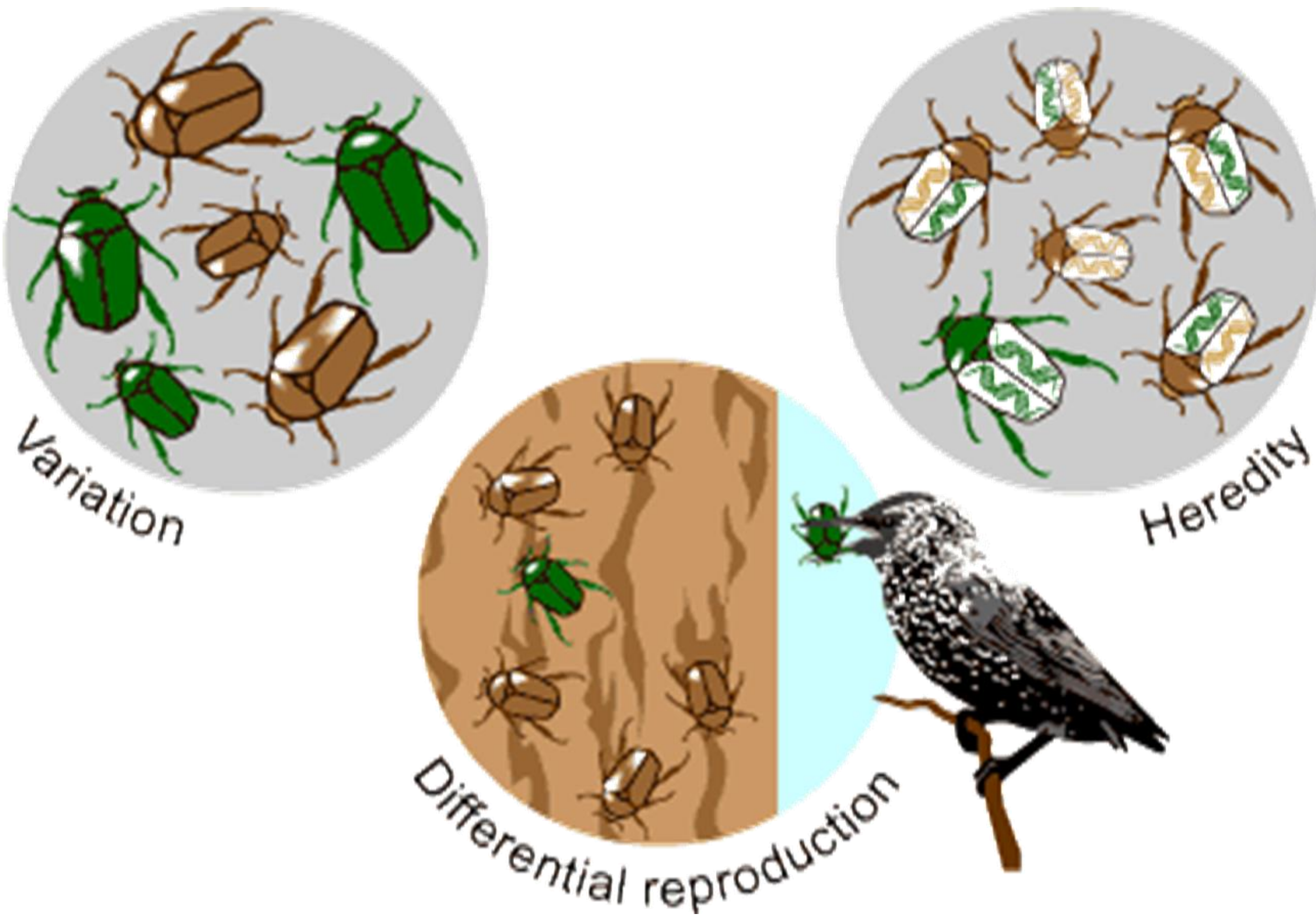
Theoretical Evolution

Formally: **Population genetics**

- Study **changes in frequency** of gene variants within populations
- The four forces of evolution:
  - **Natural selection**
  - **Random genetic drift**
  - Gene flow & recombination
  - Mutation
- Focus on **adaptation**, speciation, population subdivision, and population structure

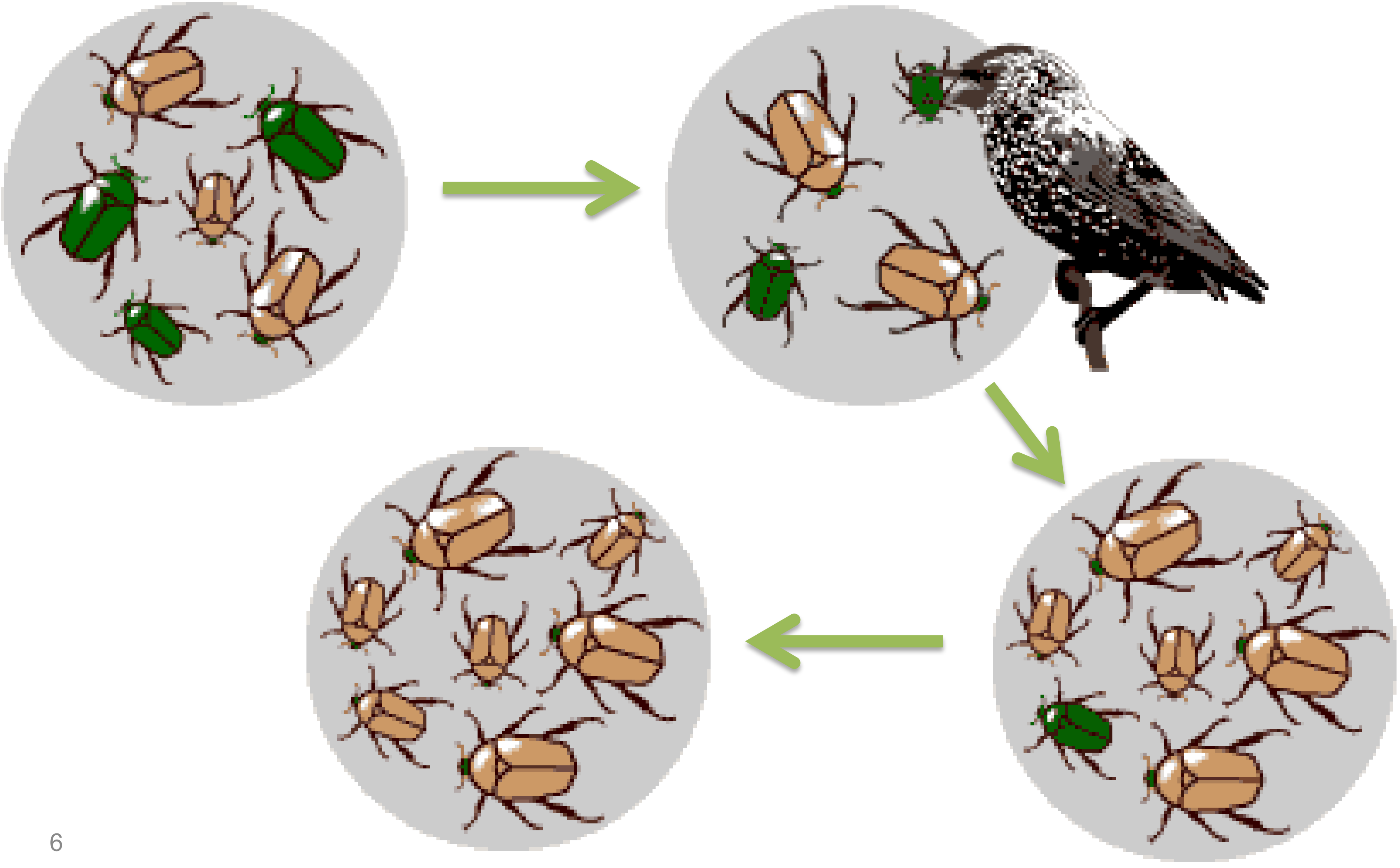
Population genetics

Evolution

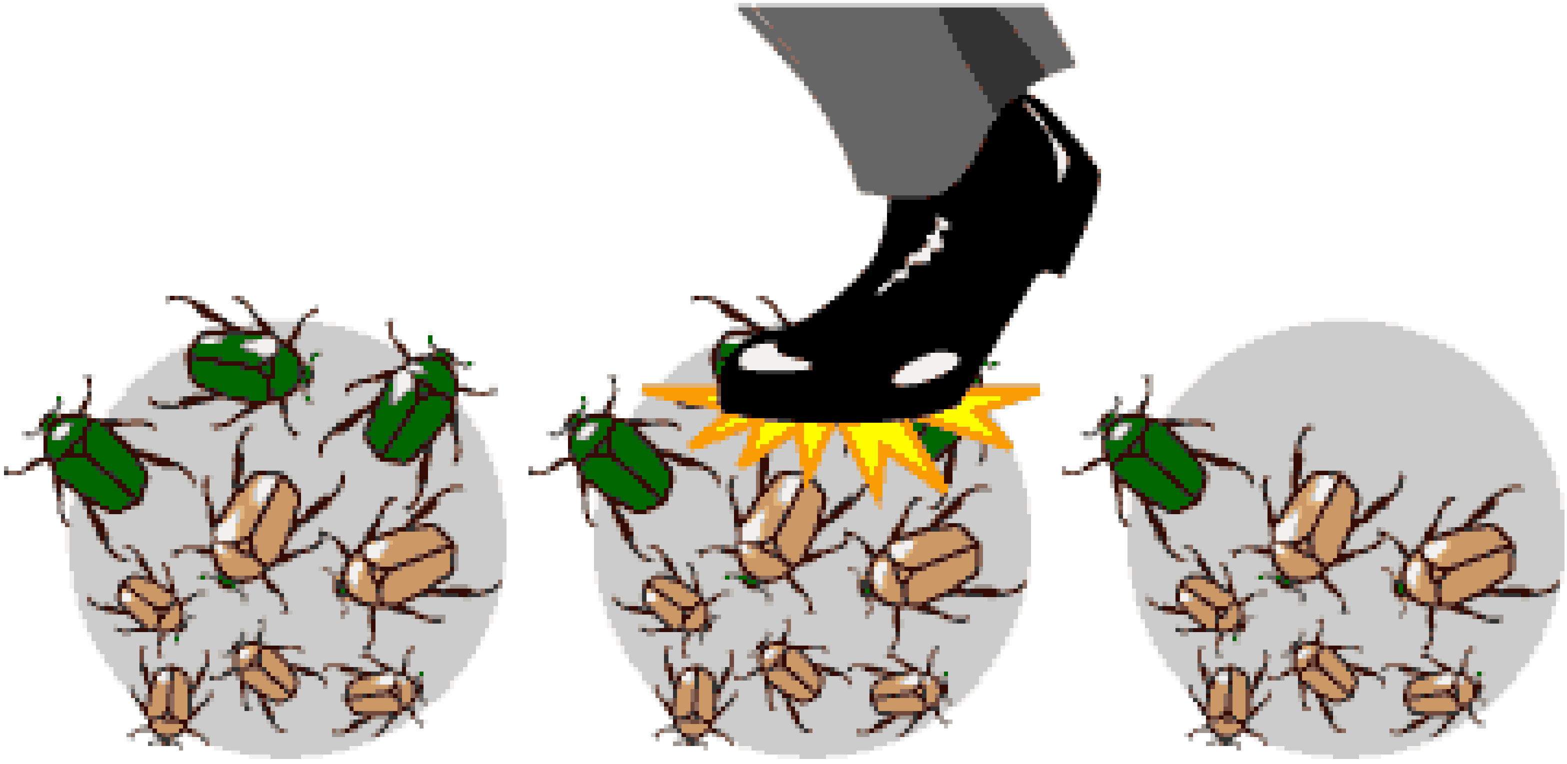


University of California Museum of Paleontology's Understanding Evolution

Natural Selection

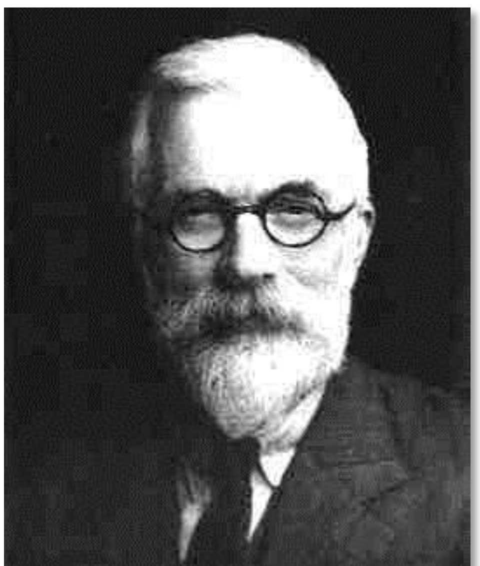


Random Genetic Drift



The Wright-Fisher Model

Standard model for change in frequency of gene variants.



R.A. Fisher
1890-1962, UK & Australia

Sewall Wright
1889-1988, USA

The Wright-Fisher Model

Standard model for change in frequency of gene variants.

Two gene variants: **0** and **1**.

Number of individuals with each variant is $\mathbf{n_0}$ and $\mathbf{n_1}$.

Total population size is $\mathbf{N = n_0 + n_1}$.

Frequency of each variant is $\mathbf{p_0 = n_0/N}$ and $\mathbf{p_1 = n_1/N}$.

The Wright-Fisher Model

Assume that variant **1** is **favored by selection** due to better survival or reproduction.

The frequency of variant **1** after the effect of selection natural (**p_1**) is:

$$p_1 = \frac{n_1 \cdot (1 + s)}{n_0 + n_1 \cdot (1 + s)}$$

s is a selection coefficient, representing **how much variant 1 is favored over variant 0.**

The Wright-Fisher Model

Random genetic drift accounts for the effect of **random sampling**.

Due to genetic drift, the number of individuals with variant **1** in the next generation (**n'_1**) is:

$$\mathrm{n}'_1 \sim \mathrm{Binomial}(\mathrm{N}, \mathrm{p}_1)$$

The **Binomial distribution** is the distribution of the number of successes in **N** independent trials with probability of success **p_1**.

Fixation Probability

Assume a single copy variant **1** in a population of size **N**.

What is the probability that variant **1** will **fix rather than go extinct**?

NumPy

The fundamental package for **scientific computing with Python**:

- Powerful N-dimensional array object
- Sophisticated (broadcasting) functions
- **Random number generators**
- Tools for integrating C/C++ and Fortran code
- Linear algebra
- Fourier transform

numpy.org

Into the code

Death to the Stock Photo

Natural Selection

$$p_1 = \frac{n_1 \cdot (1+s)}{n_0 + n_1 \cdot (1+s)}$$

Random drift

$$n_1' \sim \mathrm{Binomial}(N, p_1)$$

```
from numpy.random import binomial
n1 = 1

while 0 < n1 < N:
  n0 = N - n1
  p1 = n1*(1+s) / (n0 + n1*(1+s))
  n1 = binomial(N, p1)

fixation = n1 == N
```

Import a binomial random number generator from NumPy

Natural Selection

$$p_1 = \frac{n_1 \cdot (1+s)}{n_0 + n_1 \cdot (1+s)}$$

Random drift

$$n_1' \sim \text{Binomial}(N, p_1)$$

```
from numpy.random import binomial
n1 = 1

while 0 < n1 < N:
  n0 = N - n1
  p1 = n1*(1+s) / (n0 + n1*(1+s))
  n1 = binomial(N, p1)

fixation = n1 == N
```

Start with a single copy of variant 1

Natural Selection

$$p_1 = \frac{n_1 \cdot (1+s)}{n_0 + n_1 \cdot (1+s)}$$

Random drift

$$n_1' \sim \text{Binomial}(N, p_1)$$

```
from numpy.random import binomial
n1 = 1

while 0 < n1 < N:
  n0 = N - n1
  p1 = n1*(1+s) / (n0 + n1*(1+s))
  n1 = binomial(N, p1)


fixation = n1 == N
```

Until number of individuals with variant 1 is 0 or N: extinction or fixation

Natural Selection

$$p_1 = \frac{n_1 \cdot (1+s)}{n_0 + n_1 \cdot (1+s)}$$

Random drift

$$n_1' \sim \text{Binomial}(N, p_1)$$

```
from numpy.random import binomial
n1 = 1

while 0 < n1 < N:
  n0 = N - n1
  p1 = n1*(1+s) / (n0 + n1*(1+s))
  n1 = binomial(N, p1)

fixation = n1 == N
```

The frequency of variant 1 after selection is p1

Natural Selection

$$p_1 = \frac{n_1 \cdot (1 + s)}{n_0 + n_1 \cdot (1 + s)}$$

Random drift

$$n_1' \sim \mathrm{Binomial}(N, p_1)$$

```python
from numpy.random import binomial
n1 = 1

while 0 < n1 < N:
    n0 = N - n1
    p1 = n1*(1+s) / (n0 + n1*(1+s))
    n1 = binomial(N, p1)

fixation = n1 == N
```

Due to genetic drift, the number of individuals with variant 1 **in the next generation is** n1

Natural Selection

$$p_1 = \frac{n_1 \cdot (1+s)}{n_0 + n_1 \cdot (1+s)}$$

Random drift

$$n_1' \sim \mathrm{Binomial}(N, p_1)$$

```
from numpy.random import binomial
n1 = 1
```

Fixation: n1 **equals** N
Extinction: n1 **equals** 0

```
while 0 < n1 < N:
  n0 = N - n1
  p1 = n1*(1+s) / (n0 + n1*(1+s))
  n1 = binomial(N, p1)

fixation = n1 == N
```

NumPy vs. Pure Python

Here, **NumPy** is useful for random number generation:

```
n1 = binomial(N, p1)
```

Pure Python version would replace this with:

```
from random import random
rands = (random() for _ in range(N))
n1 = sum(1
         for r in rands
         if r < p1)
```

`random` is a standard library module

NumPy vs. Pure Python

```
%timeit simulation(N=1000, s=0.1)
%timeit simulation(N=1000000, s=0.01)
```

Pure Python version:
100 loops, best of 3: **6.42 ms** per loop
1 loop, best of 3: **528 ms** per loop

NumPy version:
10000 loops, best of 3: **150 µs** per loop **x42 faster**
1000 loops, best of 3: **313 µs** per loop

x1680 faster!


Can we do it
~~better~~ **faster**?
Malene Thyssen

Cython

- **Optimizing compiler**
- Makes **writing C extensions** for Python as easy as Python itself
- Declare the **static type** of variables
- Foreign function interface for invoking C/C++ routines

http://cython.org

```
def simulation(np.uint64_t N,
               np.float64_t s):
    cdef np.uint64_t n1 = 1
    cdef np.uint64_t n0
    cdef np.float64_t p

    while 0 < n1 < N:
        n0 = N - n1
        p1 = n1 * (1 + s) / (n0 + n1 * (1 + s))
        n1 = np.random.binomial(N, p1)

    return n1 == N
```

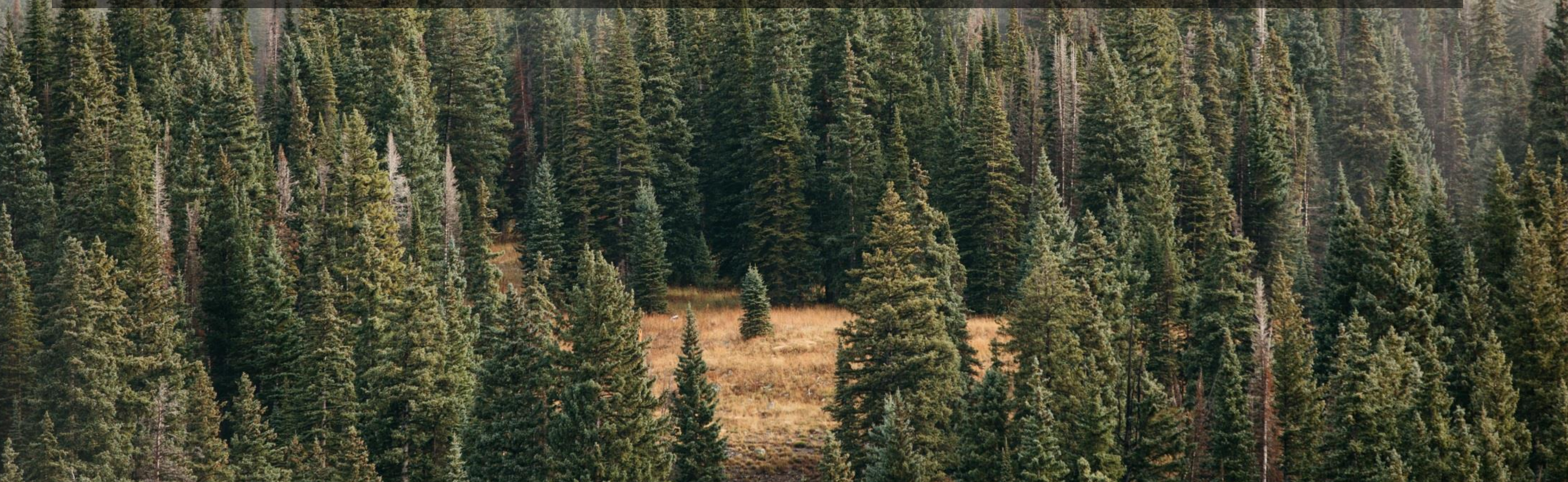
```
%timeit simulation(N=1000, s=0.1)
%timeit simulation(N=1000000, s=0.01)
```

Cython vs. NumPy:

10000 loops, best of 3: **87.8 µs** per loop **x2 faster**

10000 loops, best of 3: **177 µs** per loop **x1.75 faster**

To approximate the fixation probability we need to run **many simulations**. Thousands.



In principle, the standard error of our approximation decreases with the square root of the number of simulations: $\mathrm{SEM} \sim 1/\sqrt{m}$

Death to the Stock Photo

Multiple simulations: `for` loop

```
fixations = [
    simulation(N, s)
    for _ in range(1000)
]
sum(fixations) / len(fixations)
```

> 0.195

Multiple simulations: `for` loop

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fixations = [
    simulation(N, s)
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Multiple simulations: `for` loop

```
fixations = [
    simulation(N, s)
    for _ in range(1000)
]
sum(fixations) / len(fixations)
```

> 0.195

```
%timeit [simulation(…) for … range(1000)]
```

1 loop, best of 3: **8.05 s** per loop

Multiple simulations: NumPy

```
def simulation(N, s, repetitions):
    n1 = np.ones(repetitions)
    update = np.array([True] * repetitions)

    while update.any():
        p1 = n1 * (1 + s) / (N + n1 * s)
        n1[update] = binomial(N, p1[update])
        update = (n1 > 0) & (n1 < N)

    return n1 == N
```

Initialize multiple simulations

Multiple simulations: NumPy

```
def simulation(N, s, repetitions):
  n1 = np.ones(repetitions)
  update = np.array([True] * repetitions)

  while update.any():
    p1 = n1 * (1 + s) / (N + n1 * s)
    n1[update] = binomial(N, p1[update])
    update = (n1 > 0) & (n1 < N)

  return n1 == N
```

Natural selection:
`n1` **is an array so operations are element-wise**

Multiple simulations: NumPy

```
def simulation(N, s, repetitions):
  n1 = np.ones(repetitions)
  update = np.array([True] * repetitions)

  while update.any():
    p1 = n1 * (1 + s) / (N + n1 * s)
    n1[update] = binomial(N, p1[update])
    update = (n1 > 0) & (n1 < N)

  return n1 == N
```

Genetic drift:
`p1` **is an array so** `binomial(N, p1)` **draws from multiple distributions**

Multiple simulations: NumPy

```
def simulation(N, s, repetitions):
  n1 = np.ones(repetitions)
  update = np.array([True] * repetitions)

  while update.any():
    p1 = n1 * (1 + s) / (N + n1 * s)
    n1[update] = binomial(N, p1[update])
    update = (n1 > 0) & (n1 < N)

  return n1 == N
```

`update` **follows the simulations that didn't finish yet**

Multiple simulations: NumPy

```
def simulation(N, s, repetitions):
  n1 = np.ones(repetitions)
  update = np.array([True] * repetitions)

  while update.any():
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    n1[update] = binomial(N, p1[update])
    update = (n1 > 0) & (n1 < N)

  return n1 == N
```

`update` **follows the simulations that didn't finish yet**

Multiple simulations: NumPy

```
def simulation(N, s, repetitions):
  n1 = np.ones(repetitions)
  update = np.array([True] * repetitions)

  while update.any():
    p1 = n1 * (1 + s) / (N + n1 * s)
    n1[update] = binomial(N, p1[update])
    update = (n1 > 0) & (n1 < N)

  return n1 == N
```

`result` **is array of Booleans: for each simulation, did variant** `1` **fix?**

Multiple simulations: NumPy

```
%timeit simulation(N=1000, s=0.1)
```

10 loops, best of 3: **25.2 ms** per loop

x320 faster

Fixation probability as a function of N

```
Nrange = np.logspace(1, 6, 20,
                     dtype=np.uint64)
```

N must be an **integer** for this to evaluate to `True`:

```
(n1 > 0) & (n1 < N)
```

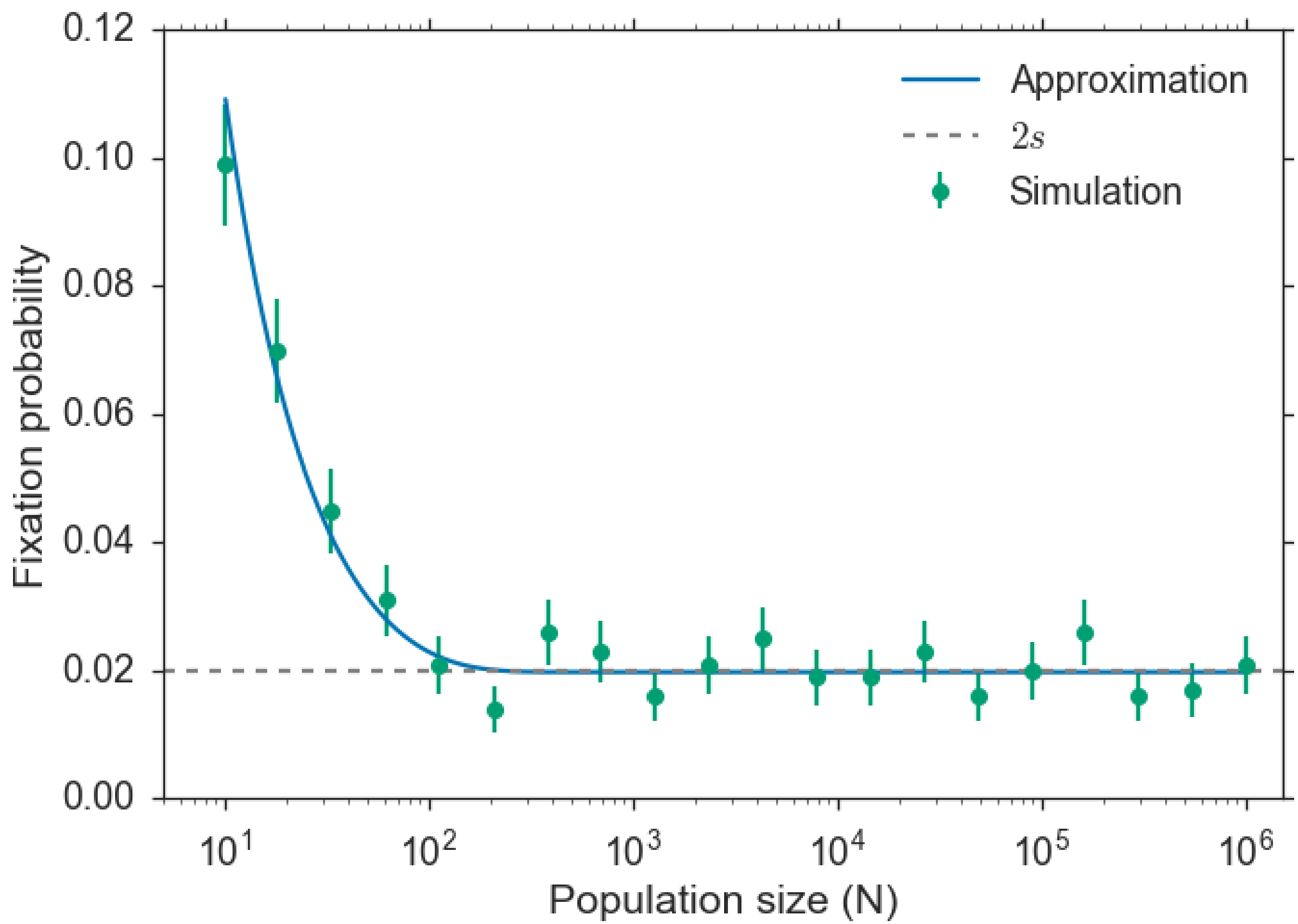
Fixation probability as a function of N

```
fixations = [
    simulation(
        N,
        s,
        repetitions
    ) for N in Nrange
]
```

Fixation probability as a function of N

```python
fixations = np.array(fixations)
mean = fixations.mean(axis=1)
sem = fixations.std(
    axis=1,
    ddof=1
) / np.sqrt(repetitions)
```

Plotting with matplotlib



http://matplotlib.org

Approximation

Motoo Kimura
1924-1994
Japan & USA

Kimura's equation:

$$\frac{e^{-2s} - 1}{e^{-2Ns} - 1}$$

```
def kimura(N, s):
    return np.expm1(-2 * s) /
           np.expm1(-2 * N * s)
```

`expm1(x)` is $\mathbf{e^x - 1}$ with better precision for small values of $\mathbf{x}$

`kimura` works on arrays out-of-the-box

```
%timeit [kimura(N=N, s=s)
                    for N in Nrange]
%timeit kimura(N=Nrange, s=s)
```

1 loop, best of 3: **752 ms** per loop

1000 loops, best of 3: **3.91 ms** per loop

X200 faster!

Numexpr

Fast evaluation of element-wise array expressions using a vector-based virtual machine.

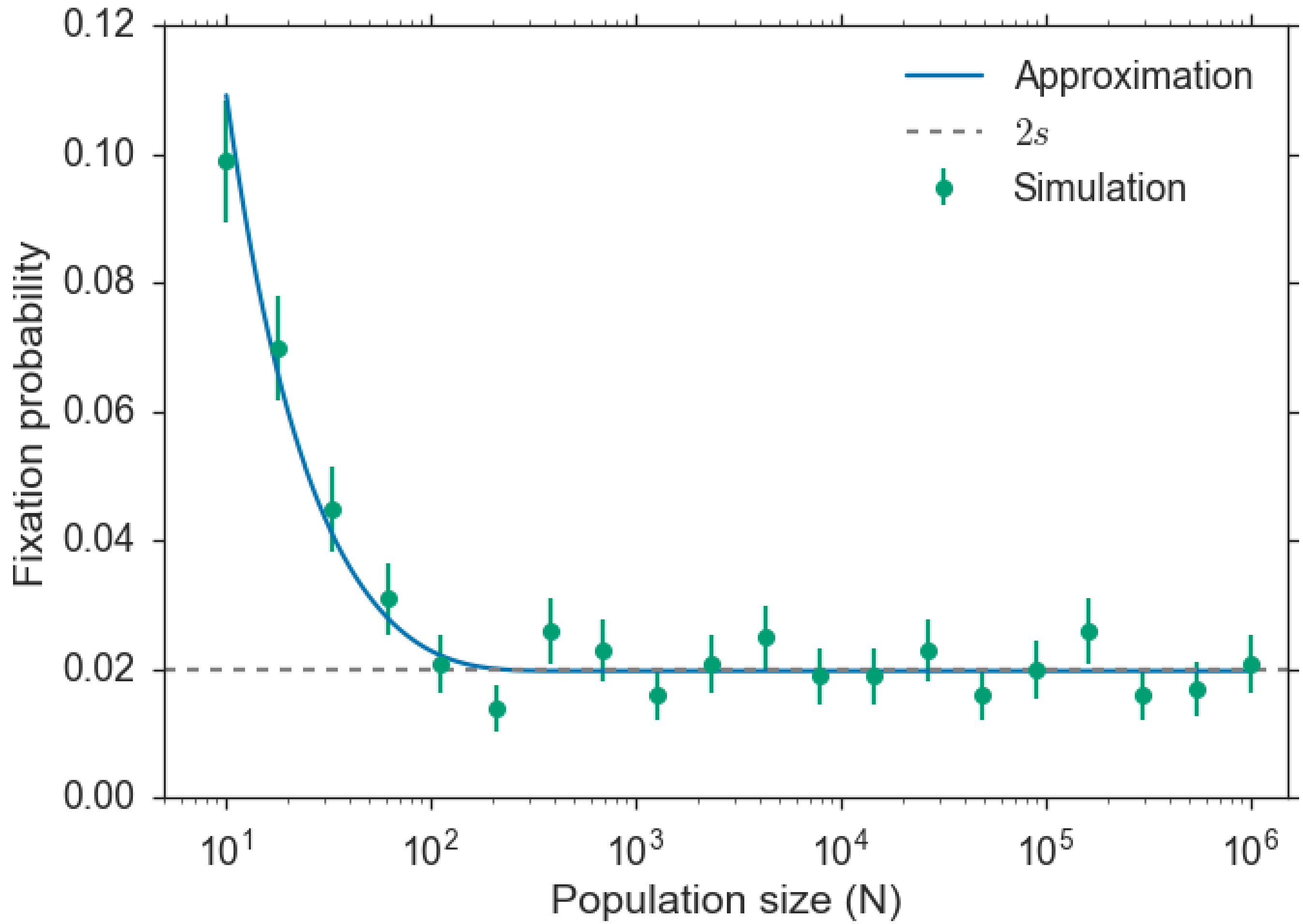
```
def kimura(N, s):
    return numexpr.evaluate(
        "expm1(-2 * s) /
        expm1(-2 * N * s)“)
```

```
%timeit kimura(N=Nrange, s=s)
```

1000 loops, best of 3: **803 µs** per loop **x5 faster**

https://github.com/pydata/numexpr

Plotting with matplotlib



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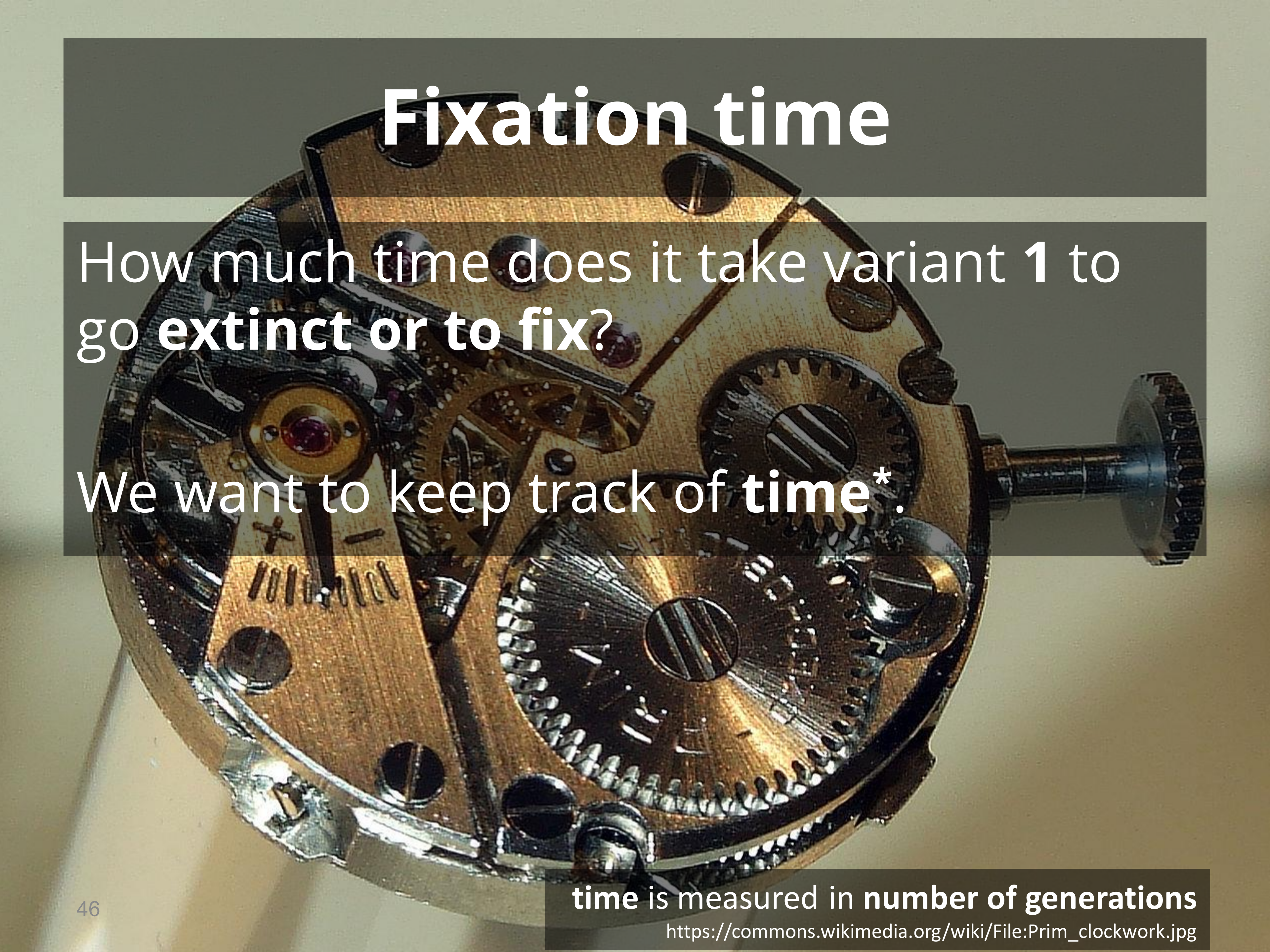


Fixation time

How much time does it take variant **1** to go **extinct or to fix**?

We want to keep track of **time***.

time is measured in **number of generations**

https://commons.wikimedia.org/wiki/File:Prim_clockwork.jpg

```python
def simulation(N, s, repetitions):
  n1 = np.ones(repetitions)
  T = np.empty_like(n1)
  update = (n1 > 0) & (n1 < N)
  t = 0

  while update.any():
    t += 1
    p = n1 * (1 + s) / (N + n1 * s)
    n1[update] = binomial(N, p[update])
    T[update] = t
    update = (n1 > 0) & (n1 < N)

  return n1 == N, T
```

`t` **keeps track of time**

```
def simulation(N, s, repetitions):
    n1 = np.ones(repetitions)
    T = np.empty_like(n1)
    update = (n1 > 0) & (n1 < N)
    t = 0

    while update.any():
        t += 1
        p = n1 * (1 + s) / (N + n1 * s)
        n1[update] = binomial(N, p[update])
        T[update] = t
        update = (n1 > 0) & (n1 < N)

    return n1 == N, T
```

T holds time for extinction/fixation

```
def simulation(N, s, repetitions):
  n1 = np.ones(repetitions)
  T = np.empty_like(n1)
  update = (n1 > 0) & (n1 < N)
  t = 0

  while update.any():
    t += 1
    p = n1 * (1 + s) / (N + n1 * s)
    n1[update] = binomial(N, p[update])
    T[update] = t
    update = (n1 > 0) & (n1 < N)

  return n1 == N, T
```

Return both Booleans and times (T)

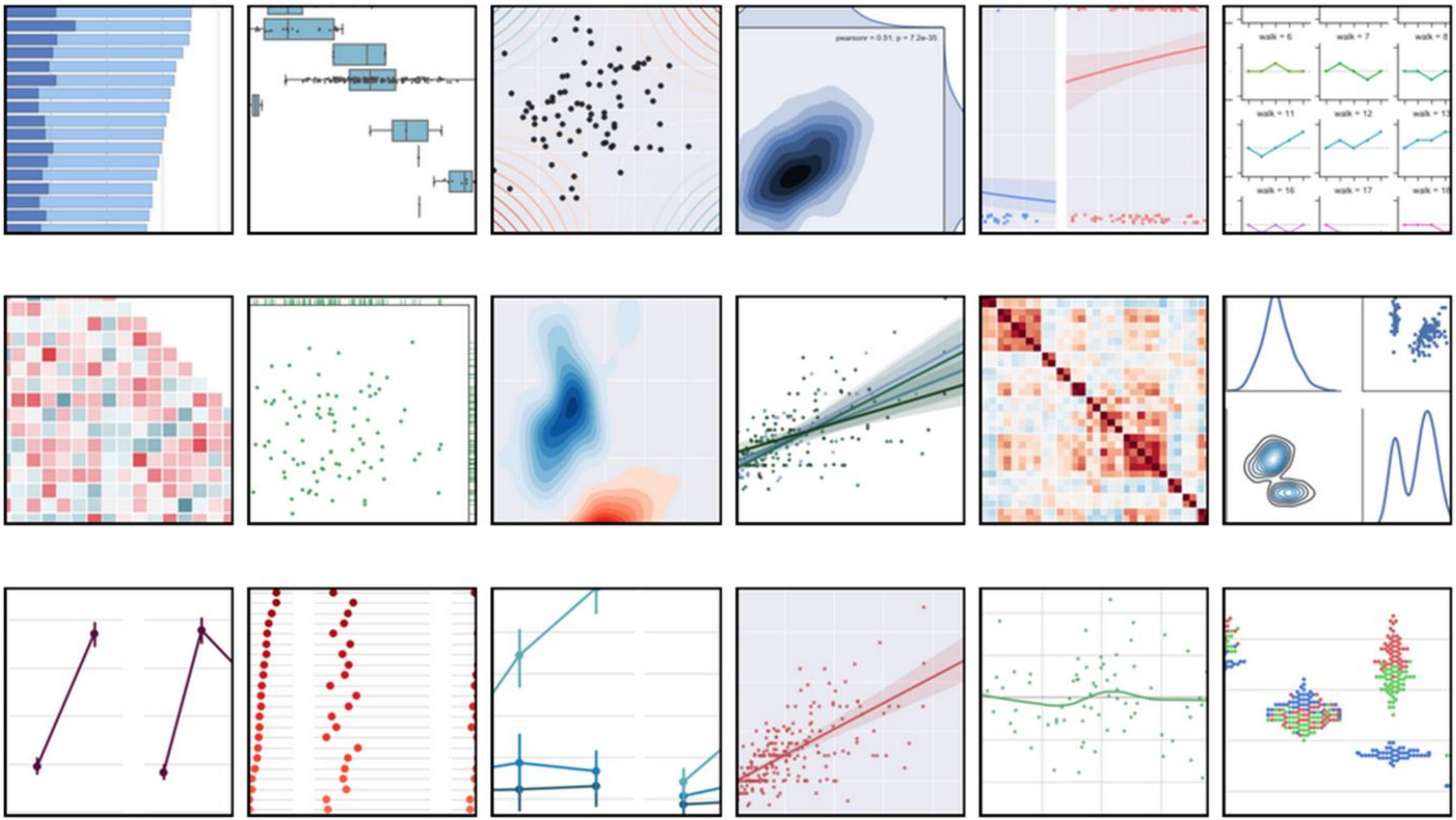
Statistical data visualization with Seaborn

- Visualization library based on **matplotlib** and **Pandas**
- High-level interface for attractive **statistical graphics**

By Michael Waskom, Stanford Ph.D. student

http://stanford.edu/~mwaskom/software/seaborn

Statistical data visualization with Seaborn



Plot with Seaborn

```
from seaborn import distplot

fixations, times = simulation(…)

distplot(times[fixations])

distplot(times[~fixations])
```

Plot with Seaborn

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Plot with Seaborn

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distplot(times[fixations])
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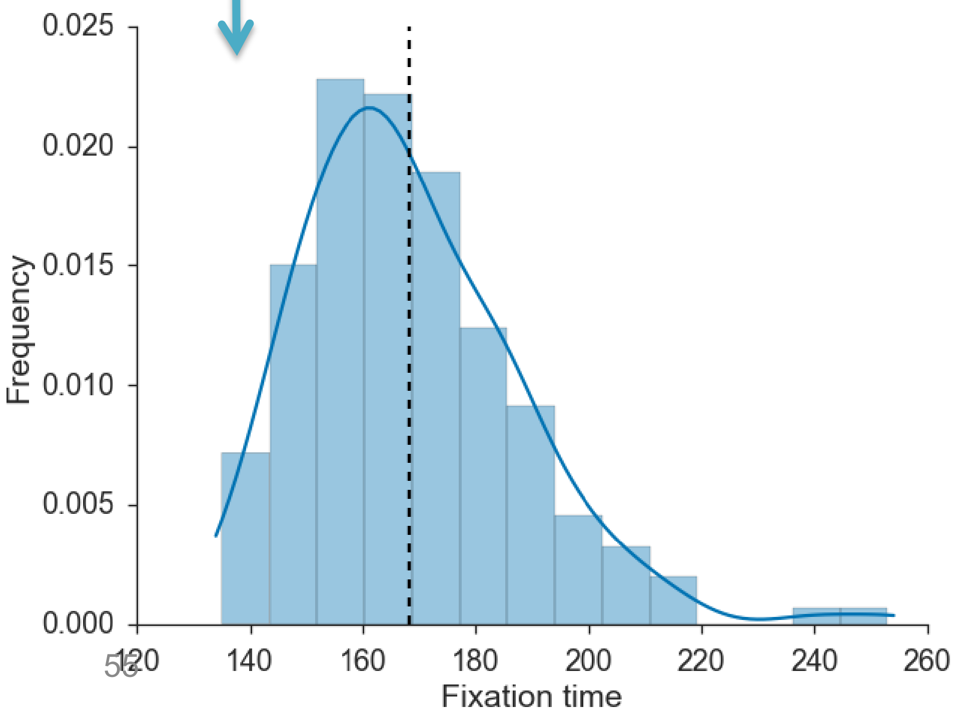
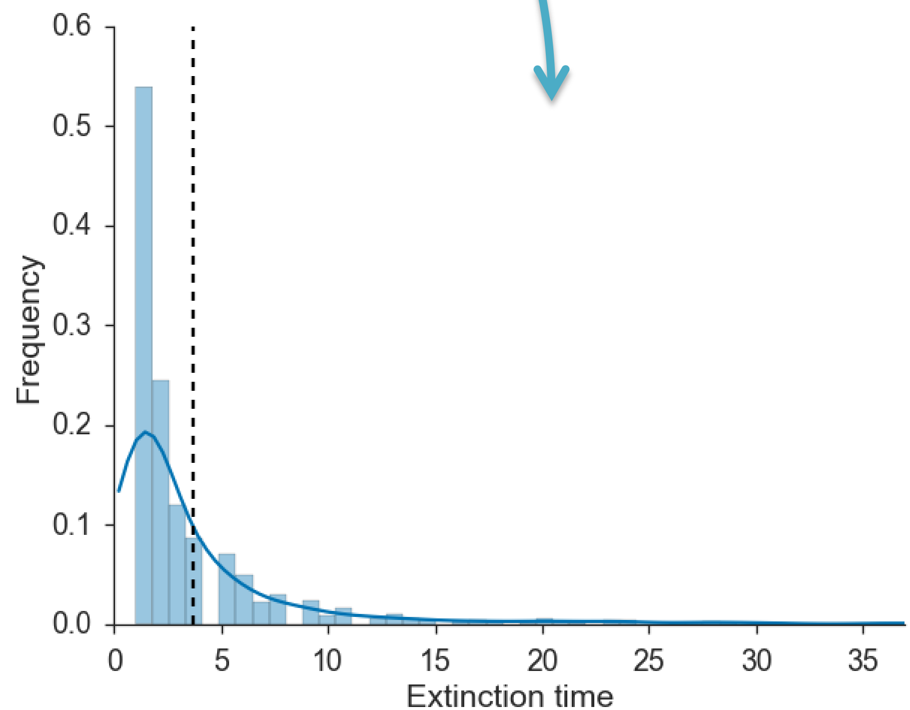
```





Diffusion equation approximation

$$I_1(x) = \frac{1 - e^{-2Nsx} - e^{-2Ns(1-x)} + e^{-2Ns}}{x(1-x)}$$

$$I_2(x) = \frac{(e^{2Nsx} - 1)(1 - e^{-2Ns(1-x)})}{x(1-x)}$$

$$J_1 = \frac{1}{s(1-e^{-2Ns})} \int_x^1 I_1(y)dy$$

$$J_2 = \frac{1}{s(1-e^{-2Ns})} \int_0^x I_2(y)dt$$

$$u = \frac{1 - e^{-2Nsx}}{1 - e^{-2Ns}}$$

$$\boxed{T_{fix} = J1 + \frac{1-u}{u} J_2}$$

Motoo Kimura
1924-1994
Japan & USA

Diffusion equation approximation

$$I_1(x) = \frac{1 - e^{-2Nsx} - e^{-2Ns(1-x)} + e^{-2Ns}}{x(1-x)}$$

$$I_2(x) = \frac{(e^{2Nsx} - 1)(1 - e^{-2Ns(1-x)})}{x(1-x)}$$

$$J_1 = \frac{1}{s(1 - e^{-2Ns})} \int_x^1 I_1(y)dy$$

$$J_2 = \frac{1}{s(1 - e^{-2Ns})} \int_0^x I_2(y)dt$$

$$u = \frac{1 - e^{-2Nsx}}{1 - e^{-2Ns}}$$

$$\boxed{T_{fix} = J1 + \frac{1-u}{u} J_2}$$

Requires integration…

Motoo Kimura
1924-1994
Japan & USA

```python
from functools import partial
from scipy.integrate import quad


def integral(f, N, s, a, b):
    f = partial(f, N, s)
    return quad(f, a, b)[0]
```

`integral` **will calculate** $\int_a^b f(N, s, x)dx$

```python
from functools import partial
from scipy.integrate import quad


def integral(f, N, s, a, b):
  f = partial(f, N, s)
  return quad(f, a, b)[0]
```

`partial` **freezes** `N` **and** `s`
in `f(N, s, x)` **to create** `f(x)`

```python
from functools import partial
from scipy.integrate import quad


def integral(f, N, s, a, b):
  f = partial(f, N, s)
  return quad(f, a, b)[0]
```

SciPy's `quad` **computes a definite integral** $\int_a^b f(x)dx$

(using a technique from the Fortran library QUADPACK)

```
def I1(N, s, x):
    ...

def I2(N, s, x):
    ...
```

$$I_1(x) = \frac{1 - e^{-2Nsx} - e^{-2Ns(1-x)} + e^{-2Ns}}{x(1-x)}$$

$$I_2(x) = \frac{(e^{2Nsx} - 1)(1 - e^{-2Ns(1-x)})}{x(1-x)}$$

$$J_1 = \frac{1}{s(1 - e^{-2Ns})} \int_x^1 I_1(y)dy$$

$$J_2 = \frac{1}{s(1 - e^{-2Ns})} \int_0^x I_2(y)dt$$

$$u = \frac{1 - e^{-2Nsx}}{1 - e^{-2Ns}}$$

$$T_{fix} = J1 + \frac{1-u}{u} J_2$$

`I1` and `I2` are defined according to the equations

```python
@np.vectorize
def T_kimura(N, s):
    x = 1.0 / N
    J1 = -1.0 / (s * expm1(-2 * N * s)) *
            integral(I1, N, s, x, 1)
    J2 = -1.0 / (s * expm1(-2 * N *s)) *
            integral(I2, N, s, 0, x)
    u = expm1(-2 * N * s * x) /
        expm1(-2 * N * s)

    return J1 + ((1 - u) / u) * J2
```

`T_kimura` is the fixation time given a single copy of variant `1`: frequency `x=1/N`

```python
@np.vectorize
def T_kimura(N, s):
    x = 1.0 / N
    J1 = -1.0 / (s * expm1(-2 * N * s)) *
            integral(I1, N, s, x, 1)
    J2 = -1.0 / (s * expm1(-2 * N *s)) *
            integral(I2, N, s, 0, x)
    u = expm1(-2 * N * s * x) /
        expm1(-2 * N * s)

    return J1 + ((1 - u) / u) * J2
```

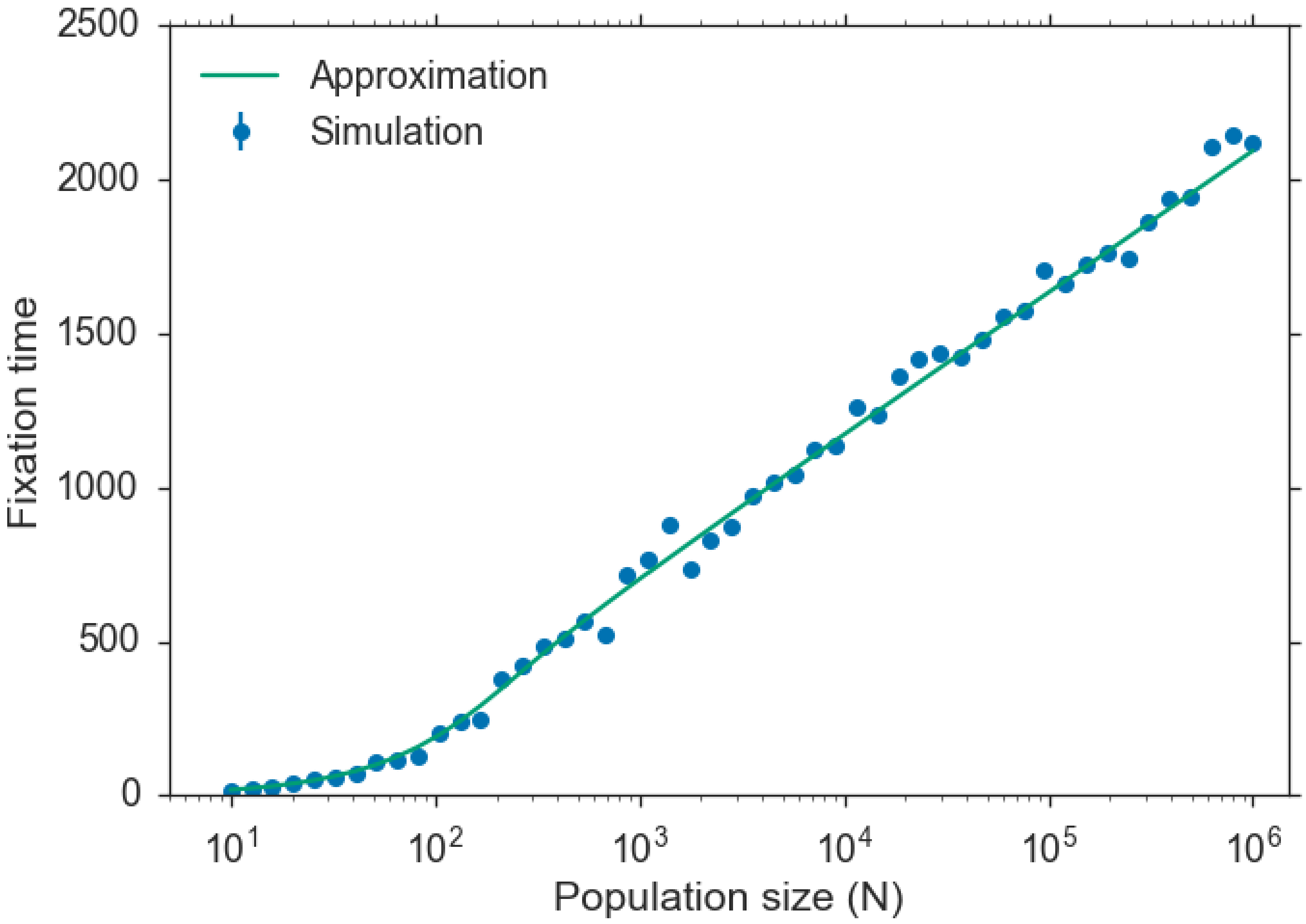
`J1` and `J2` are calculated using integrals of `I1` and `I2`

```
@np.vectorize
def T_kimura(N, s):
  x = 1.0 / N
  J1 = -1.0 / (s * expm1(-2 * N * s)) *
          integral(I1, N, s, x, 1)
  J2 = -1.0 / (s * expm1(-2 * N *s)) *
          integral(I2, N, s, 0, x)
  u = expm1(-2 * N * s * x) /
      expm1(-2 * N * s)

  return J1 + ((1 - u) / u) * J2
```

T_{fix} is the return value

```python
@np.vectorize
def T_kimura(N, s):
    x = 1.0 / N
    J1 = -1.0 / (s * expm1(-2 * N * s)) *
            integral(I1, N, s, x, 1)
    J2 = -1.0 / (s * expm1(-2 * N *s)) *
            integral(I2, N, s, 0, x)
    u = expm1(-2 * N * s * x) /
        expm1(-2 * N * s)

    return J1 + ((1 - u) / u) * J2
```

`np.vectorize` creates a function that takes a sequence and returns an array - x2 faster



Approximation
Simulation
Fixation time
2500
2000
1500
1000
500
0
10^1
10^2
10^3
10^4
10^5
10^6
Population size (N)

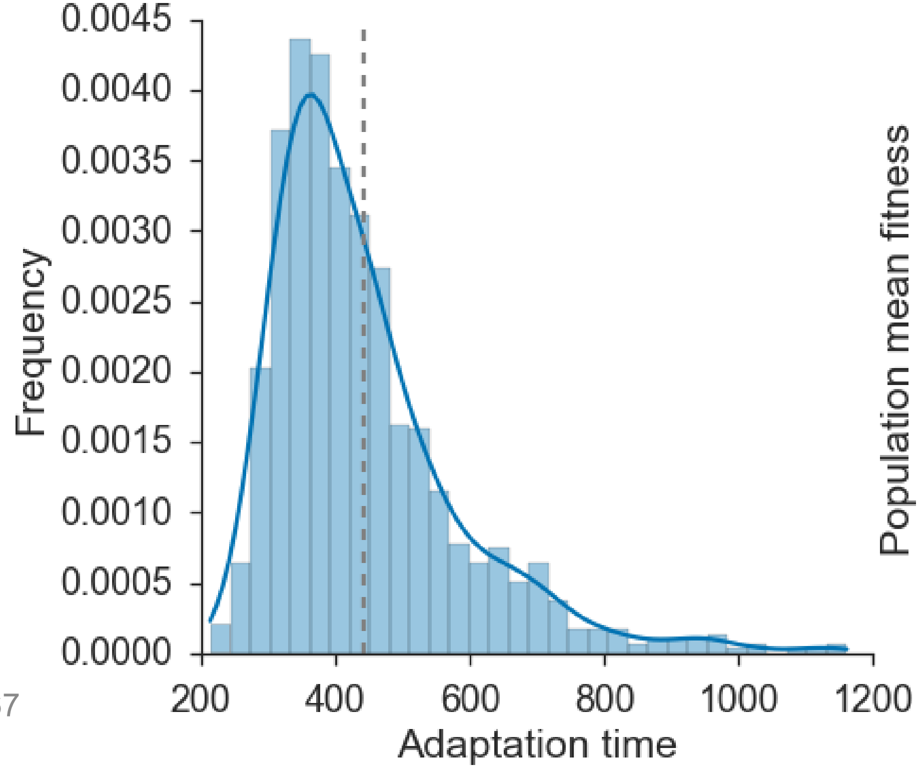
Dig Deeper

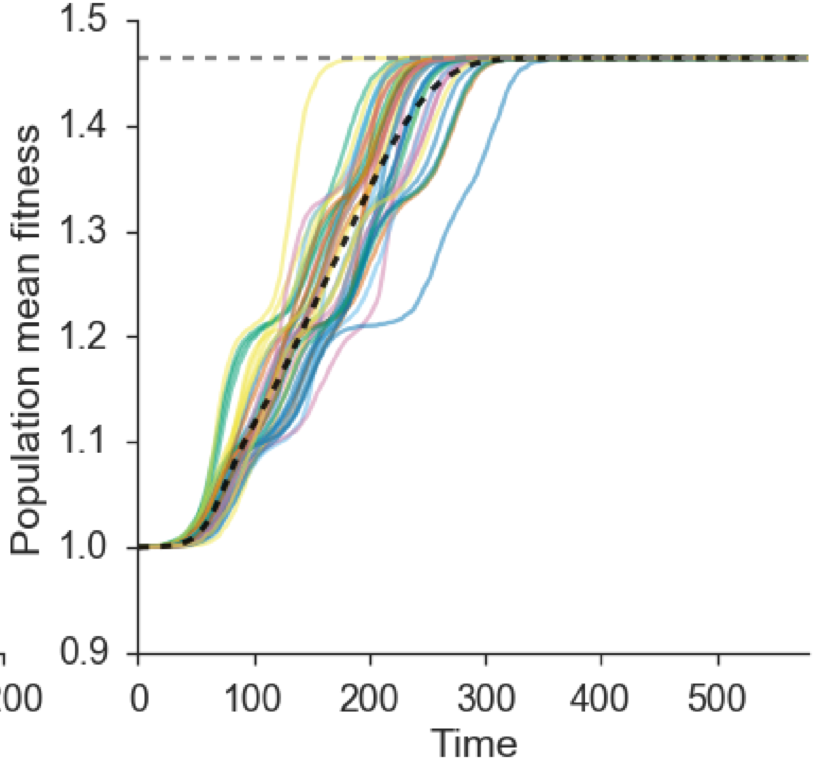
Online Jupyter notebook: github.com/yoavram/PyConIL2016

More **NumPy** - multi-type simulation:

Includes **L** variants, with mutation.

Follow $\mathbf{n_0}$, $\mathbf{n_1}$, ..., $\mathbf{n_L}$ until $\mathbf{n_L=N}$.





Dig deeper

Online Jupyter notebook: github.com/yoavram/PyConIL2016

- Pandas: high-performance, easy-to-use data structures and **data analysis tools**
- Numba: JIT compiler, **array-oriented and math-heavy** Python syntax to machine code
- IPyParallel: IPython's sophisticated and powerful architecture for **parallel** and **distributed computing**.
- IPyWidgets: **Interactive HTML Widgets** for Jupyter notebooks and the IPython kernel

Thank You!

Presentation, Jupyter notebook, and more at
github.com/yoavram/PyConIL2016

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Death to the Stock Photo