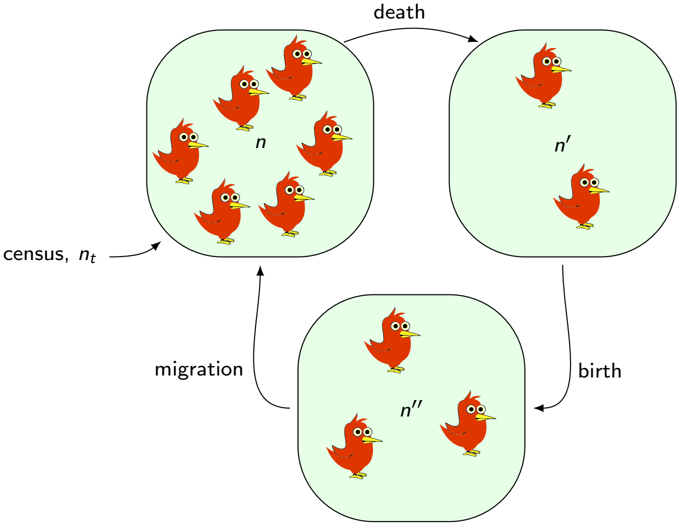
Model Construction

January 28, 2021

1. Formulate the question
   - What do you want to know?
   - Describe the model in the form of a question.
   - Simplify, Simplify!
   - Start with the simplest, biologically reasonable description of the problem.
2. Determine the basic ingredients
   - Define the variables in the model.
   - Describe any constraints on the variables.
   - Describe any interactions between variables.
   - Decide whether you will treat time as discrete or continuous.
   - Choose a time scale (i.e., decide what a time step equals in discrete time and specify whether rates will be measured per second, minute, day, year, generation, etc.).
   - Define the parameters in the model.
   - Describe any constraints on the parameters.

3. Qualitatively describe the biological system

   – Draw a life-cycle diagram for discrete-time models with multiple events per time unit.



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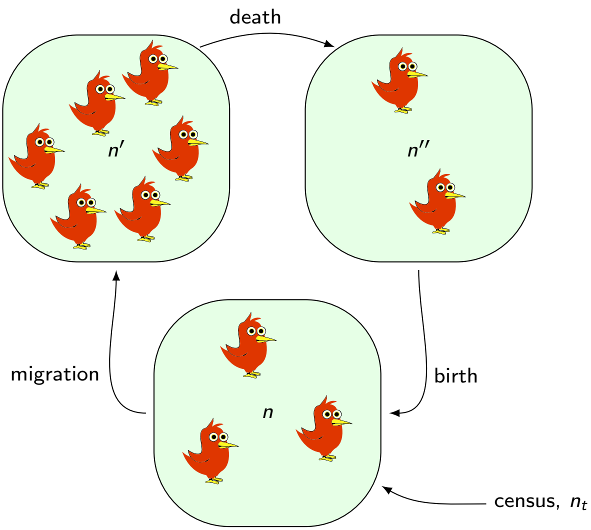
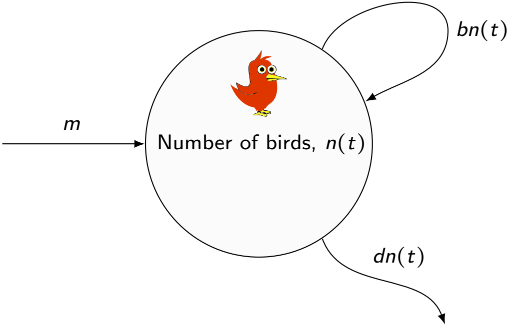


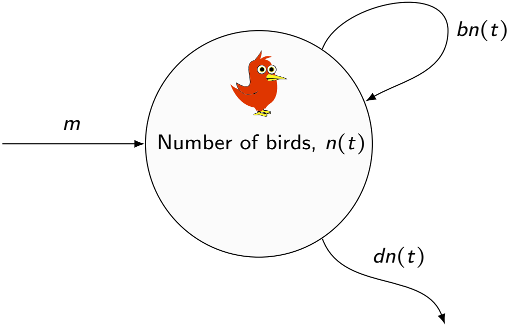
3. Qualitatively describe the biological system

   – Draw a flow diagram to describe changes to the variables over time. For models with many possible events, construct a table listing the outcome of every event.



3. Qualitatively describe the biological system

   – Using the diagrams and tables as a guide, write down the equations. Perform checks. Are the constraints on the variables still met as time passes? Make sure that the units of the right-hand side equal those on the left-hand side.



Continuous time: add rates for arrows coming in and subtract for arrows going out:

$$\frac{dn(t)}{dt} = m + bn(t) - dn(t)$$

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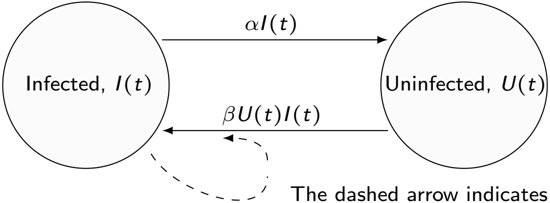
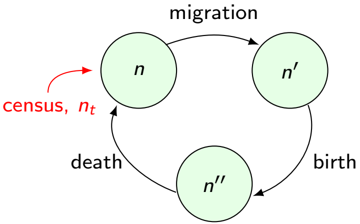


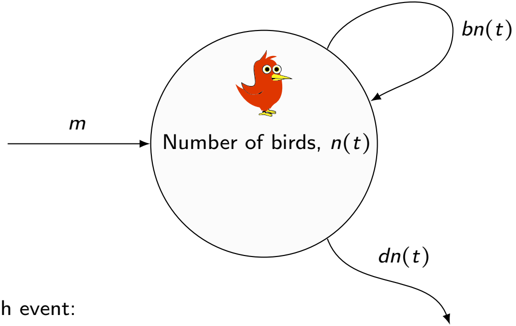
The dashed arrow indicates that the rate above the arrow from $U(t)$ to $I(t)$ also depends on the value of $I(t)$.

$$\frac{dI(t)}{dt} = \beta U(t)I(t) - \alpha I(t)$$

$$\frac{dU(t)}{dt} = \alpha I(t) - \beta U(t)I(t)$$

In **discrete time**, you must take into account the order of events when constructing equations.





First, construct equation for each event:

$$n' = n_t + m$$
$$n'' = n' + bn'$$
$$n_{t+1} = n'' - dn''$$

Next, substite to write n_{t+1} in terms of n_t:

$$\begin{aligned} n_{t+1} &= n'' - dn'' = (n' + bn') - d(n' + bn') = n'(1 + b - d - db) \\ &= (n_t + m)(1 + b - d - db) \end{aligned} \quad (1)$$

4. Analyze the equations
   - Start by using the equations to simulate and graph the changes to the system over time.
   - Choose and perform appropriate analyses.
   - Make sure that the analyses can address the problem.

5. Checks and balances
   - Check the results against data or any known special cases.
   - Determine how general the results are.
   - Consider alternatives to the simplest model.
   - Extend or simplify the model, as appropriate, and repeat steps 2-5.
6. Relate the results back to the question
   - Do the results answer the biological question?
   - Are the results counter-intuitive? Why?
   - Interpret the results verbally, and describe conceptually any new insights into the biological process.
   - Describe potential experiments.

Darwin, in 1859, published the Origin of Species, arguing that organisms evolve over time by natural selection.

As many more individuals of each species are born than can possibly survive, and as, consequently, there is a frequently recurring struggle for existence, it follows that any being, if it vary slightly in any manner profitable to itself, under the complex and sometimes varying conditions of life, will have a better chance of surviving, and thus be naturally selected.

–Charles Darwin (1859)

Natural selection requires three conditions be met:

1. Organisms vary in their traits.
2. Not all individuals survive and certain traits improve fitness.
3. Trait values are inherited.

Parents with characteristics that improve fitness are more likely to have offspring. These characteristics therefore increase in frequency over time leading the population to evolve.

Variations neither useful nor injurious would not be affected by natural selection, and would be left a fluctuating element, as perhaps we see in the species called polymorphic.

–Charles Darwin (1859)

1. Formulate the question

   - **Question:** How do gene frequencies change over time in the absence of natural selection?

   - **Description of the problem:** In a diploid population with two variant alleles at a gene (A and a), how will the frequency, p, of the A allele change over time?

   - We assume that each diploid individual (AA, Aa, and aa) has equal fitness and that individuals reproduce and then die (non-overlapping generations). We also assume that individuals produce haploid gametes that form a gamete pool. Gametes within the gamete pool unite at random to produce the next generation of diploid individuals.

2. Determine the basic ingredients

   - Variables in this model:
     x = frequency of *AA* individuals
     y = frequency of *Aa* individuals
     z = frequency of *aa* individuals

   - Constraints on these variables:

     x, y, z are positive and less than one

     $x + y + z = 1$

   - We will follow the genotype frequencies from one generation to the next, using a discrete-time model with a time scale set to one generation.

   - The frequency of allele *A* among these individuals, $p = x + \frac{y}{2}$.

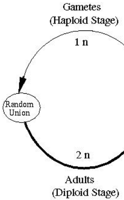
   - The frequency of allele *a* among these individuals, $q = \frac{y}{2} + z$.

   - $p + q = 1$.

   - Because all individuals are equally fit, the gamete allele frequencies are equal to parental allele frequencies.

3. Qualitatively describe the biological system

Gametes unite at random in the gamete pool to produce diploid offspring (life-cycle diagram).



To calculate offspring frequencies, we use a mating table.

		Offspring Frequencies		
Union	Frequency	AA	Aa	aa
$A \times A$	p^2	1		
$A \times a$	pq		1	
$a \times A$	qp		1	
$a \times a$	q^2			1
		p^2	$2pq$	q^2

These are known as the Hardy-Weinberg frequencies.

4. Quantitatively describe the biological system

Union	Frequency	Offspring Frequencies AA	Aa	aa
$A \times A$	p^2	1		
$A \times a$	pq		1	
$a \times A$	qp		1	
$a \times a$	q^2			1
		p^2	$2pq$	q^2

$$x' = p^2 = (x + y/2)^2$$
$$y' = 2pq = 2(x + y/2)(y/2 + z)$$
$$z' = q^2 = (y/2 + z)^2$$

Check: Does $x' + y' + z' = 1$?

5. Analyze the equations

   - Populations not at Hardy-Weinberg reach Hardy-Weinberg equilibrium after only one generation of random mating (as in the above example).
   - The frequency of allele A in the next generation? $p' =$
   - The frequency of allele a in the next generation? $q' =$
   - In the absence of selection and mutation, allele frequencies remain constant. Meiosis and random mating do not, by themselves, change allele frequencies.

6. Checks and balances

- We have made a large number of assumptions. Changing these assumptions can alter the above results

	Hardy-Weinberg attained in one generation	No change in p
With mutation	✓	✗
With selection	✗	✗
With different frequencies in the two sexes	✗	✓
Overlapping generations	✗	✓
Finite population	✗	✗
Individuals rather than games mate randomly	✓	✓

Hardy-Weinberg still holds before selection among juveniles, but not necessarily after selection among adults.

7. Relate the results back to the question

- How do gene frequencies change over time in the absence of natural selection?

  They don't.

- Data Example:

Blood Type	*M*	*MN*	*N*
Genoytpe	*MM*	*MN*	*NN*
Observed freq. in USA	0.292	0.496	0.212

- Are these at or near Hardy-Weinberg equilibrium?

  $x = 0.292, y = 0.496, z = 0.212$

  $p = x + y/2 = 0.540, q = y/2 + z = 0.460$

  $p^2 = 0.2916, 2pq = 0.4968, q^2 = 0.2116$

- The genotype frequencies appear to be very close to Hardy-Weinberg equilibrium!