Heteroplasm and Organelle Gene Dynamics

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ABSTRACT

This study assesses factors that influence the rates of change of organelle gene diversity and the maintenance of heteroplasmy. Losses of organelle gene diversity within individuals via vegetative segregation during ontogeny are paramount to resultant spatial and temporal patterns. Steady-state losses of organelle variation from the zygote to the gametes are determined by the effective number of organelles, which will be approximately equal to the number of intracellular organelles if random segregation prevails. Both rapid increases in organelle number after zygote formation and reductions at germ lines will reduce variation within individuals. Terminal reductions in organelles must be to very low copy numbers (<5) for substantial losses in variation to occur rapidly. Nonrandom clonal expansion and vegetative segregation during gametogenesis may be effective in reducing genetic variation in gametes. If organelles are uniparentally inherited, the asymptotic expectations for effective numbers of gametes and spatial differentiation will be identical for homoplasmic and heteroplasmic conditions. The rate of attainment of asymptote for heteroplasmic organelles, however, is governed by the rate of loss of variation during ontogeny. With sex-biased dispersal, the effective number of gametes is maximized when the proportional contributions of the sex having the higher dispersal rate are low.

GENETIC studies are seldom conducted solely to ascertain the status of genetic characters existing in a population. Typically, genetic observations together with spatial data are used to infer important biological information regarding behaviors, movements, and dynamics of ecological processes that influence genetic characters. Genetic information is rapidly becoming a tool that is useful for unprecedented probes for toxicological impacts of man’s activities and serves as a sensitive biomarker of individual exposures to mutagens and clastogens (Bickham and Smolen 1994; Baker et al. 1996). As such, genetic data may provide vital details of population histories and probable trajectories over space and time, as well as signatures of chemical and elemental stressors affecting individuals (Shugart and Theodorakis 1994). The effectiveness of conclusions based on observed genetic patterns depends on an understanding of which patterns may be expected under natural conditions given the behavioral ecology of the species and on the nature and dynamics of genetic material.

Accurate inference of parameters that produce observed genetic patterns is dependent on the availability of realistic theory. Interpretation of behavioral influences and historical factors on the placement of gene diversity and the rate of its change depends on (1) the mode of inheritance of specific gene characters, (2) tactics of genetic transfer (mating strategies), (3) relative sizes of families and breeding groups, and (4) the rate of genetic exchange (or lack thereof) among other breeding groups within a population. Proliferation of methods of isolation and identification of genetic characters for organelles such as mitochondrial DNA, chloroplasts, and paternal markers, as well as nuclear genes, has enhanced the power of population biologists to visualize suites of genes that may have different modes of inheritance (Avise 1994). If these techniques are used in concert, results of genetic studies may convey great power for scientists to predict the factors that give rise to observed patterns. This is particularly true if the parameters necessary to generate the various models are congruent (Chesser and Baker 1996).

Chesser and Baker (1996) showed that spatial differentiation and temporal rates of change for uniparentally inherited organelle genes may be substantially different from those for diparentally inherited nuclear genes. The only difference between the two models was the mode of inheritance of the genetic material. In addition to uniparental inheritance, their models assumed that organelles were homoplasmic; that is, specific genes for organelles were invariant within individuals and in the gametes they produced. Some organelles such as chloroplasts and mitochondria in some taxa are known to be transmitted, at least partially, by both sexes (Ohba et al. 1971; Kirk and Tilney-Bassett 1978; Neale et al. 1986; Kondo et al. 1990; Avise 1991; Gyllensten et al. 1991) allowing heteroplasmy to arise as a function of organelle variation between mates. Heteroplasmy may also arise when organelles are uniparentally inherited if the contributing gamete contains variable forms of...
genes (Birky 1975, 1994; Bermingham et al. 1986; Laipis et al. 1988; Rand and Harrison 1989). Birky et al. (1983, 1989) considered heteroplasmy in their assessment of loss of genetic diversity of organelles. They speculated that diversity present within the zygote would diminish during cytokinesis because of random assortment of organelles in vegetative segregation. Diversity would be reduced as a function of the number of cell divisions that had transpired since zygote formation. Likewise, diversity among cells would be a function of the number of cell divisions since divergence of the cell lines. Birky et al. (1983, 1989), however, did not consider that there may be variation of organelle genes among progeny produced from different gametogenic tissues in the same organism. Gametes may not covary for all genetic variance lost during their ontogeny. Losses of diversity within gametes during ontogeny may be partially offset by variation among gametes, particularly among those produced by different gametogenic tissues. Therefore, consideration of heteroplasmy of organelle genes presents some unique problems, and accurate accounting for potential losses of variation during ontogeny is of paramount importance for estimating dynamics of heteroplastic organelle genes.

This work presents an extension of several earlier models, each of which invoked various assumptions regarding development and transmission of organelle genes (Birky et al. 1983, 1988; Takahata and Palumbi 1985; Clark 1988; Chesser and Baker 1996). The works of Birky et al. (1983, 1989; also see Backer and Birky 1985; Birky 1994) set the stage for applications of theoretical and empirical research into patterns of organelle variation. Prior models have documented the negative relationship between spatial differentiation and rate of loss of genetic variation (Chesser et al. 1993, 1996). In this article I develop models to estimate the spatial patterns and temporal dynamics of organelle genes that may be heteroplastic and that may be conveyed to progeny via maternal, paternal, or diparental contributions. Because heteroplasmy may arise by variation among uniparentally contributed genes, variation between gametes of diparentally inherited genes, or by mutation of organelle genes subsequent to zygote formation (Figure 1), there is considerable attention given to the mode of inheritance and differentiation during ontogeny. The models are applicable to heteroplasmy in zygotes, potential losses of variation in the zygote during ontogeny and gametogenesis, and finally, to the genetic characterization of gametes contributed to the subsequent generation. Finally, models predicting the spatial differentiation and temporal dynamics of organelle genes are presented. The models will apply either to subdivided populations in which subunits may exchange genetic material at specified rates or to single, isolated populations with no emigration or immigration. Also, when possible, the parameter definitions and symbol denotations will follow those presented in earlier mod-

Figure 1.—Diagram depicting heteroplasmy as a function of variation between mates for diparentally inherited organelles (A) and via variation within the gamete of the contributing sex when organelles are inherited from a single parent (e.g., B). Of course mutation can cause heteroplasmy regardless of the means of organelle inheritance, and variation can be present in the gametes of either or both parents when organelle genes are dipaternally transmitted.

ORGANELLE DIVERSITY IN ONTOGENY

Determination of the dynamics of organelle gene diversity is fundamentally different from that for diploid, segregating genes. Unlike nuclear genes, variation of organelle genes within cells may be lost in the process of vegetative segregation during mitosis or meiosis (Birky et al. 1989). As a result, tissues may exhibit quite different organelle genotypes (e.g., Marchington et al. 1997) depending on the number of cell divisions that have transpired since they shared a common parental cell. Somatic variations may occur such that particular organs are homoplastic while others are either heteroplastic or homoplastic for different organelle types (Koehler et al. 1991; Ciafaloni et al. 1992; Matthews et al. 1994; Shitara et al. 1998). If organelle diversity is lost via a random, steady-state process during cell divisions, then organs derived early in ontogeny would be expected to possess greater proportions of the original variation present in the zygote. Other evidence, however, has shown that tissue-specific heteroplasmy may be a function of mitotic activity. Brain cells and oocytes have high incidence of heteroplasmy relative to tissues with greater mitotic activity (Jazin et al. 1996; Marchington et al. 1997). Heteroplasmy is also more prevalent in older individuals, showing that accumulation of mutations over time affects the diversity of organelle genes (Jazin et al. 1996).

To understand the progressive changes of organelle genetic variation, it is important to determine the fraction of the diversity in the zygote that is passed on to progeny. Therefore, the variations within and among...
the gametes are pivotal to the determination of spatial and temporal dynamics of organelle genetic diversity. Figure 2 depicts three examples of the ontogeny of gonadal tissues subsequent to zygote formation. Clearly, each progeny is expected to have lower variance of organelles due to losses in cell divisions (Birky et al. 1983, 1989). However, some portion of the original variance of the zygote potentially may be conserved among progeny born from gametes contributed by the same ovary or testis or among different gonads unless there exists some concerted mechanism for the maintenance of organelle homogeneity within organisms (e.g., Birky 1994). The determination of the rate of loss of organelle diversity during ontogeny is replete with difficulties. Birky et al. (1983, 1989) assumed a steady-state loss dependent on pairing of organelles in daughter cells or relaxed partitioning (Birky 1994). Empirical studies, however, have concluded that the process of loss may be rather abrupt with bottlenecks limiting the number of organelle types in gametes (Koehler et al. 1991; Avise 1994). Reductions in organelle numbers are often cited as the primary mechanism for relative homogeneity of gene variation within individuals and the general rarity of heteroplasmy (Brown 1985; Takahata 1985; Clark 1988; Laips et al. 1988; Rand and Harrison 1989). Others, however, have suggested that rapid clonal expansion of a limited number of organelles may reduce the heteroplasmy of gametes (Poulton 1995; Marchington et al. 1997; Meirelles and Smith 1998).

Correlations of organelle genes within and among cells may be due to either identity by state (IBS) or identity by descent (IBD; Cockerham 1969). IBS refers to genes that are identical, but there is no measure of recent common ancestry that leads to that identity. IBD denotes genes that are identical because of known processes of inheritance through which the genes are copies of one another. Whereas both modes of identity are important for assessing the status of gene diversity, it is only the IBD that confers meaningful information relative to the original variation at some (sometimes arbitrary) starting point (Cockerham 1973). The original genetic variation in the zygote is $V_0 = q_0(1 - q_0)$, where $q_0$ is the frequency of an organelle gene at time zero (zygote; cf., Cockerham 1967, 1969, 1973; Chesser 1991a,b). All identity of genes in the initial generation (zygote) is due to IBS, because there is no known ancestral history of genes. Without any systematic processes that may result in some genes leaving more descendants than others (thus, increasing IBD), then the expected genetic variance within and among cells of the developing embryo will be unchanged from the original variance, $V_0$. Therefore, it is important to define the random and systematic processes that lead to accumulations of organelle genes that are IBD if gene dynamics and spatial patterns are to be understood. The patterns of genetic variance derived from this process should accurately reflect empirical results if the assumptions of the model are not violated (Cockerham 1973, pp. 681–682; see also Sugg et al. 1996; Dobson et al. 1997). Throughout this article, therefore, I use the term “gene correlation” in derived expressions. However, these correlations could also be defined as the “probability of identity by descent.” First, I address those processes that affect changes from the amount of organelle genetic variation that an individual inherits to that which it transmits to progeny by way of gametes. Second, I consider mating and dispersal tactics that influence the variation among individuals and the dynamics of organelle genes within populations.

I define $\gamma_0$, $\gamma_2$, and $\gamma_3$ as the expected correlation of frequencies for organelle genes within gametes, among gametes within gonads (e.g., ovary or testis), and among gametes from different gonads, respectively (cf., Cockerham 1969, 1973). Each of these expected correlations (or probability of IBD) is assumed to be zero at the time the zygote is initially formed. Because I am addressing genetic changes that may take place within an individual, all identity of genes in the initial stage is considered...
Figure 3.—Graphic representation of the accumulation of gene correlations within gametes ($\gamma_c$), among gametes within the same gonad ($\gamma_b$), and among gametes of different gonads ($\gamma_a$) as a function of the number of cell divisions since divergence of sister cells. The symbols $a$, $b$, and $c$ represent the number of cell divisions until the cell lines diverge to separate gonads, separate gametocytes, and separate gametes, respectively. Organelle genes will covary for variation lost during the phases in ontogeny that they share in common. Divergence of cell lines will result in divergence among the lines for the genetic variation that remained at the time of divergence. Rates of divergence are a function of the dominant eigenvalue ($\lambda$) and the number of cell divisions occurring during each phase (see text).

to be IBS, and the initial correlations of genes are zero even if they actually may not be (Cockerham 1973, pp. 681–682). Figure 3 depicts a simple scenario for the accumulation of organelle gene correlations within and between a pair of gonads during ontogeny. Before divergence of cells leading to the separate gonads (a cell divisions) all cells covary in the amount of change in gene diversity. After divergence, each separate cell line leading to formation of the gonads covaries for the loss of gene diversity up to the time of gamete formation (b cell divisions). Loss of gene diversity within cells continues independently for the c cell divisions required for gamete formation. Thus, organelle genes for cells in separate cell lines leading to gametes for the different gonads diverge (presumably at random) for b + c cell divisions. Correlations within and among organelle genes may accumulate within an embryo because of different rates of replication for organelles, isolation (and random differentiation) of cell lines during ontogeny and reductions or increases in organelle numbers during cytokinesis. These organelle gene correlations are measured relative to the original genetic variation in the zygote, and not to other individuals in the population. Assuming no recombination of organelle genes, the gene correlations between pairs of organelles within and between cells are either zero or one, indicating that organelles are identical by descent (1), or not related during ontogeny (0; Cockerham 1969; Sugg et al. 1996). The resultant correlations are relative to the original variation in the zygote ($V_z$) such that the amount of variation remaining at any time t is $(1 - \gamma^{(t)})V_z$ within gametes, $(1 - \gamma^{(t)})V_{m}^{c}$ among gametes within the same gonad, and $(1 - \gamma^{(t)})V_{m}^{a}$ among gametes from different gonads (cf., Cockerham 1969, 1973). The probability of heteroplasmic gametes, therefore, is $V_z(1 - \gamma)$. Of course, when variation within the population disappears, no individual variation exists ($V_z = 0$), and the process of vegetative segregation is irrelevant except for the occurrence of novel mutations. Thus, the gene correlations denote the expected proportion of the original genetic variation in the zygote that has been lost within gametes, within gonads, and among gonads, due to random or systematic processes during ontogeny.

Following Figures 2 and 3, I assume there are a cell divisions before the bifurcation of cell lines that give rise to the primordial gonad tissues, b cell divisions occur before the gonad tissues are formed, and c cell divisions occur in the formation, maturation, and eventual contribution to progeny of the gametes within each gonad. Estimation of the rate of decay of organelle diversity is a function of the number of organelles within cells. For mitochondria, it appears that a reduction in number occurs before gamete formation, and that the numbers increase rapidly after zygote formation (Koehler et al. 1991). For simplicity, I assume that a zygote instantaneously increases the number of organelles ($m_r$) to result in an average of $r$ replicates per organelle in the cell, and that the number of organelles per cell thereafter is $m_r$. The replication of organelles increases the average correlation of organelle genes within the zygote because a measurable fraction of organelles will now be identical by common descent (sister organelles). The change in gene correlation within a zygote ($\gamma_c$) after organelle replication is shown in Figure 4. Therefore, after replication of organelles the average correlation of genes within the cell is

$$
\gamma_c = \frac{1}{2} \sum_{i=1}^{m_r} \frac{r_i^2 - r_i}{r} \times \frac{\sigma_i^2}{\sigma_i^2 + r(r-1)} \left( \frac{\sigma_i^2}{\sum_i \sigma_i^2 + r(r-1)} \right)
$$

where $r_i$ denotes the number of replicates of the ith organelle, $\sigma_i^2$ is the variance in the number of replicates across organelles, and $m_r (r_m - 1)/2$ is the number of pairs of different organelles within cells (see Figure 4; cf., Chesser et al. 1993).

Organelles also replicate before cell division and the organelles will be distributed between the two daughter cells during cytokinesis. Hereafter, the z subscript will be dropped because cell divisions have progressed beyond the zygote. Therefore, it is assumed that each organelle replicates, yielding a total of $m_r$ organelles to be equally divided between the two daughter cells dur-
The number of mitochondria within cells remains constant throughout future cell divisions, then whether organelle genes IBD. If the variance in replicates over organelles is zero, the effective number of organelles is approximately equal to twice the number of organelles before replication. If the variance equals the mean replication number \( \sigma^2 = 2 \), then the \( n_e \) is approximately the number of organelles before replication.

Birky (1983, 1987, 1994) suggested that often sister organelles, such as mitochondria, may remain in close proximity in the cytoplasm and therefore migrate to the same daughter cell during cytokinesis. Nonrandom sorting of sister organelles in this manner will lead to greater proportions of organelle genes IBD present within cells during vegetative segregation than if migration were random. Likewise, repulsion of sister organelles within the cytoplasm may yield lower frequency of organelle genes IBD. If \( y \) is the probability that two sister organelles will migrate to the same daughter cell after cytokinesis \( (y > \frac{1}{2}) \) yields positive association, \( y < \frac{1}{2} \) is negative association or avoidance; \( 0 \leq y \leq 1 \) then

\[
\gamma^{(1+1)} = \gamma^{(1)} + (1 - \gamma^{(0)}) \left( 2ym(\sigma^2 + r(r - 1)) \right) \frac{mr}{r(mr - 2)}
\]

\[
= \gamma^{(0)} + (1 - \gamma^{(0)}) \frac{2ym(\sigma^2 + r(r - 1))}{r(mr - 2)}
\]

and

\[
\gamma^{(1+1)} = \gamma^{(0)} + (1 - \gamma^{(0)}) \left( 2ym(\sigma^2 + r(r - 1)) \right) \frac{mr}{r(mr - 2)}
\]

\[
= \gamma^{(0)} + (1 - \gamma^{(0)}) \frac{2ym(\sigma^2 + r(r - 1))}{r(mr - 2)}
\]

Figure 4.—This graphic depicts the replication of organelles of a particular type within a cell (such as the zygote). The original cell contains 5 primary organelles. After replication, the cell contains 10 organelles, but variation in the number of replicates is evident. The initial pair-wise correlations of organelle genes are all zero. After replication, however, some organelles are identical by common descent and have correlations of unity.
\[
\lambda = 1 - \frac{2y(\sigma_i^2 + r(t - 1))}{r(mR - 2)} \quad \text{(3b)}
\]

Obviously, complete avoidance of sister organelles \((y = 0)\) will result in infinite effective numbers of organelles and no loss of organelle gene diversity. A y value of unity will half the effective number and thereby double the rate of loss of genetic diversity within cells over that of random transfer of organelles between cells.

Reduction in organelle numbers will also affect the correlations between organelle genes within cells. It would appear that Equations 2 and 3 could be used for organelle reductions as well. Organelles that are eliminated would have \(r_i = 0\) while those maintained would yield \(r_i = 1\), assuming no replication of remaining organelles. This scenario, however, will always result in the term, \(\sigma_i^2 + r(t - 1) = 0\), and thus, \(\lambda = 1\) and infinite \(n_e\). These results imply that organelle reductions would result in no loss of genetic variance. Expectations of gene correlations from the above scenario, however, are not consistent with the binomial probabilities assumed in Equations 2 and 3 because organelles with zero replicates are not considered for selection within cells. Assuming no recombination of organelle genes, the number of pairs of organelles IBD within a cell before reduction in organelle number is expected to equal \(\gamma_i^P(1)(m(m - 1))/2\). If the number of organelles is reduced from \(m\) to \(m - R\), assigning \(P = (m - R)/2\) as the number of pairs of organelles and \(i\) as the number of pairs IBD, the average correlation \((\gamma_i)\) of genes between organelles within a cell becomes

\[
\gamma_i = \gamma_i + (1 - \gamma_i) \frac{2}{(m - R)(m - R - 1)} \times \sum_{i=1}^{P} \binom{P}{i} \gamma_i(1 - \gamma_i)^{P-i}
\]

\[
= \frac{(m - R)(m - R - 1)}{m - R - 1}. \quad \text{(4)}
\]

It is clear from this equation that reductions in organelle numbers at the zygote stage would not affect the expected gene correlations for the zygote cell. Because \(\gamma_i\) at the zygote stage is zero, the expected gene correlation after reduction would remain at zero. Although this expression is undefined when \(R = m - 1\), it is obvious that reduction to a single organelle will result in a total loss of genetic variance. Figure 5 shows that the expected genetic variation for organelles within cells is virtually unchanged by reduction in numbers of organelles unless the number remaining \((m - R)\) is less than about five. Therefore, for bottlenecks in organelle numbers to serve as the primary means of promoting homoplasy (\(\gamma_i = 1.0\)) of gametes (and thus, zygotes if there is uniparental inheritance; Avise 1994, p. 62), the reduction must result in very few organelles in gametes \((m - R < 5; R > 995 \text{ in Figure 5})\). This is consistent with estimates for postulated bottlenecks during oogenesis for human mtDNA. Hauswirth and Laipis (1985) reported that the reduction yielded between 1 and 6 mitochondria, and that the segregating unit could be a single mitochondrion. Of course, nonrandom selection of organelles could take place in germ cell lines, or the value of \(\gamma_i\) could be very nearly unity before organelle reduction. Subsequent cell division beyond the stage of organelle reduction will result in an \(\gamma_i\) as defined in Equations 2 or 3, but with a reduced value of \(m\), leading to further increases in \(\gamma_i\). However, reductions are presumed to occur primarily in germ cell generations and, thus, near the final stage of cell division (Hauswirth and Laipis 1985; Avise 1994).

Homoplasy of gametes may be promoted by differential replication of organelles rather than reduction in numbers. It is possible that some organelles become quiescent during cytokinesis, while others undergo rapid proliferation. Thus, one or more organelles may replicate manyfold \((r_i \gg 1)\), whereas others would undergo no replication \((r_i = 1)\). The most rapid rate of loss of gene diversity within cells would be realized if all daughter organelles were the product of a single organelle. In this case, the variance in replicate number would equal \((m - 1)(r - 1)^2\), where \(m\) is the original number of organelles within the parental cell, and \(r\) is the average number of organelle replicates. Assuming random vegetative segregation of organelles into the separate daughter cells, the eigenvalue would become (from Equation 2b) \(\lambda = 1 - \frac{2y(m(m - 1))(r - 1)/r(mR - 2)}{n_e} \quad \text{and} \quad n_e = r(mR - 2)/(1 + m(m - 1))(r - 1)).\) Differential replication of this sort can result in dramatic reductions in organelle \(n_e\) and a rapid approach to homoplasy over successive cell divisions. For example, consider a maternal cell that contains 100 mitochondria. One mitochondrion yields 101 replicates while the
remaining 99 yield only one each (they do not duplicate themselves). The average number of replicates per organelle \((r)\) is 2, and the variance in replicate number is 99. Although there are 200 mitochondria segregating between the two cells, the effective number is only 3.9. After sixteen generations of cell divisions, approximately 99% of the original organelle gene diversity will be lost.

Reductions of organelle numbers, clonal expansion, or random segregation processes within cells will not affect the expectation of correlations between organelle genes between gametes within gonads \(\gamma_2\) or between gametes of different gonads \(\gamma_3\). This can be confirmed using \(m\) as the reduced number of organelles within gametes. The possible number of organelle pairs between cells is \(P = m^2\), and \(i\) is the number of pairs of organelles that are identical by common descent, giving the following expected gene correlations:

\[
\gamma_2 = \frac{1}{P} \sum_{i=1}^{P} \left( \frac{P}{i} \right) \gamma_3 (1 - \gamma_3)^{(P-i)} = \gamma_2
\]

\[
\gamma_3 = \frac{1}{P} \sum_{i=1}^{P} \left( \frac{P}{i} \right) \gamma_3 (1 - \gamma_3)^{(P-i)} = \gamma_3.
\]

Thus, although organelle reductions and random segregation events may alter gene diversity within cells, remaining variation among separate lineages of cells will be conserved. Even if reductions of organelle numbers or losses in diversity during vegetative segregation result in homoplasmy of gametes, there may be measurable variation between progeny produced by gametes from different gonads.

If there are \(\tau\) total gonads (Figure 2), with the \(j\)th gonad producing \(g_j\) of a total of \(G\) viable progeny produced by a female, then the expectations for the correlation of organelle genes within and among gametes are (assuming negligible effects of initial increases or terminal reductions in organelle numbers)

\[
\gamma_1 = \frac{\sum_{j=1}^{\tau} g_j (1 - \gamma_3)}{G} = 1 - \frac{\sum g_j \lambda^{\bar{h} + h}}{G}
\]

\[
\gamma_2 = \frac{\sum_{j=1}^{\tau} g_j (1 - \gamma_3)}{G} = 1 - \frac{\sum g_j \lambda^{\bar{h} + h}}{G}.
\]

Estimation of the correlation among gametes among gonads \(\gamma_3\) must be restricted to include only pairwise comparisons of gametes from different gonads. Therefore, a triangular matrix such as those shown in Figure 3 must be employed. Each element of the matrix (zeros and ones), however, will be represented by a rectangular submatrix rather than by the expected correlation between a pair of organelles. Each submatrix will contain the expected organelle gene correlation between pairs of gametes produced by two different gonads. Thus, for the \(j\)th and \(i\)th gonads, the submatrix would contain \(g_{ji}\) expected correlation values (zeros and ones). The organelle genes will coarray only for the portion of their ontogeny before bifurcation of cell lines to form different gonads (Figures 2 and 3). This expression includes the variance in progeny numbers produced by gonads \(\sigma_y^2\)

\[
\gamma_3 = \sum_{j=1}^{\tau} \sum_{i=1}^{\tau} \left( \frac{g_j g_i \gamma_3 (1 - \gamma_3)^{(P-i)}}{g_j g_i \gamma_3 (1 - \gamma_3)^{(P-i)}} \right)
\]

\[
\times \left[ \frac{g_j g_i \gamma_3 (1 - \gamma_3)^{(P-i)}}{g_j g_i \gamma_3 (1 - \gamma_3)^{(P-i)}} \right] \times (1 - \gamma_3)
\]

\[
= \left( \frac{2}{\tau (1 - \gamma_3)^{(P-i)}} \right) \sum_{j=1}^{\tau} \sum_{i=1}^{\tau} g_j g_i (1 - \gamma_3). \quad (6b)
\]

The proportion of progeny resulting from gametes produced by the same gonad \((\phi_0)\) depends on the mean \((g)\) and variance \((\sigma_y^2)\) of the number of progeny produced by individual gonads

\[
\phi_0 = \frac{1}{\gamma_3} \frac{1}{\gamma_3} \gamma_3 (1 - \gamma_3) (1 - \gamma_3).
\]

Using these expressions, the weighted average correlation of organelle types between different gametes produced by a parent is

\[
\gamma = \phi_0 \gamma_2 (1 - \gamma_3).
\]

Variations in the number of gametes contributed by gonads may affect the average correlation of genes within gametes. Thus, assigning \(\gamma_{ij}\) as the expected correlation of organelle genes within gametes of the \(i\)th gonad, the weighted average is \(\gamma = \phi_0 \gamma_{ij}\).

The proportion of genetic variation found among organelles within gametes \((f_{gt})\); the subscript \(T\) represents the total genetic variance remaining within the pool of all gametes), organelles among gametes within gonads \((f_{gg})\), and among gonads \((f_{gt})\) can be computed as

\[
f_{gt} = \frac{\gamma - \gamma_1}{1 - \gamma_1}, \quad f_{gg} = \frac{\gamma - \gamma_2}{1 - \gamma_2}, \quad f_{gt} = \frac{\gamma_3 - \gamma_3}{1 - \gamma_3}.
\]

Using Equations 6a–6b, these \(f\)-statistics for differentiation of organelle genes during ontogeny are

\[
f_{gt} = 1 - \frac{\bar{x}^{\bar{x} + \bar{x}} - 1 + \bar{x}}{\bar{x}} = 1 - \frac{\bar{x}^{\bar{x} + \bar{x}}}{\bar{x}}
\]

\[
f_{gg} = 1 - \frac{\bar{x}^{\bar{x} + \bar{x}}}{\bar{x}}
\]

\[
f_{gt} = 1 - \frac{\bar{x}^{\bar{x} + \bar{x}}}{\bar{x}}
\]

with each \(\bar{x}\) denoting the weighted averages shown in Equations 6a and 6b. Equation 10a conforms to the expectation that \((1 - f_{gt}) = (1 - f_{gg})(1 - f_{gt})\) (cf., Wright 1951).

Equation 10a can be simplified for organisms that have paired gonads (e.g., mammals) and in which the average numbers of cell divisions for intervals \(b\) and \(c\) are independent quantities \((\text{cov}(b,c) = 0)\). In such cases,
These three effective numbers are expected to be equal to one another if the processes of segregation and replication do not change throughout ontogeny. Comparisons of rates of divergence of various tissues can be useful for determining which phases of ontogeny may undergo shifts in segregation and/or replication events, thereby affecting the magnitude of heteroplasmy. Because particular diseases are often associated with mitochondrial heteroplasmy (Poulton 1995), this information may assist in predicting the processes that influence the expression of variant organelle genes and which organs may be at greater risk.

Cytoplasmic organelle DNA, particularly mitochondrial DNA, are believed to experience high mutation rates due to lack of known repair mechanisms for errors that arise during replication (Wilson et al. 1985; Avise 1994). Mutations to organelle genes may occur during cell proliferation from the zygote to the derived gonads and gametes (Bentzen et al. 1988; Bendall et al. 1996). Correlations of organelle genes within gametes and between gametes within and among gonads will usually be reduced by random mutations. When mutation rate (μ) per cell replication is included, the recursive equation for the correlation of a random pair of organelle genes within a cell is

$$\gamma_i^{(i+1)} = (1 - \lambda + \lambda \gamma_i^{(i)})(1 - \mu)^2,$$

where $$(1 - \mu)^2$$ is the probability that neither of the random pair of genes has mutated. Assuming that $$\gamma_i^{(0)} = 0$$, after a + b + c cell divisions (zygote to gamete ontogeny), the correlation of organelle genes within a gamete is (ignoring terms with $$\mu^2$$)

$$\gamma_i^{(a+b+c)} = (1 - \lambda)(1 - 2\mu) \times \frac{1 - (\lambda(1 - 2\mu))^{a+b+c}}{1 - \lambda(1 - 2\mu)}.$$  

The correlation of organelle genes among gametes within the same gonad is similar to Equation 14 above, except through a + b, rather than a + b + c cell divisions. After separation from a common daughter cell, the organelle genes for cells leading to the gametes may in fact diverge because of mutations that erode the correlations accrued before that time. The probability that neither of the pair of identical organelles has mutated after c cell divisions is $$(1 - \mu)^c$$. Therefore, the value of $$\gamma_i$$ becomes

$$\gamma_i^{(a+b+c)} = (1 - \lambda)(1 - 2\mu) \times \frac{1 - (\lambda(1 - 2\mu))^{a+b+c}}{1 - \lambda(1 - 2\mu)}.$$  

Likewise, the correlation of organelle genes among ga-
metes from different gonads will typically have greater divergence with ongoing mutation because \( b + c \) cell divisions separate the cells from their common daughter cell. Therefore,

\[
\gamma_{ij} = (1 - \lambda)(1 - 2\mu)
\]

\[
\times \left( 1 - \left( \frac{\lambda(1 - 2\mu)}{1 - \lambda(1 - 2\mu)} \right)^{x} \right)
\]

\[
- 1 + (1 - \mu)^{x^{+n+b+c}}
\]

\[
= (1 - 2\mu)^{x+c} - \left( \frac{\lambda(1 - 2\mu)}{1 - \lambda(1 - 2\mu)} \right)^{x} \times \left( 1 - \left( \frac{\lambda(1 - 2\mu)}{1 - \lambda(1 - 2\mu)} \right)^{x^{+n+b+c}} \right).
\]

These equations regarding mutation rate per cell division may seem laborious and superfluous, especially since \( \mu \) could be defined as the probability of mutation during ontogeny (zygote to gamete release), yielding much simpler forms like \( \gamma_1 = \gamma_1(1 - \mu)^{2}, \gamma_2 = \gamma_2(1 - \mu)^{2}, \gamma_3 = \gamma_3(1 - \mu)^{2} \). If mutation rates and effective sizes of cellular organelles remain constant during all phases of ontogeny, then all lines depicting organelle gene correlations in Figure 3 will be shifted downward proportionally. Thus, the divergence of organelle genes between tissues will still be relative to the times since divergence of cell lines (Equations 10 and 11). The correlations could be represented simply as\( R_{kn} \) remain unchanged from Equations 15 and 16.

The equations presented above are intended to represent a probabilistic set of scenarios for organelle differentiation during ontogeny. Estimates for cellular differentiation, effective numbers of organelles, and relative divergence times for cell lines during ontogeny may serve as null models for assessing processes affecting somatic and gametic organelle gene variation. It is likely that many alternative arrangements can be envisioned for partitioning organelle diversity and conveyance of genetic variation to progeny (see Birky 1963; 1987; 1994 for reviews). Of course, if the losses of organelle variation are not constant over cell divisions, then the correlations could be represented simply as \( \gamma_1 = 1 - \lambda_{x+b+c} \), \( \gamma_2 = 1 - \lambda_{x+b} \), and \( \gamma_3 = 1 - \lambda_{x} \) with each \( 1 - \lambda \) depicting the proportion of organelle diversity lost during the complete phase of ontogeny depicted by the subscripts. Exact functions for losses of organelle variation are probably dependent on the taxon considered and are not necessary to develop the general mathematical models presented in the next section. For expressions derived below, I am not concerned with the specific details of losses during ontogeny and present equations in terms of \( \gamma_1, \gamma_2, \gamma_3, \) and \( \gamma \). The manner in which gonads develop and gametes are formed and distributed to progeny may differ considerably between the sexes. Therefore, in equations developed below I use superscripts \( P \) and \( M \) to denote paternal and maternal gametes, respectively.

**Spatial and Temporal Dynamics**

To determine the dynamics of organelle genes through space and time, I use several parameters and methods developed in models for nuclear genes and homoplasmy and uniparental inheritance (Chesser et al. 1993; Sugg and Chesser 1994; Chesser and Baker 1996) with some refinements. A synopsis of some parameters is provided below:

\[
\psi = \frac{\sigma^2 + k(1 - 1)}{k(n - 1)}
\]

is the probability that random pairs of progeny born within breeding groups are born from the same mother,
where \( k \), \( \sigma_i^2 \) are the mean and variance, respectively, of number of progeny per female;

\[
\phi_m = \frac{\sigma_i^2 + l(l - 1)}{l(n - 1)}
\]

is the probability that random females within breeding groups mate with the same male, where \( l \), \( \sigma_i^2 \) are the mean and variance, respectively, of numbers of female mates per male;

\[
\phi_u = \frac{\sigma_u^2 + p(p - 1)}{p(k - 1)}
\]

is the probability that progeny born by a single mother are the product of the same male, where \( p \), \( \sigma_u^2 \) are the mean and variance, respectively, of number of male mates per female;

\[
\psi_m = \phi_u \psi_T + (1 - \phi_u \psi_T) \phi_m
\]

is the probability that randomly selected progeny within a group are the product of the same male parent (Chesser and Baker 1996; assumes zero covariance between family size and number of mates per female, family size and number of mates per male, and number of mates per female and number of mates per male); and \( d_m, d_i \) are the rates of dispersal of males and females, respectively, among breeding groups within the population, \( D = d_m + d_i - d_m d_i \).

In previous models using variance in group size (Chesser and Baker 1996) I assumed the probability that progeny were either male or female to be one-half (\( \eta = \eta_d = \eta_m \)), and the probability that a randomly selected pair of individuals are from the same breeding group was

\[
\eta = \frac{\sigma_i^2 + n(n - 1)}{n(ns - 1)}
\]  (18)

with \( n \) and \( \sigma_i^2 \) denoting the mean and variance of numbers of females per breeding group. Thus, the number of males and females born within breeding groups was equal. Not all males may breed, however, and \( \phi_m \) is calculated over all available males and not simply the number of breeding males (Chesser and Baker 1996). If the ratios of males and females born within breeding groups vary over the population, then the probability that randomly selected individuals, regardless of sex, were natives of the same breeding group is

\[
\eta_r = \frac{1}{2} \sum_{i=1}^{N_r} N_i - N_i \quad \frac{N_i(N_i - 1)}{2}
\]

\[
\eta_r = \frac{\sigma_i^2 + n(N - 1)}{N(N - 1)}
\]  (19)

\[
\eta_r = \frac{\sigma_m^2 + \sigma_i^2 + 2\sigma_m \eta_i + (n_m + n_i)(n_m + n_i - 1) - \sigma_m^2}{(n_m + n_i)(n_m + n_i) - 1}
\]

where \( n_m \) and \( n_i \) are the average numbers of males and females per group and \( \sigma_{m,\text{cov}} \) is the covariance of the number of male and female progeny born within groups. The covariance of male and female numbers over the breeding groups is \( 1/2 \left[ \sum_{i=1}^{N_r} (n_m(i) - \bar{n}_m)(n_i(i) - \bar{n}_i) \right] \). For males and females considered separately,

\[
\eta_m = \frac{\sigma_m^2 + n_m(n_m - 1)}{n_m(N_m - 1)}, \quad \eta_f = \frac{\sigma_f^2 + n_f(n_f - 1)}{n_f(N_f - 1)}.
\]  (20)

The probability \( \eta \) that mating occurs between a sire and dam born in different native breeding groups is

\[
\eta = 1 - (1 - d_m)(1 - d_i) - d_m(1 - d_i) \eta_m
\]

\[
- d_i(1 - d_m) \eta_f - d_m d_i \eta_{rf}
\]

\[
= d_m(1 - \eta_m) + d_i(1 - \eta_f) - d_m d_i (1 - \eta_{rf}).
\]  (21)

Inbreeding, including potential mating between siblings, half-siblings, or progeny related by group coancestry, would be expected to take place with a probability of \( 1 - \eta \). Equation 19 is obviously not necessary for characters that are inherited uniparentally; however, it could be incorporated into equations of Chesser and Baker (1996) for nuclear gene transitions, substituting \( \eta \) for \( (1 - \eta)D \) and \( D - \eta D \) for \( \eta D \). Those equations for either uniparentally transmitted genes or dipartal genes multiplied by \( d_m \) or \( d_i \) would use the corresponding equation in (20), above.

To determine the transitions of organelle types over generations I consider that the proportion of organelles contributed to a zygote by a sire is denoted by \( x \) whereas that contributed by the dam is \( 1 - x \). Because both males and females may convey organelles to the zygotes, the correlation of types within individuals must be included, unlike uniparental models. The form of this correlation is very similar to inbreeding (F) as in diploid, sexually reproducing models (Chesser et al. 1993) because the gene correlations represent the probabilities of identity by common descent or coancestry (Cockerham 1969, 1973). However, for organelle inheritance a proportion \( x \) of the types will be transmitted by the father while \( 1 - x \) are contributed by the mother and IBD of organelles within progeny may be conveyed by either or both parents. The average amount of heteroplasm in a zygote produced by a mating is \( 1 - F \). Thus, “inbreeding” will accumulate within zygotes by the expression

\[
F_{t+1} = x^2 F_t (1 - \gamma^{(p)}) + \gamma^{(p)}
\]

\[
+ (1 - x)^2 F_t (1 - \gamma^{(m)}) + \gamma^{(m)}
\]

\[
+ 2x(1 - x)((1 - \eta) \theta_i + \gamma \alpha_i)
\]

\[
= x^2 F_t (1 - \gamma^{(p)}) + \gamma^{(p)}
\]

\[
+ (1 - x)^2 F_t (1 - \gamma^{(m)}) + \gamma^{(m)} + 2x(1 - x) \theta_i
\]

\[
- (\theta_i - \alpha_i) 2x(1 - x) \left[ d_m(1 - \eta_m) + d_i(1 - \eta_f) \right].
\]  (22)

with superscripts P and M referencing paternal and maternal types, respectively, and \( \theta_i \) and \( \alpha_i \) denoting the average coancestry of organelle genes within and among breeding groups, respectively (Chesser 1991a,b). The
measures of coancestry, or gene correlations (Cockerham 1969, 1973), are relative to the genetic variation in the initial generation \(V_0 = (1/A) \Sigma_{i=1}^{A} p_i (1 - p_i); \ A \) is the total number of different alleles. Therefore, the proportion of variation remaining within and among breeding groups in the \( t \)th generation is \( V_0 (1 - \theta) \) and \( V_0 (1 - \alpha_t) \), respectively. Equation 22 incorporates the potential loss of genetic variance during ontogeny of the zygote and the development of gametes; for example, at conception the correlation of organelle types in a male is \( F_t \) and the correlation of organelle types in his gametes, upon maturation, will be \( F_t (1 - \gamma^{(P)} + \gamma^{(M)}) \) due to losses in variation during cell divisions in ontogeny and gametogenesis. The zygotes of progeny born in the population will possess a fraction of the initial organelle diversity \( V_0 \) represented as \( V_0 (1 - F_{t+1}) \).

Using \( \pi_{mm} \), \( \pi_{mf} \), and \( \pi_{ff} \) to reference the coancestry between male parents, male and female parents, and female parents within breeding groups, respectively, the coancestry for organelle types among progeny born within groups is

\[
\theta_{t+1} = x^2 \pi_{mm} + 2x(1 - x) \pi_{mf} + (1 - x)^2 \pi_{ff}. \tag{23}
\]

The origination of the two parents may be from the same or different breeding groups, depending on dispersal rates for each sex. The coancestry of male parents is complicated by the fact that \( \psi_m \) of the progeny born share the same sire via polygyny and multiple paternity (Chesser 1991a,b; Sugg and Chesser 1994; Chesser and Baker 1996). The correlation of organelle types within a male zygote is \( F_t \), and the subsequent correlation among his gametes is \( F_t (1 - \gamma^{(P)} + \gamma^{(M)}) \). Therefore, the coancestry among male parents within groups is

\[
\pi_{mm(0)} = \psi_m [F_t (1 - \gamma^{(P)}) + \gamma^{(M)}] + \theta_t (1 - \psi_m) [(1 - (1 - \eta_m)d_m) + (1 - \eta_m)d_\alpha] \tag{24}
\]

Likewise, \( \psi_f \) is the proportion of progeny born within groups that share the same mother (Chesser et al. 1993), and the coancestry of organelle types among mothers within groups is

\[
\pi_{mm(0)} = \psi_f [F_t (1 - \gamma^{(M)}) + \gamma^{(M)}] + \theta_t (1 - \psi_f) [(1 - (1 - \eta_f)d_f) + (1 - \eta_f)d_\alpha] \tag{25}
\]

Coancestry between mothers and fathers within groups is

\[
\pi_{mf(0)} = [1 - d_m (1 - \eta_m) - d_f (1 - \eta_f)] + d_m d_f (1 - \eta_f) \theta_t
+ \{d_m (1 - \eta_m) + d_f (1 - \eta_f) - d_m d_f (1 - \eta_f) \} \alpha_t
= [(1 - \theta) \theta_t + \theta_t \alpha_t]. \tag{26}
\]

Substituting Equations 24, 25, and 26 into 23, the coancestry of organelles for progeny born within breeding groups is determined as

\[
\theta_{t+1} = \psi_m x^2 \left[F_t (1 - \gamma^{(P)}) + \gamma^{(M)} \right] + \theta_t (1 - \psi_m) x^2 [(1 - (1 - \eta_m)d_m) + (1 - \eta_m)d_\alpha]
+ \psi_f (1 - x)^2 [(1 - (1 - \eta_f)d_f) + (1 - \eta_f)d_\alpha]
+ 2x(1 - x) [(1 - \theta) \theta_t + \theta_t \alpha_t]. \tag{27}
\]

Expanding \( \alpha_t \), the coancestry is

\[
\theta_{t+1} = \psi_m x^2 \left[F_t (1 - \gamma^{(P)}) + \gamma^{(M)} \right] \]
\[+ \theta_t (1 - \psi_m) x^2 [(1 - (1 - \eta_m)d_m) + (1 - \eta_m)d_\alpha]
+ \theta_t (1 - \psi_f) [(1 - x)^2 [(1 - (1 - \eta_f)d_f) + (1 - \eta_f)d_\alpha]
+ 2x(1 - x) [(1 - \theta) \theta_t + \theta_t \alpha_t]. \tag{28}
\]

The correlation of organelle types among individuals from different breeding groups \( \alpha_t \) in the total population is

\[
\alpha_{t+1} = x^2 [(1 - \gamma^{(P)}) + (1 - \gamma^{(M)})]
+ \theta_t (1 - \psi_m) [(1 - (1 - \eta_m)d_m) + (1 - \eta_m)d_\alpha]
+ \theta_t (1 - \psi_f) [(1 - x)^2 [(1 - (1 - \eta_f)d_f) + (1 - \eta_f)d_\alpha]
+ 2x(1 - x) [(1 - \theta) \theta_t + \theta_t \alpha_t]. \tag{29}
\]

From the expressions above a transition matrix, \( T \), for \( F, \theta \), and \( \alpha_t \) can be derived. For brevity, I present the expressions without expansion of \( \alpha_t \),

\[
T_{11} = x^2 (1 - \gamma^{(P)} + (1 - \gamma^{(M)})
T_{12} = 2x(1 - x)(1 - \theta)
T_{13} = 2x(1 - x) \alpha_t
T_{21} = \psi_m x^2 (1 - \gamma^{(P)}) + \psi_f (1 - x)^2 (1 - \gamma^{(M)})
T_{22} = (1 - \psi_m) x^2 [(1 - (1 - \eta_m)d_m) + (1 - \eta_m)d_\alpha]
+ 2x(1 - x)(1 - \theta)
T_{23} = (1 - \psi_m) x^2 [(1 - \eta_m)d_m + (1 - \psi_f)
+ (1 - x)^2 [(1 - \eta_f)d_f + 2x(1 - x) \alpha_t]
T_{31} = 0
\]
\[ T_{32} = x^2 \eta_m \eta_d + (1 - x)^2 \eta_d d + 2x(1 - x)(D - 3N) \]
\[ T_{33} = x^2 (1 - \eta_m \eta_d) + (1 - x)^2 (1 - \eta_d) + 2x(1 - x)(1 - D + 3N). \] (31)

Constants are accumulated into a column vector, \( \mathbf{C} \), for the accumulation of \( F \), \( \theta \), and \( \alpha \) as
\[
\begin{align*}
C_1 &= x^2 \gamma^{(p)} + (1 - x)^2 \gamma^{(n)} \\
C_2 &= \psi_m x^2 \gamma^{(p)} + \psi_d (1 - x)^2 \gamma^{(n)} \\
C_3 &= 0,
\end{align*}
\]

such that \( \mathbf{F}_{i+1}, \theta_{i+1}, \alpha_{i+1} = (\mathbf{T} \cdot \mathbf{F}_i, \theta_i, \alpha_i) + (1 - \mathbf{v})^T \mathbf{C} \). The accumulation of values for \( F \), \( \theta \), and \( \alpha \) over generations is readily determined by iteration of the matrix multiplication and scalar addition using initial values of zero for each of the state variables after parameter values have been assigned.

For each generation the proportion of remaining genetic variations for organelles found among breeding groups (\( F_{i3} \)), within individuals relative to the variation within their breeding group (\( F_{i1} \)), and within individuals relative to the total variation within the subpopulation (\( F_{i2} \)) (Wright 1969) are determined by
\[ F_{LS} = \frac{\theta_i - \alpha_i}{1 - \alpha_i}, \quad F_{IL} = \frac{F_{i} - \theta_i}{1 - \theta_i}, \quad F_{IS} = \frac{F_{i} - \alpha_i}{1 - \alpha_i}. \] (34)

(Chesser 1991a; Cockerham 1973).

Iteration of the matrix multiplication and vector addition also enables the determination of effective population sizes for organelle genes for each generation. As has previously been shown (Chesser et al. 1993) effective population sizes can be derived for each hierarchical level at which gene correlations occur. For uniparentally inherited genes the rate of change of gene diversity per generation is \( 1/N_e \), whereas rates of loss for diploid nuclear genes transmitted by sexual reproduction would be \( 1/(2N_e) \). The expressions for inbreeding, coancestral, and intergroup effective size for organelle genes that may be inherited proportionally from either or both parents are
\[ N_{el} = \frac{1 - F_i}{(1 + 4x(1 - x))(F_{i+1} - F_i)}, \]
\[ N_{el} = \frac{1 - F_i}{(1 + 4x(1 - x))(\theta_{i+1} - \theta_i)}. \] (32)

In time, the effective sizes become identical at a value referred to as the asymptotic effective size, \( \bar{N}_e \) (Chesser et al. 1993). Therefore, the expected rate of change of variation for organelle genes per generation is \( 1/(1 + 4x(1 - x))\bar{N}_e \).

Clearly, with the proliferation of techniques available to assess gene diversity for genes with variable modes of transmission and disparous contributions by parents, the concept of the effective population size becomes unclear. Wright's (1931) original intent was to describe the number of individuals of an ideal population that would confer the same rate of change of genetic variation as that of a particular nonideal population in question. For most applications of effective population size, it is indeed the rate of change of gene diversity that is sought and the \( N_e \) serves only as a vehicle to infer rates of genetic change. This inference is obscured when some rates are determined by \( 1/(2N_e) \), such as nuclear genes, and others by \( 1/N_e \) or \( 1/(1 + 4x(1 - x))N_e \). For example, organelle genes transmitted by a single parent may have the same effective size as nuclear genes; despite the equality of effective sizes, however, the rate of loss of organelle diversity will be twice that of nuclear genes (Birky et al. 1989; Chesser and Baker 1996). Also, if \( N_e \) for organelles is the number of females (\( N_i \); Avise 1994) and \( N_e \) for diploid nuclear genes is the number of breeders (\( N_i + N_m \)), then the rate of change of organelle variation is four times that for nuclear genes (Birky et al. 1989). As such, the conceptual intent of \( N_e \) is obscured by the necessity to transform the values in accordance with the mode of inheritance and proportional contributions by parents to determine rates of change. To avoid confusion, I refer to the effective rates of change of genetic variation (\( R_e \)) that are determined for any genetic character as
\[ R_{el} = \frac{F_{i+1} - F_i}{1 - F_i}, \quad R_{el} = \frac{\theta_{i+1} - \theta_i}{1 - \theta_i}, \quad R_{el} = \frac{\alpha_{i+1} - \alpha_i}{1 - \alpha_i}. \] (33)
Maximization of the effective number of gametes with equal parental contribution is evident only when there is random mating. Figure 6, A±D, demonstrates that rates of loss of genetic variation for organelles within breeding groups, of an analytical solution to rates of change or spatial terms of the ®xation indices the value of $G_e$ increases, thereby decreasing the variance among gametes. Similarly, the effective rate of inbreeding is produced by different gonads ($\gamma$), can influence the effective number of gametes. When organelle diversity is maintained among gametes from different gonads ($\gamma \to 0$) as may occur when primordial cells for gonad formation diverge early in ontogeny, then the effective number of gametes is increased. As the correlation of organelle genes among gametes from different gonads increases, thereby decreasing the variance among gametes, the $G_e$ coconically decreases.

**Heteroplasmy and uniparental inheritance:** Heteroplasmy of organelle genes need not be maintained by dipartent inheritance. Rather, heteroplasmy can be maintained by direct uniparental inheritance if genetic variance that existed in the zygote still remains in the gametes (Birky 1975, 1983). The effective number of gametes for such genetic variation can be determined by defining $x$ as either zero or one, for maternal or paternal inheritance, respectively. When $x = 0$ or $x = 1$, the dominant eigenvalue ($\lambda_m$) of the transition matrix ($T \cdot M$) is the larger of

$$\lambda_m = (1 - 2\nu)(1 - \gamma_l)$$

or

$$\lambda_m = (1 - 2\nu)\left[\frac{b + \sqrt{b^2 - 4(1 - d)(1 - \psi_1)}}{2}\right]$$

where the “dot” refers to parameter values for the contributing sex (sire or dam; cf., Chesser and Baker 1996). The asymptotic rate of decay of variance for a nonsegregating gene is $R_e = 1 - \lambda_m$; therefore,

$$\hat{R}_e^{\gamma_l} = \gamma_l + 2\nu(1 - \gamma_l)$$

or

$$\hat{R}_e^{\gamma_l} = \frac{2 - (1 - \nu)[b + \sqrt{b^2 - 4(1 - d)(1 - \psi_1)}]}{2}$$

whichever is larger. The $G_e$ values are the reciprocals...
Figure 6.—Four figures showing the influence of the proportion of male contribution of organelles ($x$; female proportion is $1 - x$) on the rate of change of organelle gene diversity ($R_e$) within a population, the correlation of organelle genes among groups ($F_{LS}$), the expected correlation of organelle genes within individuals relative to the entire population ($F_{IS}$), and correlation of organelle genes within individuals relative to their breeding group ($F_{IL}$). The straight dashed line labeled $R_D$ shows the rate of loss of gene diversity for a diploid, sexually transmitted nuclear gene. For all graphs, $s^2 = k = 2$, $s = 30$, $n_m = n_f = 8$, $s^2 = 4$, $\gamma_1 = 0.8$, $\gamma_2 = 0.6$, $\gamma_3 = 0.4$, and $\phi_g = 0$. The specific scenarios depicted are (A) $\phi_m = 0$ (random mate selection within groups), $d_m = d_f = 0.7$; (B) $\phi_m = 0.3$, $d_m = 0.7$, $d_f = 0.2$; (C) $\phi_m = 0.75$, $d_m = d_f = 0.7$; (D) $\phi_m = 0$, $d_m = 0.1$, $d_f = 0.9$.

of the $R_e$'s. These results demonstrate a fundamental difference between effective numbers for homoplasmic and heteroplasmic genes when there is strict uniparental inheritance (Chesser and Baker 1996). If there is negligible loss of gene diversity during ontogeny ($\gamma_2 \equiv 0$) then $G_e$ is infinite because all inherited variation is conferred to progeny. However, if the rate of loss of genetic variation from the zygote to the gamete of an individual is greater than the rate of loss of variance in the population during a single generation, then the population rate will dominate and control the overall rate of loss of genetic variance. A similar dichotomy was found by Birky et al. (1983, Equation 12). Normally, Equation 43b would define the asymptotic rate of decay of organelle diversity while (43a) would determine the rate at which that asymptote would be attained (cf., Birky et al. 1989, p. 519). It is unlikely that rates of loss of organelle types during ontogeny would be so small that they would govern the overall effective gamete number of the population unless the mutation rate ($\mu$) were greater than or approximately equal to the rate of loss during cell division ($\lambda$) or sister organelles preferentially migrated to separate cells during cytokinesis ($y \equiv 0$; see Equation 3b). Clearly, such scenarios are possible, however.

If mutation is ignored, the derived $G_e$ (reciprocal of Equation 43b) is numerically identical to the effective size for homoplasmic uniparental genes presented by Chesser and Baker (1996, Equation 22). Because Chesser and Baker (1996) showed that $N_e(0)$ was equal to the other half of the quadratic for the solution to the $F_{LS}$. 
incorporating mutation, and, by algebraic rearrangement, it can be shown that

\[ R_e = d \eta (1 - 2\nu) F_{LS}. \] (45)

This equation makes it clear that low rates of genetic change are dependent on low dispersal rates and not on high values of \( F_{LS} \) per se, as has been reported (Chesser et al. 1993). Figure 6 shows that, with constant dispersal rates, the rate of change of gene diversity is reduced when \( F_{LS} \) is low. Losses of organelle diversity during ontogeny (\( \gamma_I \)) will not alter the spatial heterogeneity of a heteroplasmatic trait from that seen for homoplasy. However, the time required to attain asymptote will increase with decreasing values of \( \gamma_I \) because asymptote over space cannot be attained until equilibrium within individuals is complete. For uniparental characters this equilibrium is when variation within individuals is lost completely.

**Single, isolated population:** Most applications of effective sizes for uniparentally and diparentally inherited genes have been for single, isolated populations with random mating. As a result, it is assumed that there is no substructure of the population and that mates are selected randomly from those available within the population. With these restrictions the parameter definitions become as follows: all \( \eta = 1.0 \), because all progeny born, and thus all sources of mates, are from the same population; \( \psi_i = (\sigma_i^2 + k(k - 1))/(k(kN - 1)) \), where N denotes the total number of females in the population; \( \psi_m = \psi_i \), because \( \phi_m = 0 \) with random mating; \( d_m = d_i = D = 1.0 \), because there is no continuity of family or breeding groups; further, it is assumed that \( \gamma^{(m)} = \gamma^{(n)} = \gamma \). With these definitions the dominant eigenvalue (\( \lambda_m \)) is

\[
\lambda_m = \frac{(1 - 2\nu)}{2} \left[ b + \sqrt{b^2 - \left( \frac{4(1 - 2x(1 - x))}{(1 - \gamma_I)(1 - \psi_i) + 2x(1 - x)\psi_i(\gamma - \gamma_I)} \right)} \right]
\]

\[
b = 1 + (1 - 2x(1 - x))(1 - \gamma_I - \psi_i) \] (46)

The asymptotic rate of change is \( R_e = 1 - \lambda_m \). If all variation in the zygote is lost during ontogeny and gamete production (\( \gamma = \gamma_I = 1 \)) then the dominant eigenvalue is \( \lambda_m = (1 - 2\nu)(1 - \psi_i(1 - 2x(1 - x))) \), which is equal to the result from Chesser and Baker (1996; \( N_e = \psi_i^{-1} \), Equation 33) for homoplasmic organelles when \( x = 0 \) or 1 and \( \nu = 0 \). The results of the explicit solutions above corresponded exactly to those derived from iterations of the transition matrix when the same parameters were used.

**DISCUSSION**

The dynamics of organelle genes are influenced by a variety of possible processes affecting the replication, segregation, and regulation of numbers of organelles during ontogeny, as well as tactics of mating, dispersal rates, and mode of inheritance in populations. Many of the ontogenic processes that may reduce or maintain organelle gene diversity are not well understood (Poulton 1995). Bottlenecks in organelle numbers are usually invoked to explain the high percentage of homoplasm of progeny (Hauswirth and Laipis 1985; Laipis et al. 1988; Ashley et al. 1989). High variation in the rate of transmittal of mutant genes to progeny (0–73%) suggests that random processes do, in fact, affect the change in gene diversity. However, the results of models presented here when compared to those of Chesser and Baker (1996) show that spatial variation and temporal change of heteroplasmic and homoplasmic organelle genes may not necessarily differ. If organelles are uniparentally inherited and if the rate of loss of cellular diversity (\( \gamma_I \)) is greater than the rate of loss in the population, then spatial differentiation and temporal change eventually will be identical for homoplasmic and heteroplasmic genes. This identity applies to single, isolated populations or ones exhibiting subdivision. Therefore, for organelles that are transmitted by a single sex, investigators probably need not concern themselves with the nuances of heteroplasm when considering asymptotic spatial and temporal variation.
Diparental inheritance of organelles can, under some circumstances, markedly affect the rate of loss of organelle gene diversity. When there is random mating ($\phi_m = 0$; Figure 6A) the rate of loss of gene diversity when both parents contribute equally ($x = 0.5$) to the organelle pool is less than one-half that when only one parent confers organelles to the zygote. Under this scenario, however, the rate of decay of diversity for organelle genes is still greater than for diploid nuclear genes. The dynamics of organelle genes can be considerably less than for nuclear genes when there are conditions that tend to isolate variants in different population subdivisions (Chesser and Baker 1996) as with highly social mammals (Figure 6C). Low female dispersal among different social units is the primary cause of the high effective number of gametes. Even slight paternal contributions of organelle genes to progeny erode the effective numbers of gametes, however, because high dispersal rates for males homogenize the gene frequencies in the population. High polygyny ($\phi_m = 1$) will prevent this erosion from being rapid because the effective number of gametes contributed by males is low. Lower values of $\phi_m$ will cause more rapid changes in $G_1$ as male contributions increase than will absolute polygyny. Sex-biased dispersal also affects the rate of loss of organelle diversity. Diparental contributions yielding the lowest rates of loss of gene diversity are evident when the organelle contributions of the dispersing sex are low. This situation prevents the rapid dissemination of organelle diversity throughout the population.

In some organisms, mitochondria and chloroplasts are transmitted by different sexes or mating types. Some organelles are known to be primarily maternally inherited, such as mitochondria (Avise 1994), whereas others such as chloroplasts may be contributed by males (Dong et al. 1992), females (Hackett 1980), or both (Metzlaff et al. 1981). For species in which chloroplasts and mitochondria are transmitted by males and females, respectively, the extreme values ($x = 0$ or $x = 1$) in Figure 6 show that their organelle genes may differ in their patterns of spatial and temporal variation, depending on sex-dependent dispersal rates and mating tactics. Wind pollinators may achieve relatively random mating and multiple paternity over a broad range; however, seed dispersal may be much more limited (Prout 1981). Therefore, paternally transmitted genes may be dispersed rapidly over large geographic distances while maternal genes are relatively restricted to narrow distributions from the maternal plant. Such a scenario could lead to high values for spatial differentiation ($F_{ST}$) and low rates of temporal change for mitochondrial DNA with concomitantly low differentiation and relatively high rates of change for chloroplastic DNA (see Figure 6).

Disparity of genetic patterns resultant from maternal or paternal inheritance may also be evident in the same organelle type. Several species of freshwater mussels exhibit doubly uniparental inheritance of mitochondrial DNA (Fisher and Skibinski 1990; Zouros et al. 1994; Stewart et al. 1996; Hoeh et al. 1996). Progeny apparently receive mitochondria from both parents. In the gonads of males, however, the paternal mitochondria are expressed whereas in females the maternal mitochondria persist in the gonads (Fisher and Skibinski 1990). Spatial patterns examined in some species have revealed that divergence ($F_{ST}$) among males from different regions is consistently greater than that among females and that male DNA has greater overall diversity (Liu et al. 1996). Although differential selection has been invoked to explain this disparity (Stewart et al. 1996), the expressions derived herein and in Chesser and Baker (1996) show that the differences may also be explained on the basis of differential dispersal and variance in reproductive success.

An additional complication affecting the dynamics of heteroplasmic organelle genes is ontogeny. Whether heteroplasmicity is contributed by a single parent or by both parents, the rate of change for intracellular variation of organelle genes during development of gonads and gametes is paramount to predictions of organelle gene diversity in the population. Individual gametes may confer considerably less organelle diversity to progeny ($1 - \gamma_i$) than was present in the zygote of the parent due to losses of variation during cell divisions. If bifurcation of sister cells leading to formation of separate gonads occurs early in ontogeny, however, much of the zygotic variation may be present in the form of variation among gametes ($1 - \gamma_1$). Therefore, individual progeny may be homoplasmic, yet there may be considerable variation between progeny produced by different gonads. Variation among gametes may convey large gains in the effective number of gametes particularly
when progeny numbers are high, as in a growing population. Although it is possible that variation among gametes within gonads ($\gamma_2$) could have a similar effect, it is likely that the correlation among organelle genes within gonads is high due to long development times during ontogeny. Thus, many birds that often have only one functional gonad may be expected to have lower organelle variation among gametes and possibly slightly faster rates of loss of organelle gene diversity.

If there is no loss of organelle gene diversity during ontogeny ($\gamma_1 = 0$ and it follows that $\gamma_2 = \gamma_1 = 0$), then the effective number of gametes ($G_{\text{e}}$) is essentially infinite. With no losses of diversity from zygote to gamete then all organelle variation will be conferred to progeny. Although Birky et al. (1983, 1989) and I have considered steady-state losses of organelle diversity during cell divisions, there is evidence that there may be some step(s) that dramatically increase or reduce mitochondrial numbers in daughter cells (Avise 1994). However, if random reductions of organelle numbers are responsible for promoting homoplasmy ($\gamma_1$), then the reductions must serve to dramatically limit the number of organelles within germ-cell lines (Figure 5). A paucity of information currently prevents precise formulation of the manner in which organelle variation may be reduced during ontogeny, but a general rarity of heteroplasmy in most taxa (Avise 1994; Birky 1994) indicates that losses occur. Mutation rates would necessarily be very great or nonrandom assortment of sister organelles be pervasive to offset potential losses in organelle diversity during ontogeny to a sufficient level to cause ontogenic processes to overrule the losses incurred in the population (Equations 42 and 43).

The expectations of spatial heterogeneity of heteroplasmy in organelle genes differ considerably from those for diploid, sexually transmitted nuclear genes. Values for $F_{\text{IL}}$, the correlation of genes within individuals to those available within breeding groups, are expected to be positive for heteroplastic organelle genes whereas the expectation is negative when nuclear genes are considered (Cockerham 1973; Chesser 1991a,b). Therefore, individuals should not possess greater organelle diversity within their gametes than there is present within their breeding group. Negative $F_{\text{IL}}$ values are possible due to accidents of sampling or when mixtures of progeny and adults are pooled. However, the steady-state models derived herein dictate that negative values of $F_{\text{IL}}$ are not generally expected. $F_{\text{IL}}$ values for organelle genes were always greater than those for nuclear genes.

Variance in the sizes of breeding groups will reduce the effective number of gametes (and effective population number), a result also reported by Chesser and Baker (1996). Derivations herein show that positive covariance values for male and female numbers across breeding groups will likewise lead to lower effective numbers. Prior work (Chesser 1991a,b; Chesser et al. 1993) considered groups to be of equal size and therefore would overestimate $N_e$ if there was variance in group size. Also, Wang (1996) showed that different sex ratios may affect spatial variation and temporal loss in diversity. Care should be taken, however, to differentiate between census sex ratio and breeding sex ratio. Even if sex ratios are equal, not all individuals of a particular sex may mate. In black-tailed prairie dogs the ratio of males to females is approximately 1:1; however, most males do not mate as there is only one breeding male for every 3–9 females (Hoogland and 1995). If the breeding males are considered to be selected randomly from the pool of available males, then the expectation of coancestry conveyed to progeny is the mean for all available males. Therefore, the variance in mating success ($\sigma^2$) produced would, in that case, include zeros for those males that did not mate, but the value of $\eta_m$ and $\eta_f$ would not differ. Reduction in census sex ratio would likely result in a concomitant reduction in the $\sigma^2$ and likewise could affect differences in $\eta$ between the sexes. Chesser and Baker (1996) discussed this issue and indicated that separate values for $\eta$ ($\eta_m$ and $\eta_f$) could be substituted into equations for maternally or paternally inherited characters. Their transition equations for nuclear genes used a single value of $\eta$, assuming that the available numbers of male and female mates were the same with zero covariance. The equations presented in this article permit separate values for $\eta_m$ and $\eta_f$ as well as the joint value of $\eta$, which includes the covariance for male and female numbers.

Covariance values for male and female numbers in local breeding groups must be very high to alter estimates of effective size substantially from those determined by Chesser and Baker (1996). Quantitative values for key parameters associated with mating tactics and methods of exchange among social units (see Chesser 1991a,b) were used to generate values for genetic heterogeneity that were almost identical to those produced by testing allozymes and by assessment of pedigrees in the black-tailed prairie dog (Sugg et al. 1996; Dobson et al. 1997).

Paucity of cellular mechanisms to repair damage may make organelle DNA a prime candidate for studies of genetic effects of environmental pollutants. A likely result of mutagenic exposure is the production of heteroplasmy in somatic and germ-cell lines (cf., Anderson and Weldon 1994). This study was prompted by a need to understand the expectations of organelle gene distributions so that deviations may be identified. Clearly, there are many possible alternatives for the parameters and procedures established in the models presented here and future refinements will be required to satisfy a broader realm of biological diversity and intracellular processes (cf., Birky 1994). As empirical techniques expand to encompass more areas of genetic expression, theory must attempt to keep pace to provide likely explanations of patterns and possible causation. Realistic theory together with a broad empirical base may provide...
the key to unlocking a wide array of ecological aspects and behavioral and environmental forces affecting the spatial and temporal dynamics of genes in natural populations.

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