

# **Genetic homogeneity, complex dynamics and founder flush**

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## ***Introduction***

A change in population size is a source of perturbation to the genetic composition of a population. Several theories incorporate population dynamics to scenarios of genetic change. Most outstandingly, founder-flush speciation considers repeated crash-growth cycles of population dynamics as a source of diversification (1). Founder-flush scenarios incorporate two repeated episodes: a founder phase, in which population size is abruptly reduced and a flush phase, in which population size increases. The increase in homozygosity (that is genetic homogeneity) due to repeated bottlenecks can expose previously hidden recessive alleles to new selective environments. Henceforth, the genetic change due to population dynamics could produce phenotypic divergence, if accompanied of environmental change. A problem to founder-flush scenarios is that repeated bottlenecks reduces substantially population's response to selection in new environments, due to decreasing heterozygosity. In words of Cheverud, this situation result in an evolutionary conundrum, since the homozygosity required to change the genetic environment of the population also limits the heritable additive genetic variance, needed to respond to new selection scenarios (2).

Theoretical work had pointed a solution to this problem. Following a bottleneck the genetic variance of a population might not be reduced, but augmented (3-6). The shared mechanism in those models is the conversion of epistatic variance into additive variance. This conversion provides support for founder flush theories.

The population dynamics used in these models has not been object of detailed analysis. The seminal paper from Goodnight (4) and the recent paper of Lopez-Fanjul and coworkers (6) mentioned repeated bottlenecks, without specify generational time between them. Other models consider the effect of one bottleneck, and the following “flush” phase (5). It is still to be answered which are the precise population dynamics that sustain variance increase, in founder flush scenarios. Partly, this question has been explored in a series of papers by Maruyama and Fuerst. (7-9). They did specify cyclic population dynamics, in terms of bottleneck sizes and frequencies; and in terms of the extent of “flush” phases. But their genetic models did not include epistasis nor different of population dynamics, just some types of cycles. Moreover, the cycles explored lacked any ecological justification. It is hard to connect their population dynamics with a defined ecological situation.

The objective of the present note is to evaluate the dynamics of genetic heterogeneity -heterozygosity- under well defined population dynamics, including epistatic interactions among genes. For that I use the formulation of heterozygosity developed by Goodnight (4), which considers additive by additive

epistasis. Other forms of epistasis remains to be analyzed. For modeling population dynamics I use the well known Ricker's equation (10). Here I precise which demographic circumstances, resembling founder-flush scenarios, allows some recovery of heterozygosity.

## ***Models and its analysis***

### **1) Homozygosity**

Consider a single locus in a randomly mating diploid population with discrete generations and effective population size  $N$ . Homozygosity ( $J_1$ ) or identity by descent, can be defined as the probability that a gamete has two alleles produced by the same parent. The progeny is produced by random sampling (with replacement) of pairs of gametes from a finite gamete pool to which each parent contributed equally. Since  $N$  diploid parents have  $2N$  genes at a single locus, two gametes have a chance  $1/2N$  of carrying identical genes. The chance for a gamete to carry two different parental genes is then  $1-1/2N$ . When a gamete carries identical genes, they are considered identical by descent. The probability that this occurs when the genes are different in the current generation is  $J_1(t)$ , the homozygosity carried from the previous generation. Assembling these considerations gives:

$$J_1(t) = \frac{1}{2N_{t-1}} + (1 - \frac{1}{2N_{t-1}})J_1(t) \quad (1)$$

for the homozygosity  $J_t$  as a function of the homozygosity  $J_{t-1}$  and the population size  $N_{t-1}$  in the previous generation (see Crow and Kimura, 1970 for details).

To include the effect of the mutation rate, following Nei et al (1975), I assumed that each new mutation is different from the preexisting alleles in the population.

Denoting the mutation rate by  $\nu$ , this yields:

$$J_1(t) = (1 - \nu)^2 \times \frac{1}{2N_{t-1}} + \left(1 - \frac{1}{2N_{t-1}}\right) J_1(t-1) \quad (2)$$

Nei et al (1975) did use Equation 2 as a starting point to derive particular approximations, adapted to each population dynamic scenario analyzed. Here, I do not make any further approximations. Instead I assume a certain population dynamic, that yields a time series of  $N_t$ , and then I calculate the corresponding heterozygosity at each time step, using Equation (2).

Goodnight derives an equation to calculate heterozygosity of two loci (4). This is the equivalent of Equation (1) for a two locus descendent measure, i.e. the probability that the genes at both loci are simultaneously identical by descent. Besides, two measures more are needed to cover the dynamics of homozygosity in two-loci cases. There must be a descendent measure among two-locus gene pairs in which one gene pair comes from a single gamete in one individual and the other gene pair comes from separate gametes in a second individual. And there must be another descendent measure in which one gene pair comes from separate gametes in one individual, and the other gene pair comes from separate gametes in a second individual. To keep with the notation of Goodnight, we will call the homozygosity for two loci  $J_{11}$  and the two other measures  $\gamma_{11}$  and

$\delta_{11}$  respectively. The equations for their dynamics follows (Equations 25, 26 and 27 in (4)):

$$F_{11}(t+1) = \frac{1}{N_t} \left\{ \frac{[1+F_{11}(t)]r^2 + (1-r)^2}{2} + 4F_1(t)r(1-r) \right. + \\ \left. + \left(1 - \frac{1}{N_t}\right) \left[ F_{11}(t)(1-r)^2 + 2\gamma_{11}(t)r(1-r) + \delta_{11}(t)r^2 \right] \right\} \quad (3)$$

$$\gamma_{11}(t+1) = \frac{1}{N_t} \frac{1+2J_1(t)+J_{11}(t)}{4} + \frac{2(N_{t-1}-1)}{N_{t-1}^2} \frac{J_1(t)+\gamma_{11}(t)}{2} + \\ + \frac{N_{t-1}-1}{N_{t-1}^2} \frac{J_{11}(t)(1-r)+\gamma_{11}(t)+\delta_{11}(t)r}{2} + \quad (4) \\ + \frac{(N_{t-1}-1)(N_{t-1}-2)}{N_{t-1}^2} [\gamma_{11}(t)(1-r)+\delta_{11}(t)r].$$

$$\delta_{11}(t+1) = \frac{1}{N_t^3} \frac{1+2J_1(t)+F_{11}(t)}{4} + \frac{4(N_t-1)}{N_t^3} \frac{J_1(t)+\gamma_{11}(t)}{2} + \\ \frac{2(N_t-1)}{N_t^3} \frac{J_{11}(t)+2\gamma_{11}(t)+\delta_{11}(t)}{4} + \frac{(N_t-1)}{N_t^3} \frac{1+2J_1(t)+\delta_{11}(t)}{4} + \quad (5) \\ + \frac{4(N_t-1)(N_t-2)}{N_t^3} \frac{\gamma_{11}(t)+\delta_{11}(t)}{4} + \frac{2(N_t-1)(N_t-2)}{N_t^3} \frac{J_1(t)+\delta_{11}(t)}{2} + \\ + \frac{(N_t-1)(N_t-2)(N_t-3)}{N_t^3} [\delta_{11}(t)].$$

In this set of equations, the recombination rate appears as  $r$ . The same considerations of (11) can be used to incorporate the effects of mutation in Goodnight's formula for  $F_{IT}$ . A multiplicative  $(1-v)^2$  term is added in Equation (3), to explore mutation rates. The set of equations (2), (3), (4) and (5) conform a closed representation of homozygosity, for a two locus situation.

## 2) Population dynamics

To create the time series for  $N_t$ , I used the Ricker equation (10). It considers  $N_{t+1}$  a product of  $N_t$  times a fitness function  $f(N_t)$ , which introduces density-dependent effects.

$$N_{t+1} = N_t \lambda e^{-qN_t} \quad (6)$$

$\lambda$  is the intrinsic growth rate of the population,  $q$  is considered to be a measure of how well individuals cope with competition. There is a unique equilibrium point  $N^* > 0$  that satisfies  $f(N^*) = 1$  (10). The modulus of the slope of the Ricker equation gives its dynamics, when evaluated at  $N^*$  (12). The slope at equilibrium of Ricker equation at  $N^*$  is

$$\frac{d}{dN}(N^*) = 1 - qN^* \quad (7)$$

Given a fixed  $N^*$ , changes in  $q$  produce different dynamical behaviors. Increasingly high values of  $q$  produce the well-known period-doubling route to chaos. A useful reparametrization of Ricker's equation includes the population

size at the equilibrium as a parameter. The definition  $N_{t+1} = N_t = N^*$  gives the following expression:

$$N^* = \frac{Ln\lambda}{q} \quad (8)$$

Using (8), Equation (6) takes the form:

$$N_{t+1} = N_t e^{q(N^* - N_t)} \quad (9)$$

To compare scenarios with equilibrium dynamics to those with complex dynamics, it is useful to keep the mean density of the population trajectory constant. This can be done in the Ricker equation by fixing  $N^*$  at a certain value, because in a population that neither goes extinct nor grows to infinity, the geometric mean of the fitness function is equal to one. In other words:

$$\lim_{k \rightarrow \infty} \left( \prod_k e^{q(N^* - N)} \right)^{\frac{1}{k}} = 1 \quad (10)$$

taking logarithms

$$\frac{1}{k} \sum_k (N^* - N) = 0 \quad (11)$$

finally

$$\frac{1}{k} \sum_k N = N^* \quad (12)$$

Therefore the mean population size is always equal to the population size at equilibrium, independent of whether this equilibrium is stable or not.

This property of the Ricker equation justifies its use in the following, because the equality between the population size at equilibrium, an explicit parameter of the model, and the average population size eliminates the possibility of spurious

estimates of homozygosity due to increases in average population size when the dynamical behavior changes.

Equations (2) to (5) together with Equation (9) are a discrete dynamical system. Its analysis was performed through bifurcation diagrams, which describe the behavior of a system with different sets of parameters. A bifurcation diagram is constructed iterating a dynamical system long enough time to discard transients, and afterwards plotting the values of the response variables as a function of the independent variables. Henceforth, bifurcation plots allows me to analyze the behavior of a dynamical system as function of one of its variables. In this work, I focus mainly on population dynamics and on mutation rates, as the principal factors that determine the dynamics of homozygosity. Recombination rate was set to  $\frac{1}{2}$ . In the cases in which population dynamics is studied, variations in  $q$  and fixed values of mutation rates are used. In the cases in which the mutation rate is studied, variations in  $v$  and fixed values of  $q$  are investigated.

## ***Results***

### **1) Mutation rate**

To study the effect of variations in the mutation rate, I constructed 3 bifurcation plots of the mutation rate, using three different fixed values of  $q$ , corresponding to stable, cyclic and chaotic populations dynamics, and varying the mutation rate. Bifurcation plots presented here were done plotting the last 20 values of the system after  $10^4$  generations. Some simulations were carried out to  $10^8$  generations, and the results obtained shown that the values discussed here are

qualitatively and quantitatively stable, and not an artifact of the generation time. Figure 1a plots homozygosity as  $F_1$  and Figure 1b plots homozygosity as measured by  $F_{11}$ .

Figure 1

Figure 1 points out differences between the homozygosity resulting from chaotic dynamics and that resulting from stable or cyclical population dynamics. With stable and cyclic population dynamics, identity by descent is high with low mutation rates, but starting with a mutation rate of approximately  $10^{-5}$ ,  $F$  drops to low levels. If chaotic population dynamics are assumed, higher mutation rates (almost two orders of magnitude higher) are needed for  $F$  to decline. This result is not surprising. Chaotic population dynamics had a higher variance in population numbers, so it is according to classic theory that this population dynamics would maintain low levels of heterozygosity for a broad range of mutation rates.

To provide an analytical account of the sigmoidal shape of homozygosity as a function of mutation rate (Figure 1), I calculated the asymptotic value of  $F_t$ , for the case of stable population dynamics. Beginning with equation 2 and supposing that  $F_{t+1} = F_t = F^*$  and  $N_{t+1} = N_t = N^*$ , the following equation is obtained after some algebra (derived also in (13)).

$$F_1^* = \frac{(1 - \nu)^2}{2N^* - (1 - \nu)^2(2N^* - 1)} \quad (10)$$

This function has a sigmoidal shape, which explains the shape obtained through simulations (Figure 1). The inflection point of the approximated sigmoid corresponds to a critical value of the mutation rate because where the equilibrium value  $F_1^*$  experiences a qualitative change. This critical mutation rate is a function of the population size at equilibrium. For the chaotic case, it is not possible to obtain an analytic derivation analogous to Equation 10, but the simulations suggest that the shape of the function is the same. For  $F_{11}$  the resulting formula is unwieldy, but behaves similarly, as simulations indicated.

So far I have obtained results according with standard theory and I provide some analytical reasons for aspects not covered before, as the shape of response of heterozygosity to mutation rate. Lets move to less intuitive results.

Notice that for a broad range of mutation rates, the pattern of response of  $F_1$  and  $F_{11}$  to mutation rate and population dynamics are similar. Nevertheless, two differences are worth noticing. After a critical point (circle A in Figure 1b) the heterozygosity with cyclic populations dynamics is higher than the heterozygosity under stable population dynamics. Moreover, in extreme mutations rates, (circle B in Figure 1b) the mayor heterozygosity occurs under chaotic dynamics. This results contradicts the common knowledge, since population dynamics with higher variance in population size are expected to produce higher homozygosity.

## **2) Population dynamics**

To analyze the whole range of dynamical behaviors of the system, the bifurcation diagram for population dynamics and the related heterozygosity values are

shown in Figure 2. Here I assume a mutation rate of  $10^{-6}$ . The dots plotted correspond to 100 values of the system, after  $10^4$  generations. The population sizes are plotted as individual dots, and the values of homozygosity as  $F_1$  and  $F_{11}$  are connected by two lines. Figure 2 shows the transition from simple dynamics, in which the final population sizes are the same ( $\approx q < 0.0002$ ), to cyclical dynamics with two point attractors ( $0.0002 < q < 0.00025$ ), to more complex dynamics with several points attractors ( $0.000275 < q < 0.00031$ , and the next chaotic window).

Figure 2

The bifurcation diagrams and its related  $F$  values underscores the relation among population dynamics and changes in homozygosity. As population dynamics become more complex, homozygosity after  $10^4$  generations is higher. This result is expected, since from Fisher on we know that the expected heterozygosity is the harmonic mean of the population sizes (14). More complex population dynamics have a higher harmonic mean. I have calculated the correlation among the harmonic mean of each time series and the resulting homozygosity value, obtaining correlation values higher than .8 for harmonic mean and  $F_1$ .

In despite of the expected relation between  $F_1$  and the harmonic mean of population sizes, the interesting result of Figure 2 comes from the comparison of behaviors of  $F_1$  against  $F_{11}$ . Even tough they behave quite similarly for a range of  $q$  values, they diverge for high values of  $q$ , in the range of extremely complex

population dynamics. Notice that  $F_1$  increases with  $q$ , but at the higher  $q$  values,  $F_{11}$  recedes to lower values. So, a two-locus measure of homozygosity behave differently than one-locus measurements of homozygosity, if the population undergoes highly fluctuating population dynamics. This is to say that the conditions in which epistasis elicit heterozygosity are highly complex population dynamics.

## ***Discussion***

All through this note, complex population dynamics appears as the source of unsuspected behaviors. Even though founder-flush is conceptually connected to chaotic dynamics, since both phenomena include extremely fluctuating population sizes, a relevant question holds: Are chaotic dynamics merely a mathematical consequence of a big growth rate in an un-real equation, without relevance to natural processes? While this topic is under debate, recent techniques of time series analysis suggest that chaotic behavior might be a more common feature of natural populations than previously believed. (15). On the other side, laboratory work from (16), has shown hard evidence for the existence of nonlinear and chaotic behavior in laboratory populations.

In any case, the introduction of complexity in the understanding of heterozygosity' dynamics arises from consider that the population dynamics of founder flush is adequately modeled by chaotic dynamics. Founder flush scenarios were initially described as "boom-and-bust dynamics" (17). Now we know that an adequate

description of “boom-and-bust dynamics” is provided by complex population dynamics. For chaotic dynamics to occur in ecological scenarios, we must have high rates of population growth, coupled with strong population size regulation, able to produce population crashes. Then we have a connection among complex population dynamics and founder-flush scenarios. Most interestingly, the counter-intuitive results obtained occurred under chaotic population dynamics.

After sustain the analysis of chaotic dynamics as a source of founder-flush population dynamics, lets focus in the dynamics of  $F_1$ , the single-locus measurement of homozygosity. In a still quoted paper, Nei and coworkers (11) predict high homozygosity for mutation rates of  $10^{-6}$ . I check this prediction under stable population dynamics, and add that cyclic (as among others (9,18)) and chaotic dynamics produce even higher levels of homozygosity. I show under which mutation rates heterozygosity can be maintained with highly fluctuating population sizes. Even though these results haven't been presented before, they are easily derivable from standard theory, as fluctuating population numbers increases the harmonic mean of a time series of population numbers.

Now, lets move on to the two locus measurement of homozygosity,  $F_{11}$ . If we consider standard theory, we will predict that for more complex dynamics even epistatic measurements of homozygosity will be higher. But if we consider the idea of conversion of epistatic variance into additive variance through bottlenecks, we can expect in more complex dynamics more heterozygosity. Indeed, for most of the chaotic range of population dynamics, we observe that as the dynamics becomes more complex, the heterozygosity decreases, as

standard theory predicts. But, after certain level of complexity in population dynamics, (extreme succession of bottlenecks and fast population growth) the behavior of the two loci measures of homozygosity departs from the behavior of the one-locus measures, and become less homozygous. Considering my detailed analysis of population dynamics behaviors we should predict that only extreme fluctuating population sizes are able to release heterozygosity, and not just repeated bottlenecks, as previously claimed.

To understand this result we have to consider two factors determining heterozygosity. On one side, we have the effect of fluctuating population size, which decreasing the harmonic mean of population sizes decreases the expected heterozygosity. On the other side, we have the heterozygosity due to epistatic interactions after each bottleneck (4). My simulations make apparent that only in a restricted set of conditions (highly chaotic conditions), epistasis is able to counteract the homozygosity due to population size fluctuations.

This note does not consider all the possible forms of epistatic interactions. Recent work had cover a variety of epistatic interactions and their importance to heterozygosity dynamics (6). The exploration of the plethora of genetic interactions is work to be done. In this brief note, I focus in the detail of the population dynamics behaviors. I have pointed to the interaction among population dynamics and one genetic structure, additive by additive epistatic interactions. It is my believe that future work including other forms of epistasis will produce other patterns of heterozygosity dynamics.

## ***Bibliography***

<sup>1</sup>H. L. Carson and A. R. Templeton. Genetic revolutions in relation to speciation phenomena: the founding of new populations. *Annual Review of Ecology and Systematics* ,**15**, 97-131 (1984).

<sup>2</sup>J.M. Cheverud, T.T. Vaughn, S.L. Pletscher *et al.* Epistasis and the evolution of additive genetic variance in populations that pass through a bottleneck. *Evolution* ,**53**, 1009-1018 (1999).

<sup>3</sup>A.R. Templeton. The theory of speciation via the founder principle. *Genetics* ,**94**, 1011-1038 (1980).

<sup>4</sup>Ch. J. Goodnight. On the effect of founder events on epistatic genetic variance. *Evolution* ,**41**, 80-91 (1987).

<sup>5</sup>J. M. Cheverud and E. J. Routman. Epistasis as a source of increased additive genetic variance at population bottlenecks. *Evolution* ,**50**, 1042-1051 (1996).

<sup>6</sup>C. Lopez-Fanjul, A. Fernandez, and M.A. Toro. Epistasis and the conversion of non-additive to additive genetic variance at population bottlenecks. *Theoretical Population Biology* ,**58**, 49-59 (2000).

<sup>7</sup>T. Maruyama and P. A. Fuerst. Population bottlenecks and nonequilibrium models in population genetics.I Allele number when population evolve from zero variability. *genetics* ,**108**, 745-763 (1984).

<sup>8</sup>T. Maruyama and P. A. Fuerst. Population bottlenecks and nonequilibrium models in population genetics.II Number of alleles in a small population that was formed by a recent bottleneck. *Genetics* ,**110**, 675-689 (1985).

- <sup>9</sup>T. Maruyama and P. A. Fuerst. Population bottlenecks and nonequilibrium models in population genetics.III. Genic homozygosity in populations which experience periodic bottlenecks. *genetics* ,**111**, 691-703 (1985).
- <sup>10</sup>W.E. Ricker. Stock and recruitment. *J. Fish. Res. Bd Canada* ,**11**, 559-623 (1954).
- <sup>11</sup>M Nei, T Maruyama, and R Chakraborty. The bottleneck effect and genetic variability in populations. *Evolution* ,**29**, 361-70 (1975).
- <sup>12</sup>R. M. May and G. F. Oster. Bifurcations and dynamic complexity in simple ecological models. *American Naturalist* ,**110**, 573-599 (1976).
- <sup>13</sup>S. A. Frank. Models of parasite virulence. *Quarterly Review of Biology.* ,**71**, 37-78 (1996).
- <sup>14</sup>J. F. Crow and M. Kimura, *Introduction to Population Genetics* (1970).
- <sup>15</sup>S. Ellner and P. Turchin. Chaos in a noisy world: new methods and evidence from time-series analysis. *American Naturalist* ,**145**, 343-375 (1995).
- <sup>16</sup>B. Dennis, R.A. Desharnais, J.M. Cushing *et al.* Transitions in population dynamics: equilibria to periodic cycles to aperiodic cycles. *Journal of Animal Ecology* ,**66**, 704-729 (1997).
- <sup>17</sup>H. G. Spencer, "Models of speciation by founder effect: a review," in *Speciation and the recognition concept: theory and application.*, edited by D. M. Lambert and H. G. Spencer (John Hopkins University Press, Baltimore, 1995), pp. chap 8: 141-156.

<sup>18</sup>U. Motro and G. Thomson. On heterozygosity and the effective size of populations subject to size changes. *Evolution* ,**36**, 1059-1066 (1982).

Figure 1a

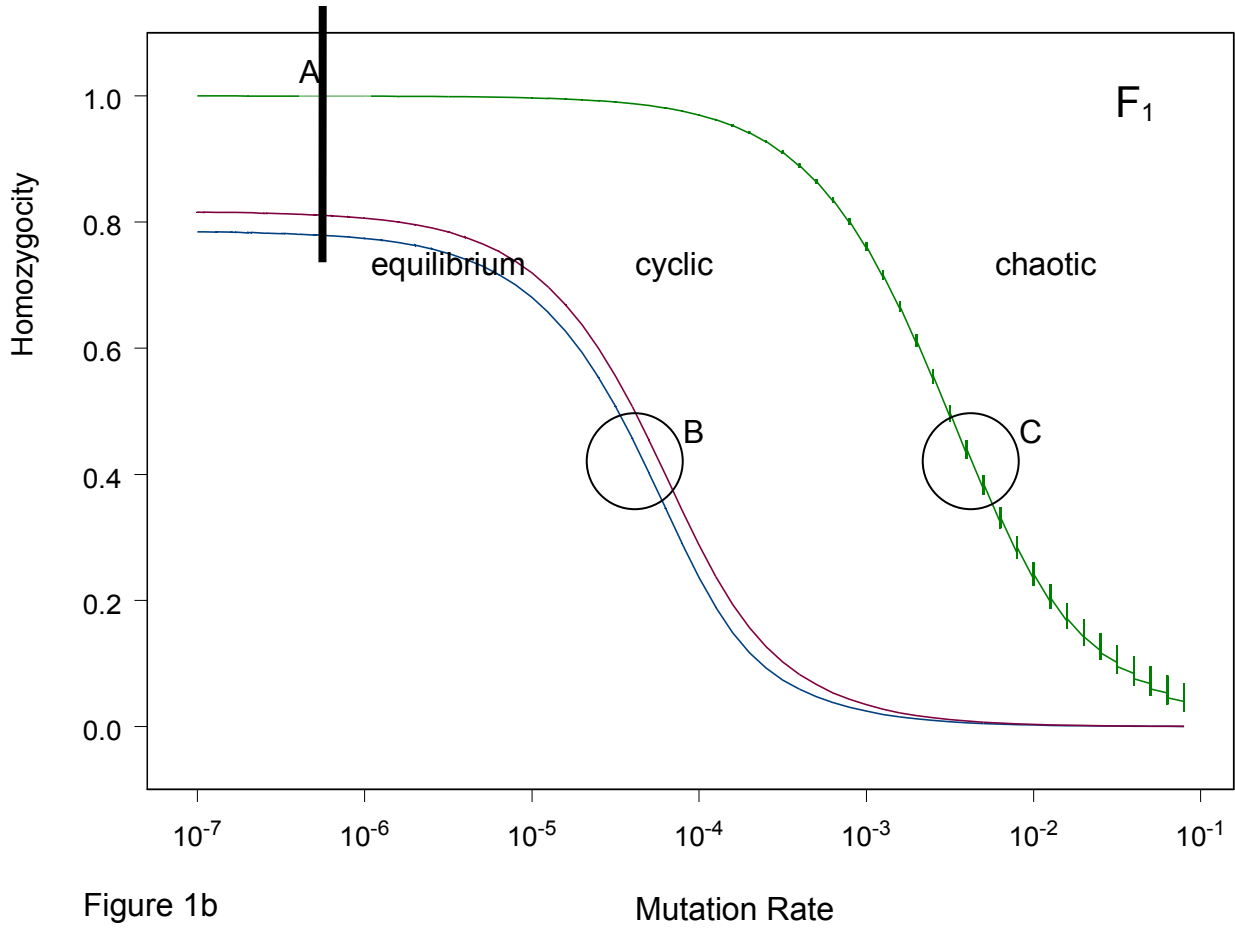


Figure 1b

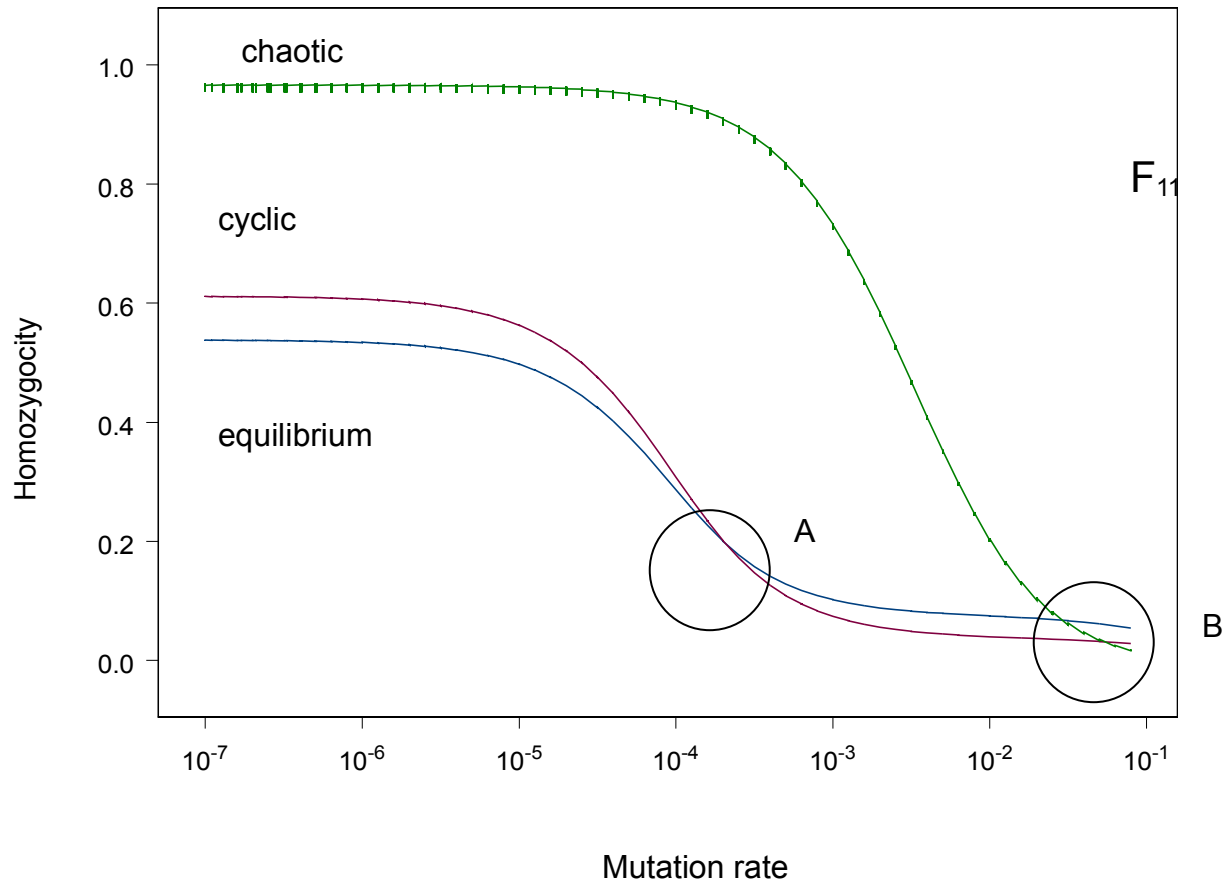


Figure 2

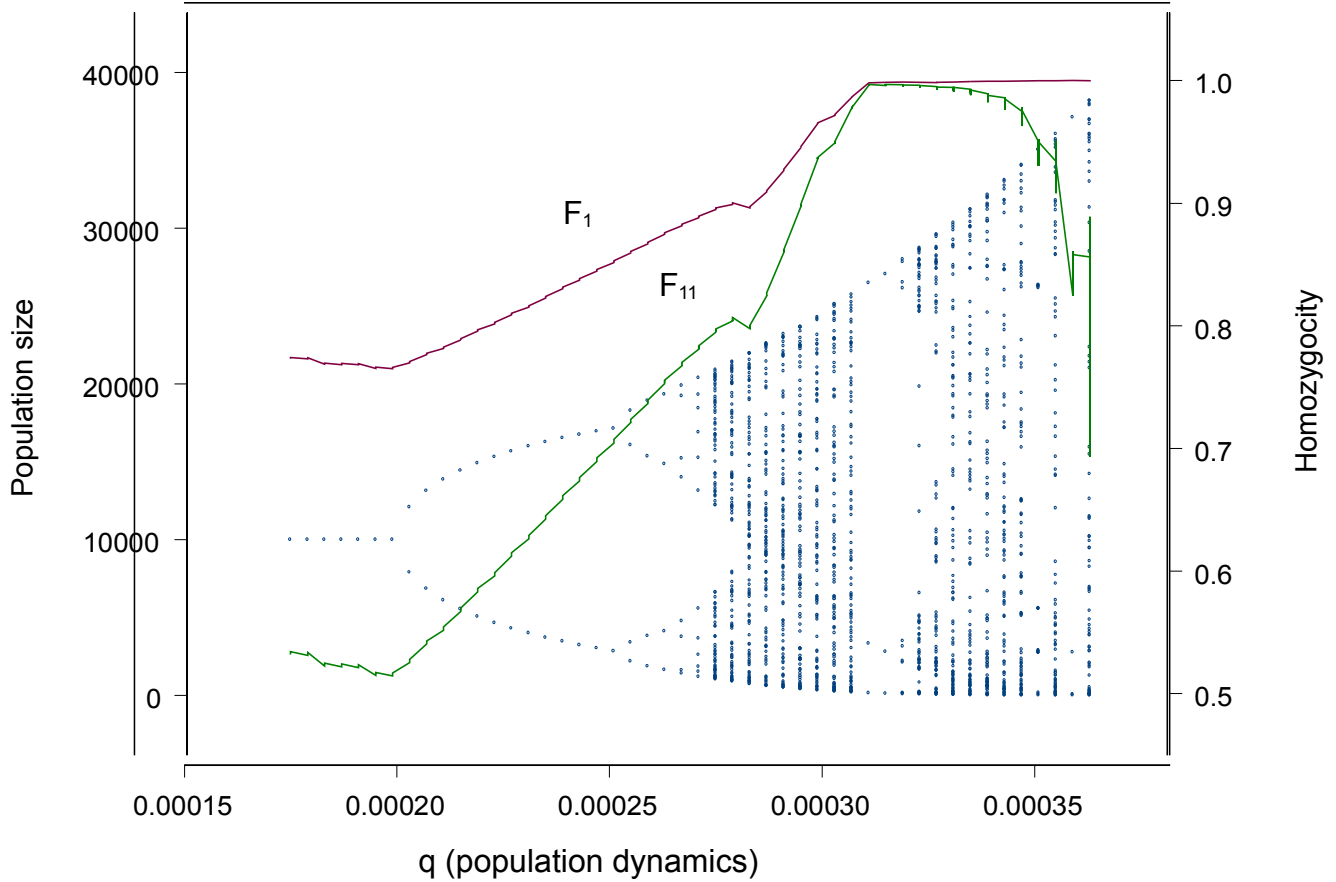


Figure 1 shows the levels of heterozygosity, calculated with one- (Figure 1a) and two-locus (Figure 1b) measurements. The independent variable of relevance is the mutation rate. Notice in Figure 1a that classic results from Nei and coworkers are repeated when conditions are equated (line A). The more outstanding difference among chaotic dynamics and stable and/or cyclic dynamics is illustrated by the circles A and B in Figure 1a. They differ in almost two orders of magnitude of mutation rates.

Figure 2 displays heterozygosity with one and two locus measures, when population dynamics is the factor investigated in detail. Notice that the measures differs importantly with extremely fluctuating population dynamics.