wright_fisher-hints

March 7, 2018

This is an ipython notebook. Lectures about Python, useful both for beginners and experts, can be found at http://scipy-lectures.github.io.

I recommend installing the Anaconda distribution. Make sure not to pay for it! Click Anaconda Academic License; it should be free for those with academic e-mail addresses.

Open the notebook by (1) copying this file into a directory, (2) in that directory typing ipython notebook and (3) selecting the notebook.

In this exercise, we will build a Wright-Fisher simulation model, which will be the basis of most of our simulation efforts.

1 Wright-Fisher model

1.1 Motivation

Population genetics seeks to describe and understand patterns of genetic diversity found in natural and artificial populations. In previous exercises, we've focused on the description part, measuring statistical differences among populations. We were able to interpret these differences in qualitative terms. Some populations seemed more related to each other, some were more distinct, and we could tell stories about that: maybe the more distinct groups were separated for a longer time. However, if we want to really understand the data, we need to go beyond describing it. We need to build models for the data that make predictions and can be falsified. The Hardy-Weinberg equilibrium model was a good start in that direction, but it only predicts a specific aspect of the data: the relationship between allele frequency and heterozygosity. It told us nothing about the number or frequency of variants in a population, or the amount of differences across populations. It didn't tell us how things change over time.

In this exercise, we will study the evolution of allele frequencies in a finite population. This notebook implements a very simple model of allele frequency evolution that we will use over and over in this course. To build an actual evolutionary model, we need to specify a number of parameters: the population size, the structure of the genome (e.g., the number of chromosomes, its ploidy), the mode of reproduction of the population (e.g., sexual vs asexual), the structure of the population, the distribution of offspring by individual, how new alleles are created, how alleles are transmitted from parent to offspring. We also have to decide on the starting point in our model, the ancestral population from which we will consider evolution. Since this is our first model, we'd like to keep everything as simple as possible:

- Population size: constant, N
- Structure of the genome: one single haploid chromosome of length 1 base pair.

- Mode of reproduction: asexual
- Mutation process: No mutation
- Transmission: Asexual transmission (clonal reproduction)
- Distribution of offspring: ?

It was straightforrward to come up with the simplest parameters so far, but here we need to think a bit more. Since we have a haploid population of constant size, the average number of offspring per individual must be one. If every individual has exactly one offspring, the population will never change and the model will be useless, so we need to let parents have different number of offspring.
If we let each parent independently pick a random number of offspring, the population size could change a little bit at every generation. That's not really a big deal, since real populations sizes do fluctuate, but we'd like to be able to control those fluctuations for two reasons. First, if we happen to know the size of the population we want to model, we don't want to waste time simulating populations of the wrong size. Second, if we want to model a population for a long period of time, the size fluctuations will add up and the population will either go extinct or grow uncontrollably.

If parents vary in their number of offspring, how can they synchronize to produce exactly one offspring, on average? One way would be to add feedback, reducing the mean number of offspring when the population size increases, and increasing it when the population size decreases. That could work, but there are many parameters to fix, and even there we're not immune to the occasional population extinction.

There are a few elegant but slightly strange ways of solving this problem by keeping the population size at an exact, predefined N. First, you can imagine that each parent produces very many offspring, but that only N offspring from the entire population are allowed to survive, and these are selected at random among all offspring. You can also turn the table and imagine that each of the allowed N offspring "picks" a parent at random. If the idea of children picking their parents is confusing, you can imagine that there are N child-bearing permits available, and each permit is offered to a randomly-chosen parent.

Interestingly, these approaches are exactly equivalent, in that they make the exact same predictions about the number of surviving offsprings per parent. **Take the time to convince yourself that this is the case.**

This sampling approach defines the Wright-Fisher model. We can add many features to this model, such as selection, recombination, mutation, and so forth, but as long as you have this discrete generations and random selection of parents, you're within the Wright-Fisher model.

I'll just mention one alternative, called the Moran Model, which involves replacing a single, randomly selected individual by the genotype of another, randomly selected individual, and repeating this N times per generation. The Moran model is not exactly equivalent to the Wright-Fisher model, and there are cases where it is more convenient. But we'll stick to Wright-Fisher for this notebook.

Optional Mathematical exercises

1. What is the distribution of offspring number per individual in the Wright-Fisher model?

The distribution of number of children for next generation:
0 - (1-(1/N))N
1 - N C1 x (1-(1/N))(N-1) x (1/N)

..
i - N Ci x (1-(1/N))(N-i) x (1/N)i
..
N - N CN x (1/N)N
This is the binomial distribution with n=N and probability p = 1/N

2. Convince yourself that, for large enough populations, this distribution is approximately Poisson with mean 1.

Mean of binomial = np = N*(1/N) = 1
As a binomial distribution reaches infinity(large number of trials) it can be approximated using the poisson distribution as long as the mean remains constant.

1.2 Libraries

We'll need the following python plotting libraries.

```
In [3]: ### 1
        %matplotlib inline
        #If you run into errors with %matplotlib, check that your version of ipython is >=1.0
        import numpy as np #numpy defines useful functions for manipulating arrays and matrices.
        import matplotlib.pyplot as plt #matplotlib is plotting library
```

1.3 Implementation

We have specified almost everything we needed in the model, except for the initial state of the population. We will suppose that the single site has two alleles labeled 0 and 1. We need to specify the number of individuals nInd in the initial population and the proportion $p0$ of 1 alleles

```
In [4]: ### 2
        p0   = 0.1  # initial proportion of "1" alleles
        nInd = 100  # initial population size (number of individuals)
```

Now we need to create an initial population with the given number of individuals, and the appropriate proportion of 1 alleles. We'll store the population as a np.array called "initial_population", of length nInd containing 0s and 1s.

```
In [5]: ### 3
        # Initialize a population of length nInd with only 0 alleles.
        initial_population = np.zeros(nInd)

        # Set the first p0*nInd alleles to 1.

        initial_population[:int(p0*nInd)] = 1;

        # For added realism, shuffle the population so that the ones are distributed across the
        # You can use np.random.shuffle to do this.

        np.random.shuffle(initial_population);
```

To take finite samples from this population, we can use the np.random.choice function. When taking a sample from a population, we can pick each sample only once--the "replace=False" option below tells us that we don't replace the sampled individual in the population before drawing a new one. Read the np.random.choice documentation for more detail!

```
In [6]: ### 4
        sample_size = 10
        np.random.choice(initial_population, sample_size, replace=False );
```

When we take repeated samples from the same population, we can find very different numbers of alternate alleles--we'll have to take this into account when looking at real data!

Optional Mathematical exercise

```
1-What is the distribution of the number of alternate alleles if we sample s individuals in a po
```

The distribution that is obtained can be seen as the probability of obtaining k successes from n draws without replacement which is similar to the distribution defined by hypergeometric distribution.

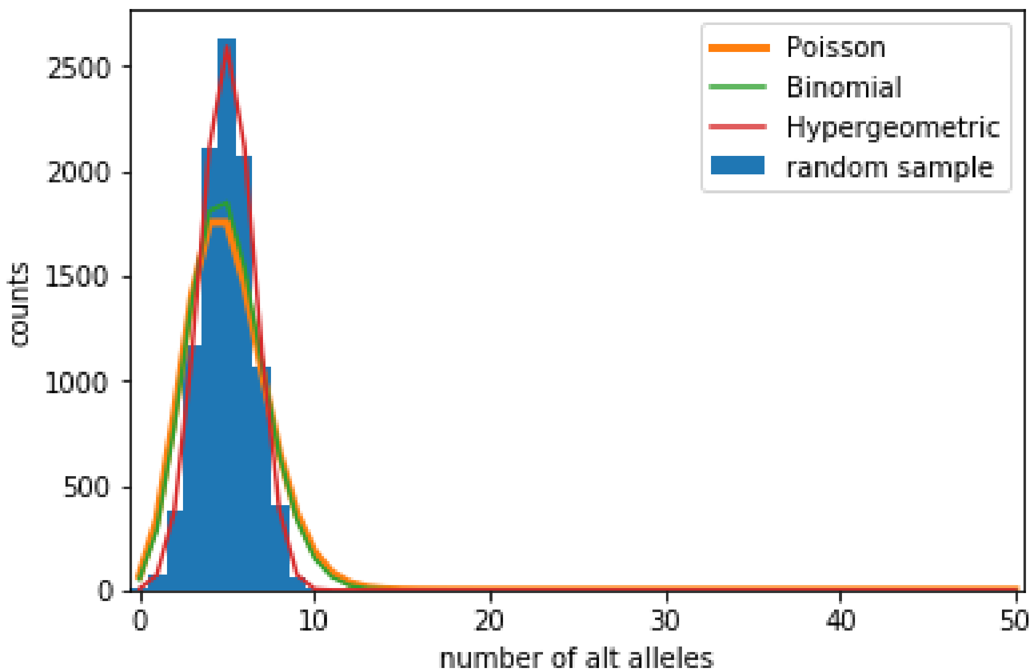
The number

I generated a bunch of samples below, and compare the resulting histogram to plausible probability distributions so that you can pick the one that fits best. If you don't do the math problems, read a bit about the best-fitting one and check that it makes sense.

```
In [7]: ### 5
        import scipy
        from scipy import stats

        iterations = 10000  # the number of times to draw.
        sample_size = 50  # the size of each sample
        alt_counts = []  # number of alternate alleles (i.e., 1's) for each draw

        for i in range(iterations):
            sample=np.random.choice(initial_population, sample_size, replace=False)
            # get the number of alt alleles
            alt_counts.append(sample.sum())

        # plot a histogram of sampled values
        plt.hist(alt_counts, sample_size + 1, range=(-0.5, sample_size + 1 - 0.5), label="random
        plt.xlabel("number of alt alleles")
        plt.ylabel("counts")

        # Compare this to some discrete distributions
        x_range = range(sample_size + 1) # all the possible values

        p = np.sum(initial_population) * 1. / len(initial_population)  # initial fraction of alt

        # poisson with mean sample_size * p
        y_poisson = stats.poisson.pmf(x_range, sample_size*p) * iterations
        # binomial with probability p and  sample_size draws
```

```
y_binom = stats.binom.pmf(x_range, sample_size,p) * iterations
# hypergeometric draw of sample_size from population of size len(initial_populationpop)
# with np.sum(initial_population) ones.
y_hypergeom = stats.hypergeom.pmf(x_range, len(initial_population), np.sum(initial_popul
                * iterations

plt.plot(x_range, y_poisson, label="Poisson", lw=3)
plt.plot(x_range, y_binom, label="Binomial")
plt.plot(x_range, y_hypergeom, label="Hypergeometric")
plt.xlim(-0.5, sample_size + 0.5)
plt.legend()
```

```
Out[7]: <matplotlib.legend.Legend at 0x7fd9bf1bbc90>
```



Now comes the time to code up the Wright-Fisher model. Remember that there were two ways of thinking about Wright-Fisher reproduction:

```
1- We generate a very large number of offspring for each parent, and than we take a sample from
2- Each offspring picks a parent at random.
```

In 2-, each parent can be chosen multiple times. This is equivalent to taking a sample from the previous generation, but *with replacement*. Convince yourself that this is true. This is *not* optional! If you are not convinced, try programming it both ways, or ask questions.

Now code a function that takes in a parental population as an array (such as "initial_population", above), and returns an offspring population.

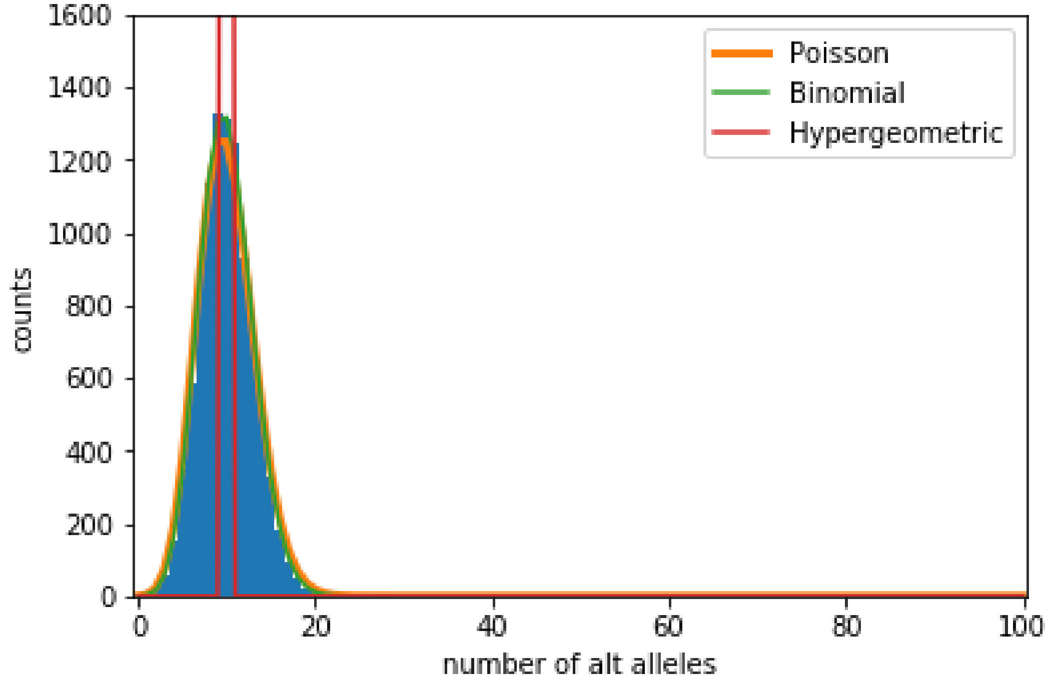
In [8]:
```
### 6
def generation(pop):
    """Takes in a list or array describing an asexual parental population.
    Return a descendant population according to Wright-Fisher dynamics with constant siz
    nInd = pop.shape[0] #number of individuals. We could use the global definition of nI
    #but it's better to use the information that is passed to the function
    #now generate the offspring population.
    return np.random.choice(pop, nInd, replace=True);

generation(initial_population)

np.sum(initial_population)
```

Out[8]: 10.0

As for regular sampling, we get a different number of ones every time we run the "generation" function. Here again, I generated a bunch of samples just to get an idea of how much variation there is, and overlaid some plausible distribution. Which one fits best? Does it make sense to you?

In [9]:
```
### 7


nsample = 10000  # the number of samples to draw.
alt_counts = []  # number of alternate alleles (i.e., 1's) for each draw

for i in range(nsample):
    offspring = generation(initial_population)
    alt_counts.append(offspring.sum())

hist = plt.hist(alt_counts, len(initial_population)+1, range=(0-0.5, len(initial_populat
plt.xlabel("number of alt alleles")
plt.ylabel("counts")

#Here I just check that the initial population is still a list of length nInd
assert nInd==len(initial_population),"initial_population doesn't have the same length as

x_range=range(nInd+1)                    #all the possible values
p=np.sum(initial_population)*1./nInd     #the initial frequency

#Compare this to some distributions
y_poisson=stats.poisson.pmf(x_range, nInd*p) * nsample
y_binom=stats.binom.pmf(x_range, nInd, p) * nsample
y_hypergeom=stats.hypergeom.pmf(x_range, nInd, np.sum(initial_population), nInd) * nsamp

plt.plot(x_range, y_poisson, label="Poisson",lw=3)
plt.plot(x_range, y_binom, label="Binomial")
plt.plot(x_range, y_hypergeom, label="Hypergeometric")
plt.xlim(-0.5, nInd+0.5)
plt.ylim(0, 1.2*max(hist[0]))
plt.legend()
```

Out[9]: <matplotlib.legend.Legend at 0x7fd9befbccd0>



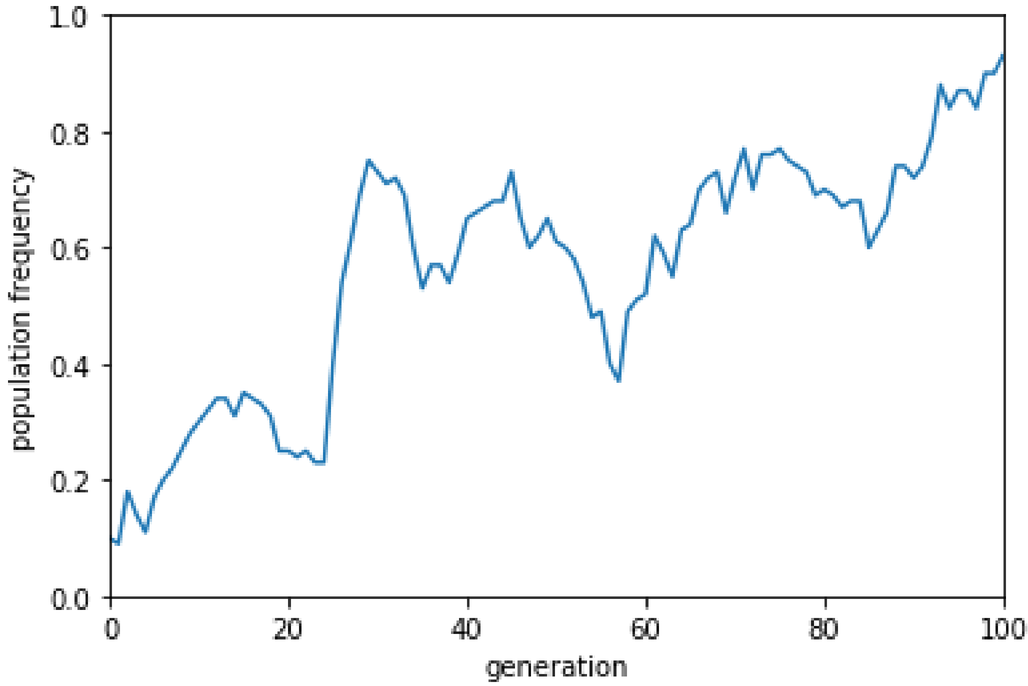
Now we are ready to evolve our population for 100 generations. Let's store the entire genotypes for each generation in a list.

```
In [10]: ### 8
         nGen = 100  # number of generations to simulate
         history = [initial_population]  # a container list for our simulations. It will contain
                                               # state after generations 0 to nGen
         for i in range(nGen):
             # evolve the population for one generation, and append the result to history.
             history.append(generation(history[i]));
         history = np.array(history)  # convert the list into an array for convenient manipulati
```

Now we want to look at the results. Let's compute the allele frequency at each generation and plot that as a function of time.

```
In [11]: ### 9
         #compute the allele frequency at each generation.
         #freqs should be a list or array of frequencies, with one frequency per generation.
         #history is a np array and has two methods that can help you here: sum, and mean.
         #Mean is probably the best bet here.
         freqs = np.mean(history, axis=1)
         plt.plot(freqs)
         plt.axis([0, 100, 0, 1]);#define the plotting range
         plt.xlabel("generation")
         plt.ylabel("population frequency")
```

Out[11]: Text(0,0.5,u'population frequency')



Now we would like to experiment a bit with the tools that we have developed. Before we do this, we will organize them a bit better, using a Python "class" and object-oriented programming. We have defined above variables that describe a population (such as the population size nInd, and the ancestral frequency g0). We have also defined functions that apply to a population, such as "generation". A class is used to keep track of the relation between objects, variables, and functions.

If you are not familiar with classes and are having issues, have a look at this tutorial.

In [12]:
```
### 10
class population:
    """
    Initialization call:

    population(nInd,p0)
    requires a number of individuals nInd and an initial frequency p0

    Variables:
    nInd: The number of individuals
    p0: the initial allele frequency
    initial_population: an array of nInd alleles
    history: a list of genotypes for each generation
    traj: an allele frequency trajectory; only defined if getTraj is run.
    Methods:
    generation: returns the offspring from the current population, whish is also the la
    evolve: evolves the population for a fixed number of generations, stores results to
```

```
getTraj: calculates the allele frequency history for the population
plotTraj: plots the allele frequency history for the population

"""
def __init__(self, nInd, p0):
    """initialize the population. nInd is the number of individuals. p0 is the init
    __init__ is a method that, when run, creates a "population" class and defines s
    Here we define this __init__ method but we don't run it, so there is no "popula
    In the meantime, we'll refer to the eventual population object as "self".
    We'll eventually create a population by stating something like
    pop = population(nInd,p0)
    This will call the __init__ function and pass a "population" object to it in li
    """
    self.nInd = nInd
    self.p0 = p0
    #initialize the population
    self.initial_population = np.zeros([nInd])
    self.initial_population[0 : int(p0*self.nInd)] = 1
    np.random.shuffle(self.initial_population)
    #history is a container that records the genotype at each generation.
    #we'll update this list
    self.history = [self.initial_population]

def generation(self):
    """class methods need "self" as an argument in they definition to know that the
    The class structure
    gives you a more readable way of calling this function: If we have a population
    the population as the first argument. Putting the object name upfront often mak
    Takes the last element of the history.
    Return a descendant population according to Wright-Fisher dynamics with constan
    """
    return np.random.choice(self.history[-1], self.nInd, replace=True)

def evolve(self,nGen):
    """
    This is a method with one additional argument, the number of generations nGen.
    To call this method on a population "pop", we'd call pop.evolve(nGen).
    This function can be called many times on the same population.
    pop.evolve(2)
    pop.evolve(3)
    would evolve the population for 5 generations.
    For each step, we make a call to the function generation() and append the popul
    """
    for i in range(nGen):
        self.history.append(self.generation());
    self.getTraj()

def getTraj(self):
```

```
        """
        calculates the allele frequency history for the population
        """
        history_array = np.array(self.history)
        self.traj = history_array.mean(axis=1)
        return self.traj

    def plotTraj(self,ax="auto"):
        """
        plots the allele frequency history for the population
        """

        plt.plot(self.traj)
        if ax=="auto":
            plt.axis([0, len(self.history), 0, 1])
        else:
            plt.axis(ax)
```

2 Exploration

2.1 Drift

We can now define multiple populations, and let them evolve from the same initial conditions.

In [13]:
```
### 11
nInd = 100
nGen = 30
nRuns = 10
p0 = 0.3
# Create a list of length nRuns containing initial populations
# with initial frequency p0 and nInd individuals.
pops = [population(nInd, p0) for i in range(nRuns)]
```

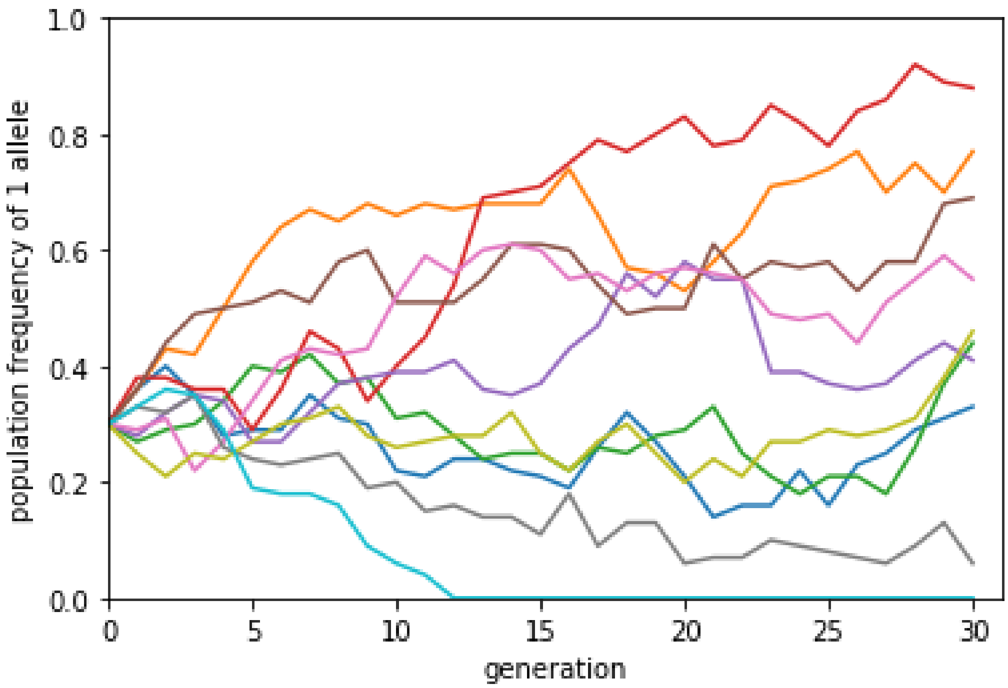
Evolve each population for nGen generations. Because each population object has it's own internal storage for the history of the population, we don't have to worry about recording anything.

In [14]:
```
### 12
for pop in pops:
    pop.evolve(nGen);
```

Now plot each population trajectory, using the built-in method from the population class.

```
In [15]: ### 13
         for pop in pops:
             pop.plotTraj();
         plt.xlabel("generation")
         plt.ylabel("population frequency of 1 allele")
```

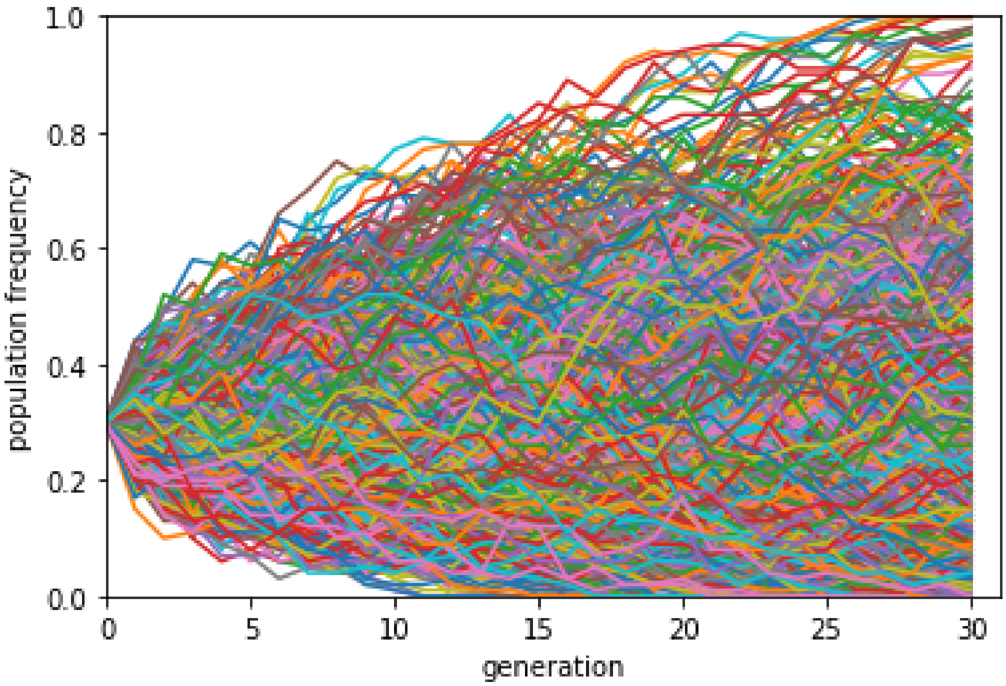
```
Out[15]: Text(0,0.5,u'population frequency of 1 allele')
```



Now that we know it works, let's explore this a bit numerically. Try to get at least 1000 runs, it'll make graphs prettier down the road.

```
In [16]: ### 14
         nInd = 100
         nGen = 30
         nRuns = 1000
         p0 = 0.3
         pops = [population(nInd, p0) for i in range(nRuns)]
         for pop in pops:
             pop.evolve(nGen)

         for pop in pops:
             pop.plotTraj();

         plt.xlabel("generation")
         plt.ylabel("population frequency")
```

Out[16]: Text(0,0.5,u'population frequency')



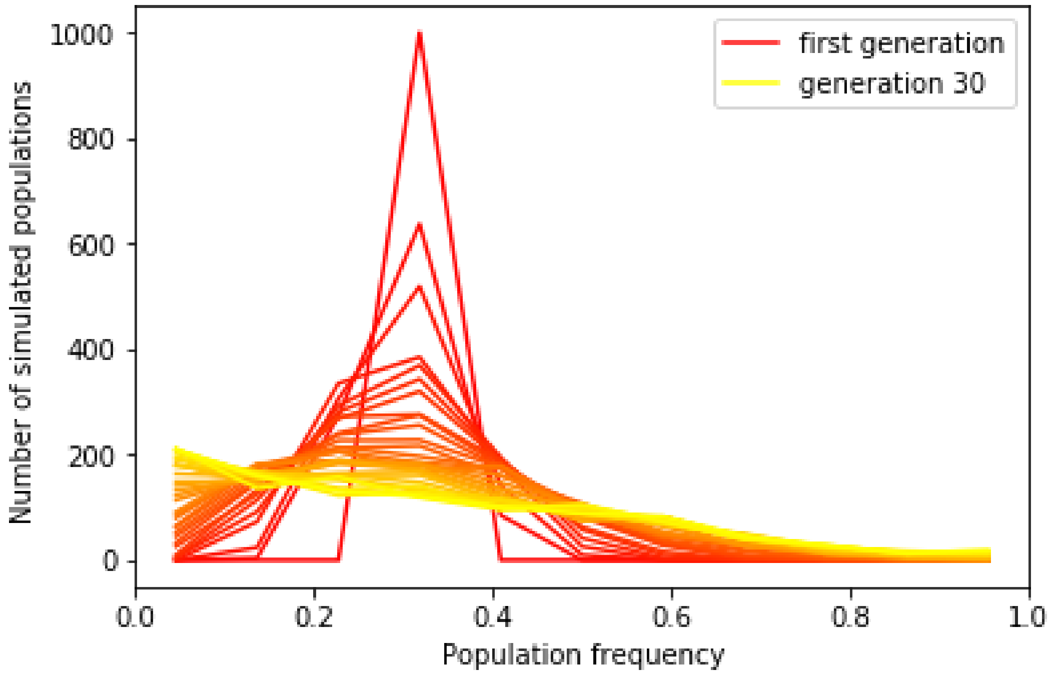
So there is a lot of randomness in there, but if you run it multiple times you should see that there is some regularity in how fast the allele frequencies depart from the initial values. To investigate this, calculate and plot the distribution of frequency at each generation.

In [17]:
```
### 15
def frequencyAtGen(generation_number, populations, nBins=11):
    """calculates the allele frequency at generation genN for a list of populations pop
     Generates a histogram of the observed values"""
    counts_per_bin, bin_edge_positions = np.histogram([pop.traj[generation_number] for

    bin_centers=np.array([(bin_edge_positions[i+1]+bin_edge_positions[i]) / 2 for i in
    return bin_centers, counts_per_bin # Return the data from which we will generate th
```

In [18]:
```
### 16
nBins = 11 # The number of frequency bins that we will use to partition the data.
for i in range(nGen+1):

    bin_centers, counts_per_bin = frequencyAtGen(i, pops, nBins);
    if i==0:
        plt.plot(bin_centers, counts_per_bin, color=plt.cm.autumn(i*1./nGen), label="fi
                                                                    #  color with u
    elif i==nGen:
        plt.plot(bin_centers, counts_per_bin, color=plt.cm.autumn(i*1./nGen), label="ge
    else:
```

```
        plt.plot(bin_centers, counts_per_bin, color=plt.cm.autumn(i*1./nGen))
    plt.legend()
    plt.xlabel("Population frequency")
    plt.ylabel("Number of simulated populations ")
```

Out[18]: Text(0,0.5,u'Number of simulated populations ')



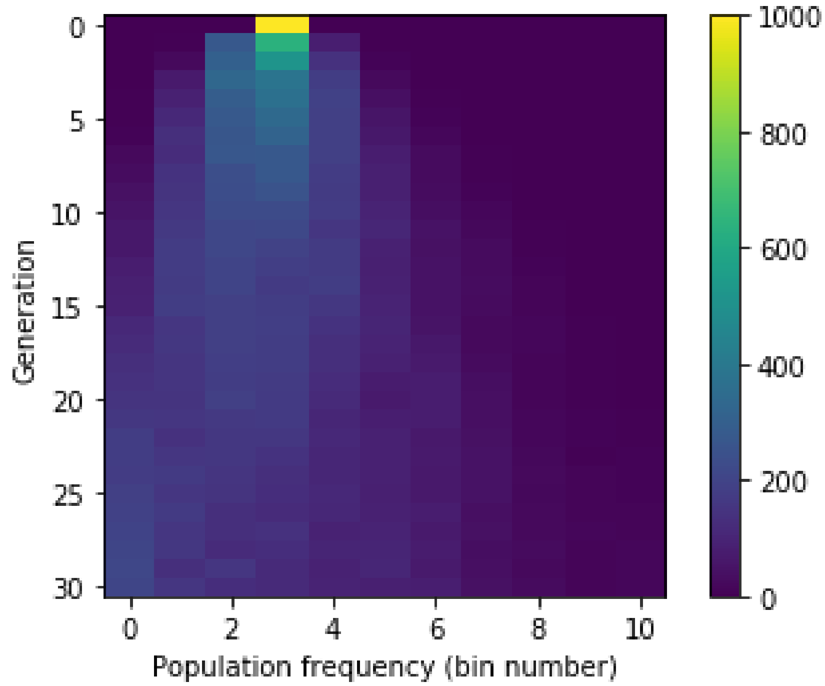
There are three important observations here:

```
1-Frequencies tend to spread out over time
2-Over time, there are more and more populations at frequencies 0 and 1. (Why?)

Consider the binomial distribution with which the next generation is created. The probability th

3-Apart from the 0 and 1 bins, the distribution becomes entirely flat.
```

A few alternate ways of visualizing the data: first a density map

In [19]:
```
### 17
nBins = 11
sfs_by_generation = np.array([frequencyAtGen(i, pops, nBins=nBins)[1] for i in range(0,
bins = frequencyAtGen(i, pops, nBins=nBins)[0]
plt.imshow(sfs_by_generation, aspect=nBins*1./nGen, interpolation='nearest')
plt.xlabel("Population frequency (bin number)")
plt.ylabel("Generation")
plt.colorbar()
```

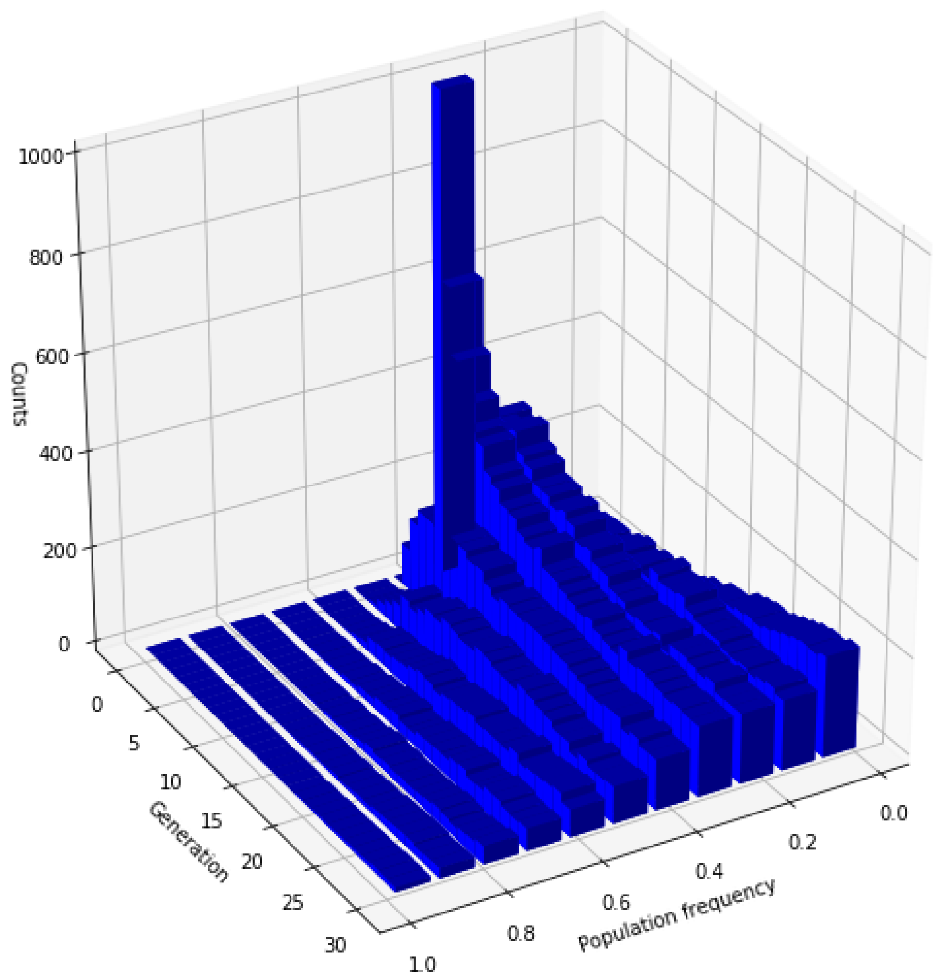
Out[19]: <matplotlib.colorbar.Colorbar at 0x7fd9bdd75650>



Then a 3D histogram, unfortunately a bit slow to compute.

In [215]:
```
### 18
from mpl_toolkits.mplot3d import Axes3D

fig = plt.figure(figsize=(10,10))
ax = fig.add_subplot(111, projection='3d', elev=90)
xedges = bins
yedges = np.arange(nGen+1)

xpos, ypos = np.meshgrid(xedges-.4/nBins, yedges-0.5)

xpos = xpos.flatten()
ypos = ypos.flatten()
zpos = 0 * ypos
dx = .8 / nBins
dy = 1
dz = sfs_by_generation.flatten()

ax.bar3d(xpos, ypos, zpos, dx, dy, dz, color='b', edgecolor='none', alpha=0.15)

ax.view_init(elev=30., azim=60)
ax.set_xlabel("Population frequency")
ax.set_ylabel("Generation")
```

```python
ax.set_zlabel("Counts")

plt.show()
```



Now let's dig into the effect of population size in a bit more detail. Consider the change in frequency after just one generation:

Mathematical exercise (NOT optional):

- What is the expected distribution of allele frequencies after one generation, if they start at frequency p in a population of size N? (Hint: we explored this numerically above!)

The frequencies follow a binomial distribution. The binary choice is of selection between two alleles and the selection occurs with a probability p for first allele and 1-p for second allele. This represents a binomial distribution.

Number of alternate alleles in the starting generation: pN

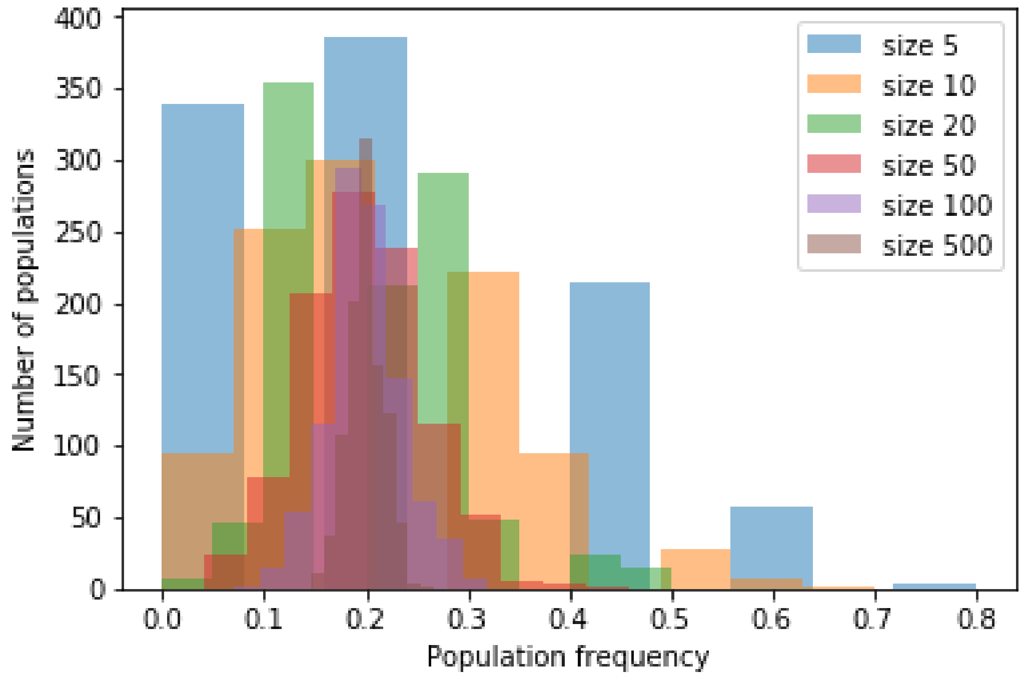
Probability that the next generation has the following number of alleles of:
Frequency - Count - probability
0 - 0 - N C0 p0 x (1-p)N
1/N - 1 - N C1 p1 x (1-p)(N-1)
...
i/N - i - N Ci pi x (1-p)(N-i)
...
1 - N - CN pN

- What is the variance of this distribution? (Look it up if you don't know--wikipedia is useful for that kind of stuff)

Variance : $(p/N)[1\text{-}p]$

To study the effect of population size on the rate of change in allele frequencies, plot the distribution of allele frequencies after nGen generation. Start with nGen=1 generation.

```
In [255]: ### 19
          histograms = []
          variances = []
          p0 = 0.2
          sizes = [5, 10, 20, 50, 100, 500]
          nGen = 1
          for nInd in sizes:
              pops=[population(nInd,p0) for i in range(1000)]
              [pop.evolve(nGen) for pop in pops]
              sample = [pop.getTraj()[-1] for pop in pops]
              variances.append(np.var(sample))
              histograms.append(plt.hist(sample, alpha=0.5, label="size %d" % (nInd,) ))

          plt.xlabel("Population frequency")
          plt.ylabel("Number of populations")
          plt.legend()

Out[255]: <matplotlib.legend.Legend at 0x7f22f5d29290>
```



So how does population size affect the change in allele frequency after one generation? Can you give a specific function describing the relationship between variance and population size?

You can get this relationship from the math exercise above, or just try to guess it from the data. If you want to try to guess, start by plotting the variances (stored in "variances") against the population sizes (stored in "sizes"). Then you can either try to plot different functinoal forms to see if they fit, or you can change the way you plot the data such that it looks like a straight line. If you do the latter, make sure you update the labels!

Here I'm giving you a bit more room to explore--there are multiple ways to get there.

2.1.1 Answer

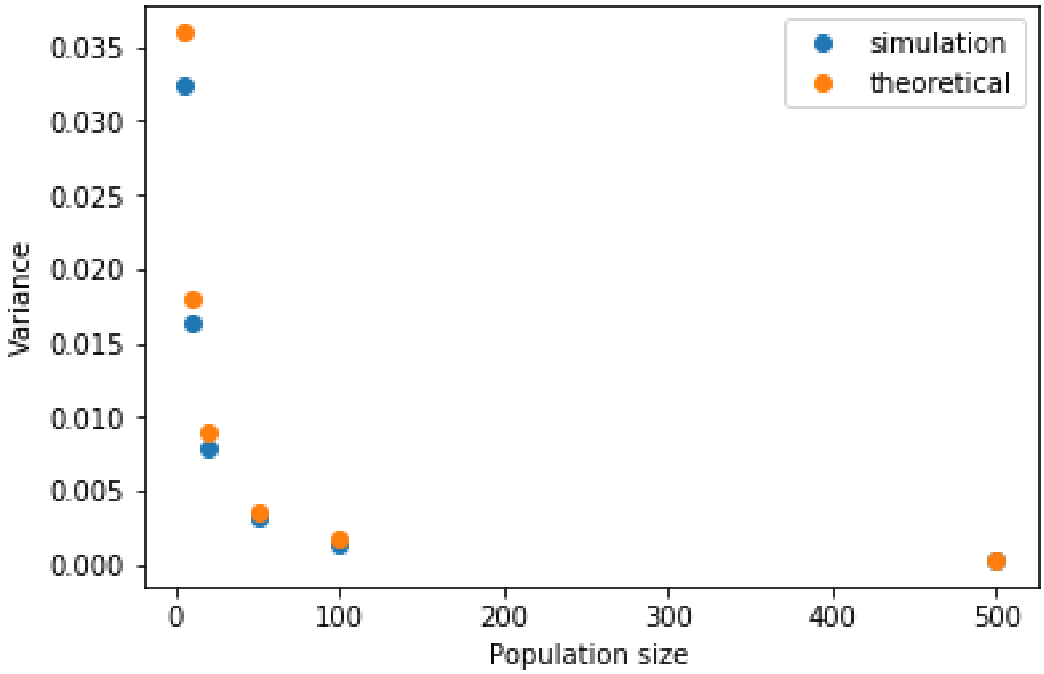
The allele frequency gradually changes for larger populations compared to smaller populations for which it is seen that the allele frequency distribution quickly changes and spreads. The variance is lesser for higher populations because there is less sampling error(in a high level a population represents samples from a distribution).

Relation between variance and population size: Variance = (p/N)[1-p] , Here N is the population size

```
In [258]: ### 20
          plt.plot(np.array(sizes), variances, 'o', label="simulation") #this is a starting poin
          # Your theory.
          # ...

          computed_variance = [ (p0*1./N)*(1-p) for N in sizes ];

          plt.plot(np.array(sizes), np.array(computed_variance), 'o', label="theoretical")
```

```
plt.legend()
plt.xlabel("Population size")
plt.ylabel("Variance")
```

Out[258]: Text(0,0.5,u'Variance')

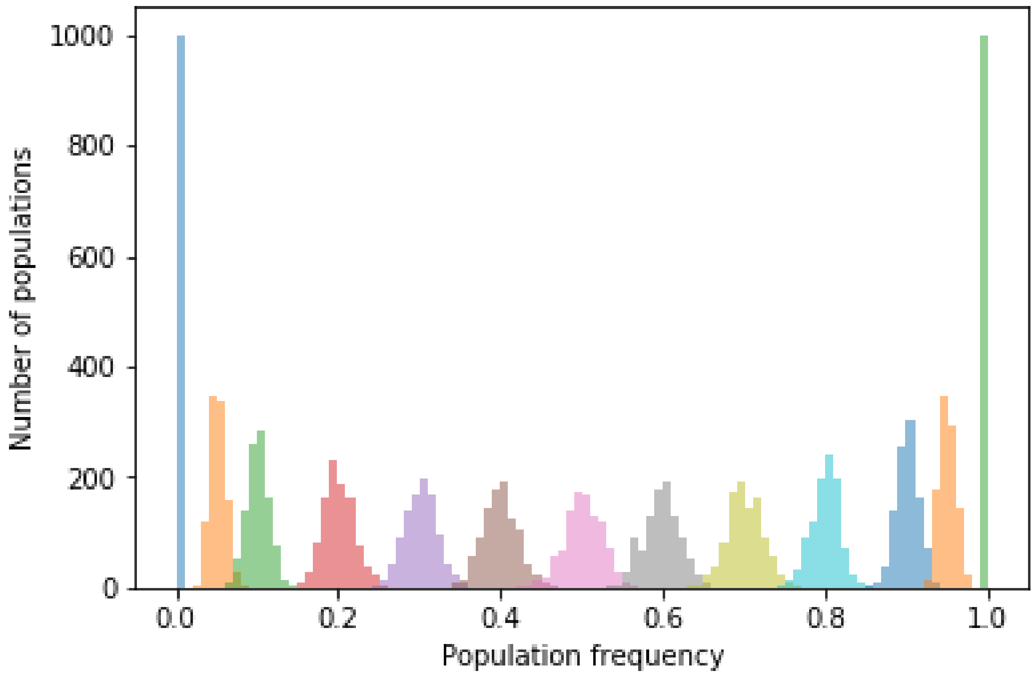


For short times, the expected changes in allele frequencies, $Var\left[E[(x-x_0)^2)\right]$, are larger for smaller population, a crucial result of population genetics.

The next question is: How does the rate of change in allele frequency depend on the initial allele frequency? We can plot the histograms of allele frequency as before:

In [261]:
```
### 21
histograms = []
variances = []
p0_list = np.array([0, 0.05, 0.1, 0.2, 0.3, 0.4, 0.5, .6, .7, .8, 0.9, 0.95, 1])
nGen = 1
for p0 in p0_list:
    pops = [population(nInd, p0) for i in range(1000)]
    [pop.evolve(nGen) for pop in pops]
    sample = [pop.getTraj()[-1] for pop in pops]
    variances.append(np.var(sample))
    histograms.append(plt.hist(sample, 100, alpha=0.5, range=(0,1), label="size %d" %
plt.xlabel("Population frequency")
plt.ylabel("Number of populations")
```

Out[261]: Text(0,0.5,u'Number of populations')



Find the relationship between initial frequency and variance. Again, this can be from the math exercise above, from looking it up, but you can also just try to guess it from the data--it's a simple function.

Tips for guessing:

First, make the plot of variance vs frequency below

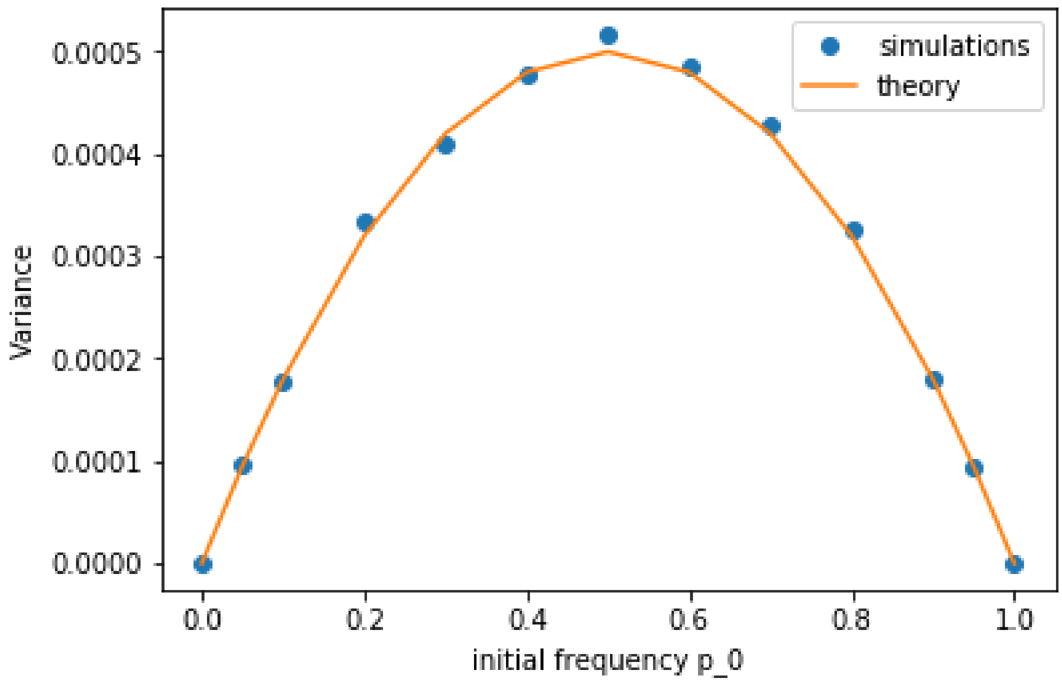
Then consider how much variance there is for p0=0 and p0=1.

Can you come up with a simple function that has these values? Hint: it's simpler than a trigonometric function.

Variance = $(p/N)[1\text{-}p]$

In [263]:
```
### 22
plt.plot(np.array(p0_list), variances, 'o', label="simulations")
plt.plot(np.array(p0_list), np.array([(p/nInd)*(1-p) for p in p0_list]), '-', label="t
plt.ylabel("Variance")
plt.xlabel(r"initial frequency p_0")
plt.legend()
```

Out[263]: <matplotlib.legend.Legend at 0x7f22f3d2dc10>



Can you explain why this function is symmetrical around $p_0 = 0.5$?

Mathematically the function is a second degree polynomial with a critical at 0.5. Since second degree polynomials are symmetric around maxima, the function is symmetric around maxima. Intuitively it can be seen that the probability that the next generation has higher or lower frequency depends directly on the initial frequency and this does not depend on what the alleles represent(allele 0 could be p or 1-p), since they have the same importance the function does not favour any particular allele.

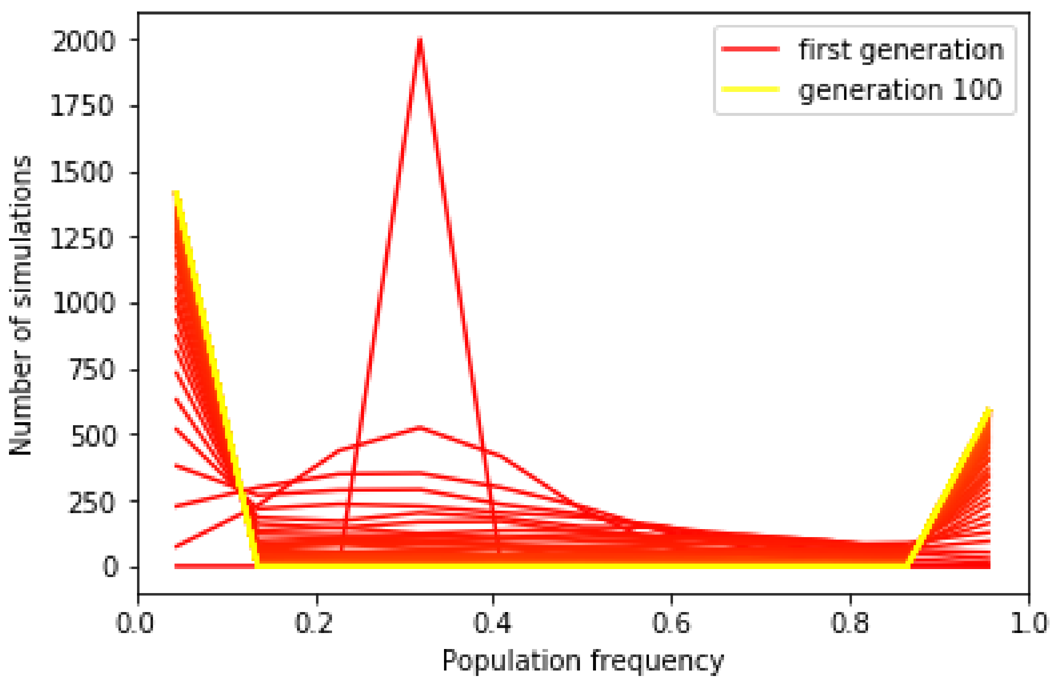
2.2 Mutation

New mutations enter the population in a single individual, and therefore begin their journey at frequency $\frac{1}{N}$. Numerically estimate the probability that such a new mutation will eventually fix (i.e., the probability that the mutation reaches frequency 1) in the population, if no subsequent mutations occur.

In [266]:
```
### 23


nInd = 10
nGen = 100
nRuns = 2000
#enter the initial allele frequency for new mutations
p0 = 0.3
pops = [population(nInd, p0) for i in range(nRuns)]
[pop.evolve(nGen) for pop in pops];
```

We can plot the number of populations at each frequency, as we did above.

```
In [267]: ### 24
          nBins = nInd + 1  # We want to have bins for 0,1,2,...,N copies of the allele.
          proportion_fixed = []  # fixation rate
          for i in range(nGen+1):
              x,y = frequencyAtGen(i, pops);
              if i==0:
                  plt.plot(x, y, color=plt.cm.autumn(i*1./nGen), label="first generation")  # cm
                                                                                   #color wit
              elif i==nGen:
                  plt.plot(x, y, color=plt.cm.autumn(i*1./nGen), label="generation %d"% (nGen,)
              else:
                  plt.plot(x, y, color=plt.cm.autumn(i*1./nGen))

              #we'll consider a population "fixed" if it is in the highest-frequency bin. It's
              #an approximation, but not a bad one if the number of bins is comparable to the
              #population size.
              proportion_fixed.append((i, y[-1]*1./nRuns))

          plt.legend()
          plt.xlabel("Population frequency")
          plt.ylabel("Number of simulations")

Out[267]: Text(0,0.5,u'Number of simulations')
```



Here you should find that most mutations fix at zero frequency--only a small proportion survives.

What is the probability that a new mutation fixes in the population?--solve this problem both mathematically and numerically.

The mathematical part requires almost no calculation or mathematical knowledge, once you think about it in the right way.

Your mathematical solution:

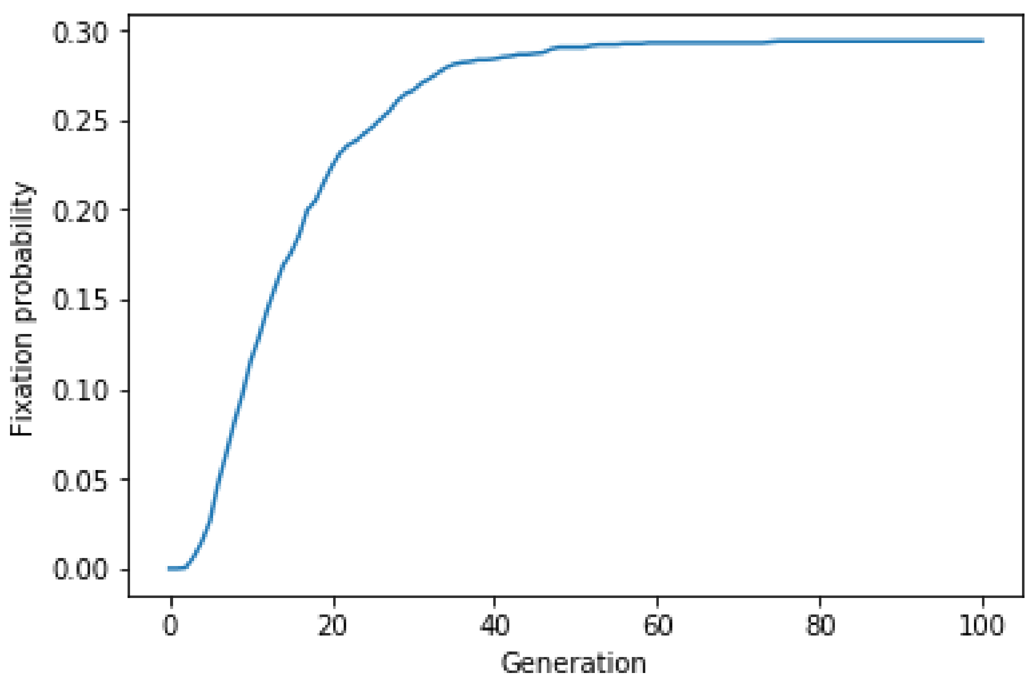
2.2.1 Answer

The probabilty that a mutation fixes is equal to the initial frequency of the mutation. This can be intuitively analysed as all inidividuals after some generations will be descendants of either one type of allele and the probability that initial allele is a given mutation is the mean.

For the computational part, note that we already computed the proportion of fixed alleles vs time in the "proportion_fixed" variable. Make sure that the numerical value agrees with the mathematical expectation.

```
In [270]: ### 25e
          proportion_fixed = np.array(proportion_fixed)
          plt.plot(proportion_fixed[:,0], proportion_fixed[:,1])
          plt.xlabel("Generation")
          plt.ylabel("Fixation probability")
```

```
Out[270]: Text(0,0.5,u'Fixation probability')
```



3 Summary

Some important things that we've seen in this notebook: * The Wright-Fisher model. Despite its simplicity, it is the basic building block of a large fraction of population genetics. * In finite populations, sampling fluctuations are an important driver of allele frequency change. * These sampling fluctuations cause larger frequency changes in smaller populations. * These fluctuations mean that alleles eventually fix one way or another -- We need new mutations to maintain diversity within a population. * For neutral alleles, the probability of new mutations fixing in the population is inversely proportional to the population size

4 Something to think about.

We'll get to selection, recombination, and linkage in the next exercises. In the meantime, you can think about the following:

- Verify numerically that different reproductive models gives similar behavior. You may look up the Moran Model, or come up with your own evolutionary model.
- How much time will it take for a typical new mutation to reach fixation for different population sizes?
- If you add a constant influx of new mutations, how will the distribution of allele frequency look like at any given point in time?