Continuous Model of Frequency of Phenotype and its Equilibria and Stability

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April 26, 2017

Abstract

Introduction: In class we analysis a genetic population model in discrete time step. And what if want to develop a genetic population model that links a continuous time population dynamics to the genotype and allele frequencies of a single gene with two allele types A and a. With the assumption that the fitness of genotypes differ only in the natural death rate dAA , dAa and daa respectively, and all genotypes have the same birth rate b. The purpose is to explore the question of whether the allele frequencies (associated with a particular gene) change in a given population over time as individuals within that population mate and reproduce, specifically determine the equilibrium and its stability of the allele frequency model and compare it with discrete models.

Start with modeling population change, which is "BIDE" Balance Law for total population size $N(t)$:

$$N(t+\Delta t) = N(t) + Births + Immigration - Deaths - Emigration$$

Then we want to specify the values of B, I, D, and E over the time interval $(t, t+\Delta t)$, and in the assumption we want to develop a genotype and allele frequencies of a single gene with two allele types A and a. Thus we ignore the immigration and emigration. Assuming that the fitness of genotypes differ only in the natural death rate (all genotypes have the same constant birth rate b), and constant per capita death rates d_{AA}, d_{Aa} and d_{aa}. Let N_{AA}, N_{Aa}, N_{aa} represents the number of total population with AA, Aa, aa genotypes separately in the t-generation. Then we have

$$N(t+\Delta t) = N(t) + b\Delta t N(t) - [d_{AA}N_{AA}(t) + d_{Aa}N_{Aa}(t) + d_{aa}N_{aa}(t)]\Delta t$$
$$\frac{dN}{dt} = lim_{\Delta t \to 0}\frac{N(t+\Delta t) - N(t)}{\Delta t} = bN(t) - d_{AA}N_{AA}(t) - d_{Aa}N_{Aa}(t) - d_{aa}N_{aa}(t)$$

Then, we want to determine $\frac{dN_{AA}}{dt}$, and $\frac{dN_{aa}}{dt}$, it is necessary to consider all possible matings, their frequency, and all possible of spring and their frequency.

	AA	Aa	aa
AA	1AA	$\frac{1}{2}$AA $\frac{1}{2}$Aa	1Aa
Aa	$\frac{1}{2}$AA $\frac{1}{2}$Aa	$\frac{1}{4}$AA $\frac{1}{2}$Aa $\frac{1}{4}$aa	$\frac{1}{2}$Aa $\frac{1}{2}$aa
aa	1Aa	$\frac{1}{2}$Aa $\frac{1}{2}$aa	1aa

Let p_{AA}, p_{Aa}, p_{aa} denote the genotype frequencies at time t, that is $p_{AA} = \frac{N_{AA}}{N}, p_{Aa} = \frac{N_{Aa}}{N}, p_{aa} = \frac{N_{aa}}{N}$. Notice that the birth rate for AA is not b, but b times the probability that an individuals offspring is AA, and similarly for aa. Only $\frac{N_{AA}}{dt}$, $\frac{N_{aa}}{dt}$ need to be determine, since $N_{Aa} = N - N_{AA} - aa$.

Applying the result from the above table. We get

$$
\begin{aligned}
N_{AA}(t+\Delta t) &= N_{AA}(t) + b\Delta t N_{AA}(t)(p_{AA} + \frac{1}{2}p_{Aa})\Delta t \\
&\quad + b\Delta t N_{AA}(t)(\frac{1}{2}p_{AA} + \frac{1}{4}p_{Aa})\Delta t - d_{AA}N_{AA}(t)\Delta t \\
\frac{dN_{AA}}{dt} &= lim_{\Delta t\to 0}\frac{N_{AA}(t+\Delta t) - N_{AA}(t)}{\Delta t} \\
\frac{dN_{AA}}{dt} &= bN_{AA}(t)(p_{AA} + \frac{1}{2}p_{Aa}) + bN_{Aa}(t)(\frac{1}{2}p_{AA} + \frac{1}{4}p_{Aa}) - d_{AA}N_{AA}(t) \\
N_{aa}(t+\Delta t) &= N_{aa}(t) + b\Delta t N_{aa}(t)(p_{aa} + \frac{1}{2}p_{Aa})\Delta t \\
&\quad + b\Delta t N_{aa}(t)(\frac{1}{2}p_{aa} + \frac{1}{4}p_{Aa})\Delta t - d_{aa}N_{aa}(t)\Delta t \\
\frac{dN_{aa}}{dt} &= lim_{\Delta t\to 0}\frac{N_{aa}(t+\Delta t) - N_{aa}(t)}{\Delta t} \\
\frac{dN_{aa}}{dt} &= bN_{aa}(t)(p_{aa} + \frac{1}{2}p_{Aa}) + bN_{Aa}(t)(\frac{1}{2}p_{aa} + \frac{1}{4}p_{Aa}) - d_{aa}N_{aa}(t)
\end{aligned}
$$

We denote the allele frequency of A at t time as $p_A(t)$. Want the equilibrium of frequency of phenotype model, firstly determine $\frac{dp_A}{dt}$

$$
\begin{aligned}
p_A(t) &= p_{AA} + \frac{1}{2}p_{Aa} = \frac{N_{AA}(t)}{N(t)} + \frac{N_{Aa}(t)}{2N(t)} \\
&= \frac{N_{AA}(t) + \frac{1}{2}(N(t) - N_{AA}(t) - N_{aa}(t))}{N(t)} \\
&= \frac{N_{AA}(t) - N_{aa}(t)}{2N(t)} + \frac{1}{2}
\end{aligned}
$$

$$
\begin{aligned}
\frac{dp_A}{dt} &= \frac{d\{\frac{N_{AA}(t)-N_{aa}(t)}{2N(t)} + \frac{1}{2}\}}{dt} \\
&= \frac{1}{2}\cdot\frac{(N_{AA}(t) - N_{aa}(t))'\cdot N(t) - N'(t)(N_{AA}(t) - N_{aa}(t))}{N^2(t)}
\end{aligned}
$$

Know from previous that

$$\begin{aligned}
\frac{dN}{dt} &= bN(t) - d_{AA}N_{AA}(t) - d_{Aa}N_{Aa}(t) - d_{aa}N_{aa}(t) \\
\frac{dN_{AA}}{dt} &= bN_{AA}(t)(p_{AA} + \frac{1}{2}p_{Aa}) + bN_{Aa}(t)(\frac{1}{2}p_{AA} + \frac{1}{4}p_{Aa}) - d_{AA}N_{AA}(t) \\
\frac{dN_{aa}}{dt} &= bN_{aa}(t)(p_{aa} + \frac{1}{2}p_{Aa}) + bN_{Aa}(t)(\frac{1}{2}p_{aa} + \frac{1}{4}p_{Aa}) - d_{aa}N_{aa}(t)
\end{aligned}$$

And plug those equations in, we can get

$$\begin{aligned}
(N_{AA}(t) - N_{aa}(t))' &= bN_{AA}(t)(p_{AA} + \frac{1}{2}p_{Aa}) + bN_{Aa}(\frac{1}{2}p_{AA} - \frac{1}{2}p_{aa}) \\
&\quad - bN_{aa}(p_{aa} + \frac{1}{2}p_{Aa}) + d_{aa}N_{aa} - d_{AA}N_{AA} \\
\frac{(N_{AA}(t) - N_{aa}(t))'}{N(t)} &= bp_{AA}(t)(p_{AA} + \frac{1}{2}p_{Aa}) + bp_{Aa}(\frac{1}{2}p_{AA} - \frac{1}{2}p_{aa}) \\
&\quad - bp_{aa}(p_{aa} + \frac{1}{2}p_{Aa}) + d_{aa}p_{aa} - d_{AA}p_{AA}
\end{aligned}$$

$$\begin{aligned}
\frac{dp_A(t)}{dt} &= \frac{(N_{AA}(t) - N_{aa}(t))'}{2N(t)} \\
&- \frac{[bN(t) - d_{AA}N_{AA}(t) - d_{Aa}N_{Aa}(t) - d_{aa}N_{aa}(t)](N_{AA}(t) - N_{aa}(t))}{2N^2(t)} \\
&= \frac{(N_{AA}(t) - N_{aa}(t))'}{2N(t)} \\
&- \frac{1}{2}[b - d_{AA}\frac{N_{AA}(t)}{N(t)} - d_{Aa}\frac{N_{Aa}(t)}{N(t)} - d_{aa}\frac{N_{aa}(t)}{N(t)}](\frac{N_{AA}(t)}{N(t)} - \frac{N_{AA}(t)}{N(t)}) \\
&= \frac{1}{2}\left\{bp_{AA}(p_{AA} + \frac{1}{2}p_{Aa}) + bp_{Aa}(\frac{1}{2}p_{AA} - \frac{1}{2}p_{aa}) - bp_{aa}(p_{aa} + \frac{1}{2}p_{Aa}) + d_{aa}p_{aa} - d_{AA}p_{AA}\right\} \\
&- \frac{1}{2}\{b - d_{AA}p_{AA} - d_{Aa}p_{Aa} - d_{aa}p_{aa}](p_{AA} - p_{AA}) \\
&= \frac{1}{2}\{b[(p_{AA}^2 - p_{aa}^2) + p_{AA}p_{aa} - p_{Aa}p_{aa} - p_{AA} + p_{aa})] \\
&+ d_{aa}(p_{aa} + p_{aa}p_{AA} - p_{aa}^2) + d_{AA}(p_{AA}^2 - p_{AA} - p_{AA}p_{aa}) + d_{Aa}(p_{Aa}p_{AA} - p_{Aa}p_{aa})\} \\
&= \frac{1}{2}\{b[(p_{AA} + p_{aa} + p_{Aa})(p_{AA} - p_{aa}) - p_{AA} + p_{aa}] \\
&+ d_{aa}(p_{aa} + p_{aa}p_{AA} - p_{aa}^2) + d_{AA}(p_{AA}^2 - p_{AA} - p_{AA}p_{aa}) + d_{Aa}(p_{Aa}p_{AA} - p_{Aa}p_{aa})\} \\
&= \frac{1}{2}\left\{d_{aa}(p_{aa} + p_{aa}p_{AA} - p_{aa}^2) + d_{AA}(p_{AA}^2 - p_{AA} - p_{AA}p_{aa}) + d_{Aa}(p_{Aa}p_{AA} - p_{Aa}p_{aa})\right\}
\end{aligned}$$

Then to get the equilibrium p^*, p^* should satisfy the equation $\frac{dp_A(t)}{dt} = 0$, that is

$$\frac{dp_A(t)}{dt} = \frac{1}{2}\{d_{aa}(p_{aa} + p_{aa}p_{AA} - p_{aa}^2) + d_{AA}(p_{AA}^2 - p_{AA} - p_{AA}p_{aa}) + d_{Aa}(p_{Aa}p_{AA} - p_{Aa}p_{aa}\} = 0$$

Let $\frac{d_{AA}}{d_{Aa}} = 1 - s$, $\frac{d_{aa}}{d_{Aa}} = 1 - r$, where $r, s \leq 1$

$$\frac{d_{aa}}{d_{Aa}}(p_{aa} + p_{aa}p_{AA} - p_{aa}^2) + \frac{d_{AA}}{d_{Aa}}(p_{AA}^2 - p_{AA} - p_{AA}p_{aa}) + \frac{d_{Aa}}{d_{Aa}}(p_{Aa}p_{AA} - p_{Aa}p_{aa}) = 0$$

$$(1-r)(p_{aa} + p_{aa}p_{AA} - p_{aa}^2) + (1-s)(p_{AA}^2 - p_{AA} - p_{AA}p_{aa}) + (p_{Aa}p_{AA} - p_{Aa}p_{aa}) = 0$$

$$(p_{aa} + p_{aa}p_{AA} - p_{aa}^2 + p_{AA}^2 - p_{AA} - p_{AA}p_{aa} + p_{Aa}p_{AA} - p_{Aa}p_{aa}) - r(p_{aa} + p_{aa}p_{AA} - p_{aa}^2)$$

$$-s(p_{AA}^2 - p_{AA} - p_{AA}p_{aa}) = 0$$

$$r(p_{aa} + p_{aa}p_{AA} - p_{aa}^2) + s(p_{AA}^2 - p_{AA} - p_{AA}p_{aa}) = 0$$

$$rp_{aa}(1 + p_{AA} - p_{aa}) + sp_{AA}(p_{AA} - 1 - p_{aa}) = 0$$

The equality is always satisfied when $r = s = 0$, that is

$$\left.\begin{aligned} \frac{d_{AA}}{d_{Aa}} &= 1 \\ \frac{d_{aa}}{d_{Aa}} &= 1 \end{aligned}\right\} \Rightarrow d_{AA} = d_{Aa} = d_{aa}$$

$d_{AA} = d_{Aa} = d_{aa}$ means that there is no variation in the deaths rate of different genotypes. The equality $\frac{dp_A}{dt} = 0$ is always satisfied, which means phenotype frequencies remain constant from generation to generation.

What if $d_{AA} = d_{Aa} = d_{aa}$ does not hold, is there still an equilibrium for the model? Since for the equation $rp_{aa}(1 + p_{AA} - p_{aa}) + sp_{AA}(p_{AA} - 1 - p_{aa}) = 0$ there are two variables and only one equation, to solve the equilibrium, we need to find the equilibrium for p_{AA}, and p_{aa} separately.

$$\begin{aligned}
p_{AA} &= \frac{N_{AA}(t)}{N(t)} \\
\frac{dP_{AA}}{dt} &= \frac{N'_{AA}(t)N(t) - N'(t)N_{AA}(t)}{N^2(t)} = \frac{N'_{AA}(t) - N'(t)p_{AA}}{N(t)} \\
&= bp_{AA}(p_{AA} + \frac{1}{2}p_{Aa}) + bp_{Aa}(\frac{1}{2}p_{AA} + \frac{1}{4}p_{Aa}) - d_{AA}p_{AA} \\
&- p_{AA}(b - d_{AA}p_{AA} - d_{Aa}p_{Aa} - d_{aa}p_{aa}) \\
&= b(\frac{1}{4} + \frac{1}{4}p_{AA}^2 + \frac{1}{4}p_{aa}^2 - \frac{1}{2}p_{AA}p_{aa} - \frac{1}{2}p_{AA} - \frac{1}{2}p_{aa}) + d_{AA}(p_{AA}^2 - p_{AA}) \\
&+ d_{Aa}(p_{AA} - p_{AA}^2 - p_{AA}p_{aa}) + d_{aa}p_{AA}p_{aa} \\
&= b(\frac{1}{4} + \frac{1}{4}p_{AA}^2 + \frac{1}{4}p_{aa}^2 - \frac{1}{2}p_{AA}p_{aa} - \frac{1}{2}p_{AA} - \frac{1}{2}p_{aa}) - s(p_{AA}^2 - p_{AA}) - rp_{AA}p_{aa}
\end{aligned}$$

Similarly, we can get

$$\frac{dP_{aa}}{dt} = b(\frac{1}{4} + \frac{1}{4}p_{aa}^2 + \frac{1}{4}p_{AA}^2 - \frac{1}{2}p_{AA}p_{aa} - \frac{1}{2}p_{aa} - \frac{1}{2}p_{AA}) + d_{aa}(p_{aa}^2 - p_{aa})$$
$$+ d_{Aa}(p_{aa} - p_{aa}^2 - p_{aa}p_{AA}) + d_{AA}p_{aa}p_{AA}$$
$$= b(\frac{1}{4} + \frac{1}{4}p_{aa}^2 + \frac{1}{4}p_{AA}^2 - \frac{1}{2}p_{AA}p_{aa} - \frac{1}{2}p_{aa} - \frac{1}{2}p_{AA}) - r(p_{aa}^2 - p_{aa}) - sp_{aa}p_{AA}$$

Then we can find $(p_{AA}, p_{aa}) = (0, 1)$ and $(p_{AA}, p_{aa}) = (1, 0)$ are the solution, thus we know that $p^* = \frac{1}{2} + \frac{p_{AA} - p_{aa}}{2}$, plug in $(0, 1)$ and $(1, 0)$ we can get two possible equilibria $p^* = 0$ and $p^* = 1$. Then we want to see if the equilibria satisfy the equality $\frac{dp_A}{dt} = 0$

First try $p_A = p^* = 0$, then $p_{AA} = 0$ and $p_{aa} = 1$, plug into the equality

$$LHS = rp_{aa}(1 + p_{AA} - p_{aa}) + sp_{AA}(p_{AA} - 1 - p_{aa})$$
$$= r \cdot 1 \cdot (1 + 0 - 1) + s \cdot 0 \cdot (0 - 1 - 1) = 0$$
$$= RHS$$

Similarly, let $p_A = p^* = 1$, then $p_{AA} = 1$ and $p_{aa} = 0$, plug into the equality

$$LHS = rp_{aa}(1 + p_{AA} - p_{aa}) + sp_{AA}(p_{AA} - 1 - p_{aa})$$
$$= r \cdot 0 \cdot (1 + 1 - 0) + s \cdot 1 \cdot (1 - 1 - 0) = 0$$
$$= RHS$$

Hence, both 0 and 1 are also equilibria of the continuous model. Is $p^* = \frac{r}{r+s}$ an equilibrium for our model? Let $p_A = p^* = \frac{r}{r+s}$, then $p_{AA} = (\frac{r}{r+s})^2$ and $p_{aa} = (1 - \frac{r}{r+s})^2$, plug into the equality

$$LHS = rp_{aa}(1 + p_{AA} - p_{aa}) + sp_{AA}(p_{AA} - 1 - p_{aa})$$
$$= r \cdot (1 - \frac{r}{r+s})^2(1 + (\frac{r}{r+s})^2 - (1 - \frac{r}{r+s})^2) + s \cdot (\frac{r}{r+s})^2((\frac{r}{r+s})^2 - 1 - (1 - \frac{r}{r+s})^2)$$
$$= r \cdot (\frac{s}{r+s})^2(1 + \frac{r^2 - s^2}{(r+s)^2}) + s \cdot (\frac{r}{r+s})^2(\frac{r^2 - s^2}{(r+s)^2} - 1)$$
$$= r \cdot (\frac{s}{r+s})^2(\frac{2r}{r+s}) + s \cdot (\frac{r}{r+s})^2(\frac{-2s}{r+s})$$
$$= \frac{2r^2s^2}{(r+s)^2} - \frac{-2s^2r^2}{(r+s)^2}$$
$$= 0 = RHS$$

Thus, $p^* = \frac{r}{r+s}$ is an equilibrium of the model. Recall that In class we consider a discrete model under assumption of different genotypes have different fitness. We define ω_{AA}, ω_{Aa} and ω_{aa} be the survival rates of genotypes AA, Aa and aa. Let $\frac{\omega_{AA}}{\omega_{Aa}} = 1 - s$ and $\frac{\omega_{aa}}{\omega_{Aa}} = 1 - r$, and we find three equilibrium 0, 1 and $p^* = \frac{r}{r+s}$.Compare with the equilibria we get from continuous model, we can conclude that the continuous and discrete models have the same equilibria.

Now we want to analysis the stability for those three equilibria, and wonder if the equilibria in continuous model have the same behaviour in discrete model.

To determine the stability for the equilibira, need to get the Jacobin matrix for p_{AA}, p_{aa}. Let $\widetilde{p_{AA}} = \frac{dP_{AA}}{dt}, \widetilde{p_{aa}} = \frac{dP_{aa}}{dt}$. From above, we know that

$$\begin{aligned}
\frac{dP_{AA}}{dt} &= b(\frac{1}{4} + \frac{1}{4}p_{AA}^2 + \frac{1}{4}p_{aa}^2 - \frac{1}{2}p_{AA}p_{aa} - \frac{1}{2}p_{AA} - \frac{1}{2}p_{aa}) + d_{AA}(p_{AA}^2 - p_{AA}) \\
&\quad + d_{Aa}(p_{AA} - p_{AA}^2 - p_{AA}p_{aa}) + d_{aa}p_{AA}p_{aa} \\
\frac{dP_{aa}}{dt} &= b(\frac{1}{4} + \frac{1}{4}p_{aa}^2 + \frac{1}{4}p_{AA}^2 - \frac{1}{2}p_{AA}p_{aa} - \frac{1}{2}p_{aa} - \frac{1}{2}p_{AA}) + d_{aa}(p_{aa}^2 - p_{aa}) \\
&\quad + d_{Aa}(p_{aa} - p_{aa}^2 - p_{aa}p_{AA}) + d_{AA}p_{aa}p_{AA}
\end{aligned}$$

Partial derivative $\widetilde{p_{AA}}, \widetilde{p_{aa}}$ with respect to p_{AA}, p_{aa} to get the Jacobian matrix.

$$\begin{aligned}
\frac{d\widetilde{p_{AA}}}{dp_{AA}} &= b(\frac{1}{2}p_{AA} - \frac{1}{2}p_{aa} - \frac{1}{2}) + d_{AA}(2p_{AA} - 1) + d_{Aa}(1 - 2p_{AA} - p_{aa}) + d_{aa}p_{aa} \\
\frac{d\widetilde{p_{aa}}}{dp_{AA}} &= b(\frac{1}{2}p_{AA} - \frac{1}{2}p_{aa} - \frac{1}{2}) - d_{Aa}p_{aa} + d_{AA}p_{aa} \\
\frac{d\widetilde{p_{AA}}}{dp_{aa}} &= b(\frac{1}{2}p_{aa} - \frac{1}{2}p_{AA} - \frac{1}{2}) - d_{Aa}p_{AA} + d_{aa}p_{AA} \\
\frac{d\widetilde{p_{aa}}}{dp_{aa}} &= b(\frac{1}{2}p_{aa} - \frac{1}{2}p_{AA} - \frac{1}{2}) + d_{aa}(2p_{aa} - 1) + d_{Aa}(1 - p_{AA} - 2p_{aa}) + d_{AA}p_{AA}
\end{aligned}$$

plug in $(p_{AA}, p_{aa}) = (0, 1)$, we can get

$$\frac{d\widetilde{p_{AA}}}{dp_{AA}}(0,1) = b(0 - \frac{1}{2} - \frac{1}{2}) + d_{AA}(-1) + d_{Aa}(1-1) + d_{aa} = -b - d_{AA} + d_{aa}$$
$$\frac{d\widetilde{p_{aa}}}{dp_{AA}}(0,1) = -b - d_{Aa} + d_{AA}$$
$$\frac{d\widetilde{p_{AA}}}{dp_{aa}}(0,1) = b(\frac{1}{2} - \frac{1}{2}) = 0$$
$$\frac{d\widetilde{p_{aa}}}{dp_{aa}}(0,1) = d_{aa} - d_{Aa}$$
$$\text{Then we can get } J = \begin{bmatrix} -b - d_{AA} + d_{aa} & 0 \\ -b - d_{Aa} + d_{AA} & d_{aa} - d_{Aa} \end{bmatrix}$$

$$\begin{aligned} \frac{dN}{dt} &= bN(t) - d_{AA}N_{AA}(t) - d_{Aa}N_{Aa}(t) - d_{aa}N_{aa}(t) \\ &= N(t)(b - d_{AA}p_{AA} - d_{Aa}p_{Aa} - d_{aa}p_{aa}) \\ &= N(t)(b - d_{aa}) \end{aligned}$$

The two eigenvalue are $\lambda_1 = -b - d_{AA} + d_{aa}, \lambda_2 = d_{aa} - d_{Aa}$. To guarantee the population does not die out, we want $\frac{dN}{dt} > 0 \Rightarrow (b - d_{aa}) > 0$, then we see the $\lambda_1 = -b - d_{AA} + d_{aa} = -(b - d_{aa}) - d_{AA} < 0$, that is $\lambda_1 < 0$, and if $\lambda_2 < 0 \Rightarrow d_{aa} - d_{Aa} < 0 \Rightarrow (1 - r) - 1 = -r < 0 \Rightarrow r > 0$. Thus if $r > 0$, then $p^* = 0$ is a asymptotically stable.

Similarly, let $p^* = 1$, then $(p_{AA}, p_{aa}) = (1, 0)$, and then plug $(p_{AA}, p_{aa}) = (1, 0)$ in $\frac{dN}{dt} = N(t)(b - d_{AA})$, and to guarantee the population does not die out, we want $\frac{dN}{dt} > 0 \Rightarrow (b - d_{AA}) > 0$. Plug $(p_{AA}, p_{aa}) = (1, 0)$ in the Jacobin matrix, we can get

$$J = \begin{bmatrix} d_{AA} - d_{Aa} & -b - d_{Aa} + d_{aa} \\ 0 & -b - d_{aa} + d_{AA} \end{bmatrix}$$

And then $\lambda_2 = -b - d_{aa} + d_{AA} = -(b - d_{AA}) - d_{aa} < 0$, let $\lambda_1 = d_{AA} - d_{Aa} = (1 - s) - 1 = -s < 0 \Rightarrow s > 0$, that is $\lambda_1 < 0, \lambda_2 < 0$. Thus if $s > 0$, then $p^* = 1$ is asymptotically stable.

Let $p^* = \frac{r}{r+s}$, then $(p_{AA}, p_{aa}) = \left((\frac{r}{r+s})^2, (\frac{s}{r+s})^2 \right)$, and $0 < p^* < 1 \Rightarrow < 0 \frac{r}{r+s} < 1 \Rightarrow r < 0$ and $s < 0$, or $r > 0$ and $s > 0$, that is r, s have the same sign. First, we want the population does not die out, plug $\left((\frac{r}{r+s})^2, (\frac{s}{r+s})^2\right)$ in $\frac{dN}{dt}$

$$\begin{aligned}
\frac{dN}{dt} &= N(t)(b - d_{AA}p_{AA} - d_{Aa}p_{Aa} - d_{aa}p_{aa}) > 0 \\
\Rightarrow & b - d_{AA}\cdot(\frac{r}{r+s})^2 - d_{Aa}\cdot\frac{2rs}{(r+s)^2} - d_{aa}(\frac{s}{r+s})^2 > 0 \\
\Rightarrow & b - d_{Aa}\left((1-s)\frac{r^2}{(r+s)^2} + \frac{2rs}{(r+s)^2} + (1-r)\frac{s^2}{(r+s)^2}\right) > 0 \\
\Rightarrow & b - d_{Aa}\left(\frac{r^2 - sr^2 + 2rs + s^2 - rs^2}{(r+s)^2}\right) > 0 \\
\Rightarrow & b - d_{Aa}\left(\frac{r+s-rs}{r+s}\right) > 0
\end{aligned}$$

To analysis the stability of the equilibrium, plug $\left((\frac{r}{r+s})^2, (\frac{s}{r+s})^2\right)$ in Jacobin matrix,we can get.

$$\begin{aligned}
&\frac{d\widetilde{p_{AA}}}{dp_{AA}}\left((\frac{r}{r+s})^2, (\frac{s}{r+s})^2\right) \\
&= b\frac{1}{2}\cdot(\frac{r-s}{r+s} - 1) + d_{AA}(2\cdot(\frac{r}{r+s})^2 - 1) + d_{Aa}(1 - 2(\frac{r}{r+s})^2 - (\frac{s}{r+s})^2) + d_{aa}(\frac{s}{r+s})^2 \\
&= \frac{-bs}{r+s} + d_{AA}\cdot\frac{r^2 - s^2 - 2rs}{(r+s)^2} + d_{Aa}\cdot\frac{2rs - r^2}{(r+s)^2} + d_{aa}\cdot\frac{s^2}{(r+s)^2} \\
&= \frac{-bs}{r+s} + d_{Aa}\cdot\left(\frac{(1-s)(r^2 - s^2 - 2rs) + 2rs - r^2 + (1-r)(s^2)}{(r+s)^2}\right) \\
&= \frac{-bs}{r+s} + d_{Aa}\cdot\frac{rs^2 - sr^2 + s^3}{(r+s)^2} \\
&\frac{d\widetilde{p_{aa}}}{dp_{AA}}\left((\frac{r}{r+s})^2, (\frac{s}{r+s})^2\right) = \frac{-bs}{r+s} - d_{Aa}\frac{s^2 + (1-s)s^2}{(r+s)^2} = \frac{-bs}{r+s} - d_{Aa}\frac{s^3}{(r+s)^2} \\
&\frac{d\widetilde{p_{AA}}}{dp_{aa}}\left((\frac{r}{r+s})^2, (\frac{s}{r+s})^2\right) = \frac{-br}{r+s} - d_{Aa}\cdot\frac{r^3}{(r+s)^2} \\
&\frac{d\widetilde{p_{aa}}}{dp_{aa}}\left((\frac{r}{r+s})^2, (\frac{s}{r+s})^2\right) = \frac{-br}{r+s} + d_{Aa}\cdot\frac{(1-r)(2s^2 - (r+s)^2) + (2rs - s^2) + (1-s)r^2}{(r+s)^2} \\
&= \frac{-br}{r+s} + d_{Aa}\cdot\frac{r^3 + r^2 s - rs^2}{(r+s)^2}
\end{aligned}$$

$$J = \begin{bmatrix} \frac{-bs}{r+s} + d_{Aa}\cdot\frac{rs^2 - sr^2 + s^3}{(r+s)^2} & \frac{-br}{r+s} - d_{Aa}\cdot\frac{r^3}{(r+s)^2} \\ \frac{-bs}{r+s} - d_{Aa}\frac{s^3}{(r+s)^2} & \frac{-br}{r+s} + d_{Aa}\cdot\frac{r^3 + r^2 s - rs^2}{(r+s)^2} \end{bmatrix}$$

$$Tr(J) = \frac{-bs}{r+s} + d_{Aa} \cdot \frac{rs^2 - sr^2 + s^3}{(r+s)^2} + \frac{-br}{r+s} + d_{Aa} \cdot \frac{r^3 + r^2 s - rs^2}{(r+s)^2} = -b + d_{Aa} \cdot \frac{r^3+s^3}{(r+s)^2}$$
$$= -b + d_{Aa} \cdot \frac{r^2+s^2-rs}{r+s} = -(b - d_{Aa} \cdot \frac{r+s-rs}{r+s}) + d_{Aa} \cdot \frac{r(r-1)+s(s-1)}{r+s}$$

Since $b - d_{Aa}\left(\frac{r+s-rs}{r+s}\right) > 0$, then $-\left(b - d_{Aa}\left(\frac{r+s-rs}{r+s}\right)\right) < 0$. $r, s < 1 \Rightarrow r-1 < 0, s-1 < 0$, since r and s have the same sign we only need to consider 2 case. When $r, s < 0$ then $r+s < 0$ and $r(r-1)+s(s-1) > 0 \Rightarrow d_{Aa} \cdot \frac{r(r-1)+s(s-1)}{r+s} < 0$. When $r, s > 0$, then $r+s > 0$ and $r(r-1)+s(s-1) < 0$ $\Rightarrow d_{Aa} \cdot \frac{r(r-1)+s(s-1)}{r+s} < 0$. For both case $r(r-1)+s(s-1) < 0 \Rightarrow d_{Aa} \cdot \frac{r(r-1)+s(s-1)}{r+s} < 0$, and known that $-\left(b - d_{Aa}\left(\frac{r+s-rs}{r+s}\right)\right) < 0$, then

$$Tr(J) = -b + d_{Aa} \cdot \frac{r^2+s^2-rs}{r+s} = -(b - d_{Aa} \cdot \frac{r+s-rs}{r+s}) + d_{Aa} \cdot \frac{r(r-1)+s(s-1)}{r+s} < 0$$

$$det(J) = \left(\frac{-bs}{r+s} + d_{Aa} \cdot \frac{rs^2 - sr^2 + s^3}{(r+s)^2}\right) \cdot \left(\frac{-br}{r+s} + d_{Aa} \cdot \frac{r^3 + r^2 s - rs^2}{(r+s)^2}\right)$$
$$- \left(\frac{-bs}{r+s} - d_{Aa} \frac{s^3}{(r+s)^2}\right) \cdot \left(\frac{-br}{r+s} - d_{Aa} \cdot \frac{r^3}{(r+s)^2}\right)$$
$$= \frac{b^2 rs}{(r+s)^2} + bd_{Aa}\left(\frac{2r^2s^2}{(r+s)^3}\right) + d_{Aa} \cdot \frac{rs(rs - r^2 + s^2)(r^2 + rs - s^2)}{(r+s)^4}$$
$$- \left(\frac{b^2 rs}{(r+s)^2} + bd_{Aa} \frac{sr^3 + rs^3}{(r+s)^3} + d_{Aa}^2 \frac{r^3 s^3}{(r+s)^4}\right)$$
$$= -bd_{Aa}\left(\frac{rs(r-s)^2}{(r+s)^3}\right) + d_{Aa}^2 \cdot \frac{rs(r^2-s^2)^2}{(r+s)^4}$$

Since r, s have the same sign $\Rightarrow rs > 0 \Rightarrow d_{Aa}^2 \cdot \frac{rs(r^2-s^2)^2}{(r+s)^4} > 0$, and also $b > 0, d_{Aa} > 0$, $\frac{(r-s)^2}{(r+s)^2} > 0$, then the sign of $-bd_{Aa}\left(\frac{rs(r-s)^2}{(r+s)^3}\right)$ is depend on $-\frac{1}{r+s}$. And we want $det(J) > 0$, that is $-bd_{Aa}\left(\frac{rs(r-s)^2}{(r+s)^3}\right) + d_{Aa}^2 \cdot \frac{rs(r^2-s^2)^2}{(r+s)^4} > 0$, since $d_{Aa}^2 \cdot \frac{rs(r^2-s^2)^2}{(r+s)^4} > 0$, we want $-bd_{Aa}\left(\frac{rs(r-s)^2}{(r+s)^3}\right) > 0 \Rightarrow -\frac{1}{r+s} \Rightarrow r+s < 0$, and we know from previous that r and s have the same sign, then to satisfy $r+s < 0$, $r < 0, s < 0$.

Since $det(J) = \lambda_1 \cdot \lambda_2$ and $Tr(J) = \lambda_1 + \lambda_2$, then $det(J) > 0$, and $Tr(J) < 0$ indicate that the real part of two eigenvalues of Jacobian matrix are negative. Thus, we can conclude that if $r < 0, s < 0$, then $p^* = \frac{r}{r+s}$ is asymptotically stable.

$r > 0 \Rightarrow 1 - r < 1 \Rightarrow \frac{d_{aa}}{d_{Aa}} < 1 \Rightarrow d_{aa} < d_{Aa}$, $s > 0 \Rightarrow 1 - s < 1 \Rightarrow \frac{d_{AA}}{d_{Aa}} < 1 \Rightarrow d_{AA} < d_{Aa}$, and $r < 0 \Rightarrow d_{aa} > d_{Aa}$, $s < 0 \Rightarrow d_{AA} > d_{Aa}$. Thus, if $d_{aa} < d_{Aa}, p^* = 0$ is an asymptotically stable; if $d_{AA} < d_{Aa}$, $p^* = 1$ is an asymptotically stable; if $d_{Aa} < min(d_{AA}, d_{aa})$, then $p^* = \frac{r}{r+s}$ is an asymptotically stable.

Recall that for discrete model if $\omega_{aa} > \omega_{Aa}$, $p^* = 0$ is asymptotically stable; if $\omega_{AA} > \omega_{Aa}$, $p^* = 1$ is asymptotically stable;if $\omega_{Aa} > min\{\omega_{AA}, \omega_{aa}\}$, $p^* = \frac{r}{r+s}$ is asymptotically stable ($\omega_{AA}, \omega_{Aa}, \omega_{aa}$ represents different fitness of genotypes). Since for our model the fitness of genotypes differ only in the natural death rate and smaller death rate indicate a greater fitness rate. Thus we observed that the continuous and discrete models have the same equilibria and stability.

Conclusion

The model of preceding paper are examined the allele frequencies under the condition that different genotypes have different fitness. There is three equilibria for the model 0, 1 and $\frac{r}{r+s}$. If $r > 0(d_{aa} < d_{Aa})$, then $p^* = 0$ is an asymptotically stable. If $s > 0(d_{AA} < d_{Aa})$, then $p^* = 1$ is asymptotically stable If $r, s < 0(d_{Aa} < min(d_{AA}, d_{aa})$, $p^* = \frac{r}{r+s}$ is locally asymptotically stable. And those equilibria and stability are the same with what we get in class under the same condition but with a discrete population model.

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