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Evolution of the Plant Mitochondrial Genome: Dynamics of Duplication and Deletion of Sequences

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Abstract. Several descriptive models have been proposed to explain the occurrence of deletion-duplication events in the plant mitochondrial genome. In order to investigate the dynamics of these events, we have simulated them using a computer model. The simulation shows that whatever the recombination rates between repeats, if a mitochondrial sequence becomes unnecessary for the proper function of mitochondria, this sequence can be deleted and another sequence can be duplicated in consequence. Furthermore, the model shows that the organization of the sequences with respect to the origin of replication has a great influence over the dynamics of the deletion-duplication events.

Key words: Recombination rates — Selection — Mitochondrial genome

The plant mitochondrial genome has an unusually dynamic structure due to recombination between repeated sequences which generates a population of molecules of different sizes and molecular configurations (an example is given in Fig. 1). Although most genomes evolve principally by point mutations, the plant mitochondrial genome has a very low substitution rate, and its evolution is characterized by frequent structural rearrangements (Palmer and Herbon 1988). These rearrangements correspond to variation in the stoichiometry of the different molecules and/or the creation of new sequence arrangements.

Highly variable proportions of different mitochondrial molecules have been observed experimentally: Some sequences frequent in one mitotype are substoichiometric or totally deleted in another, and others are duplicated. There are several examples where two sets of direct repeats are involved in these alterations. One example of a coupled duplication-deletion of sequences is the case of *Zea mays* mitotypes (Small et al. 1989). The comparison of the modern maize mitochondrial genome (N) with the RU mitochondrial genome from more primitive maize types reveals a 12-kb duplication and a deletion in the N mitochondrial genome. Again in maize, Fauron et al. (1990) described a 165-kb duplication associated with a 0.423-kb deletion of the *urf*13 chimeric gene in fertile revertant plants obtained after culture of *cms*T tissue. Another example is A-58 *cms* mitochondrial DNA, which presents a 100-kb duplication and an 8-kb deletion compared to that of the cultured Chinsurah Boro II line (Yamato et al. 1992).

Small et al. (1989) proposed a model involving two sets of direct repeats to explain coupled duplication-deletion events. Considering the circles in Fig. 1, an infrequent homologous recombination between short direct repeats (1) in the master circle 1 generates two subgenomic circles (circles 2 and 3). Independently, an infrequent recombination between a second pair of direct repeats (2) gives rise to two other subgenomic circles

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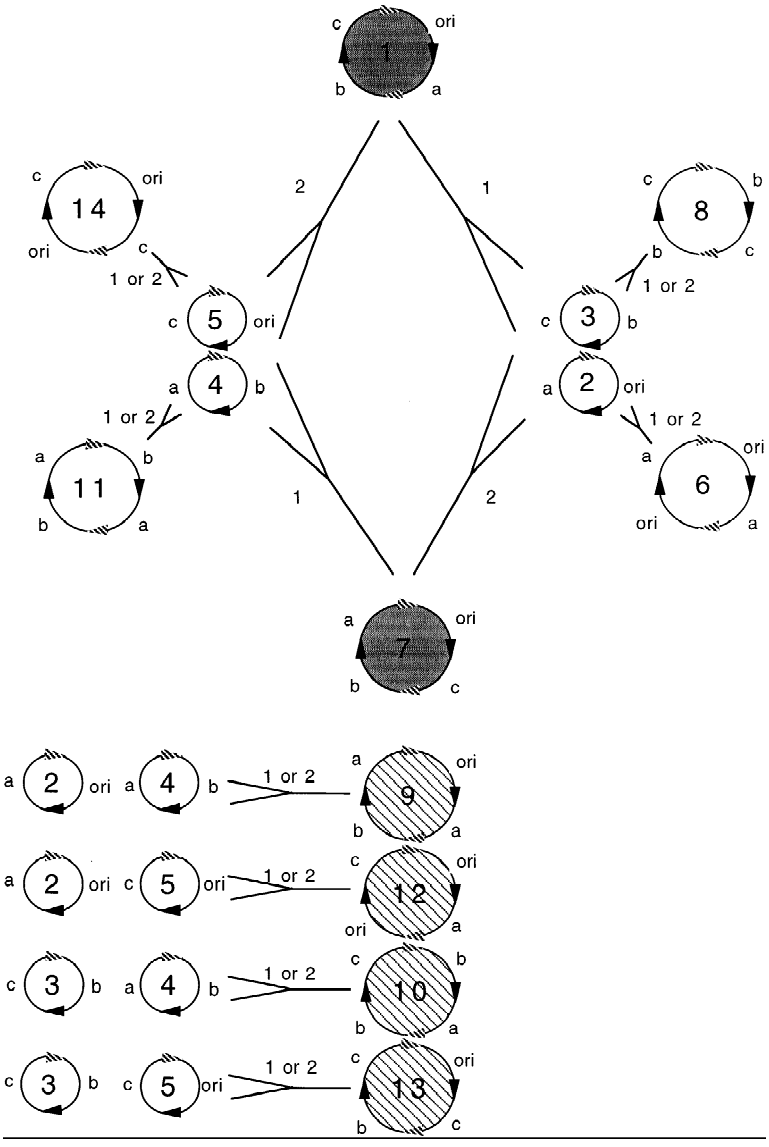

Fig. 1. Population of mitochondrial molecules. A master circle (*circle 1*) containing several types of sequences was chosen; *a*, *b*, and *c* are regions with coding and noncoding sequences. The origin of replication is represented by *ori.* There are two sets of direct repeats numbered *1* and *2;* repeat *1* is represented by a *gray arrow* and repeat *2* by a *black* one. The *direction of the arrow* indicates the orientation of the repeat. The master *circle 1* generates *circles 2 to 14* through recombination between the repeats. Circles which generate each other through recombination are joined by *lines.* The type of repeat involved in the recombination is indicated above the line. The *end of the line* indicates whether the recombination event happens within or between molecules (for example: from *circles 2* and *3* to *1* the recombination is intermolecular, and from *circle 1* to *2* and *3* the recombination is intramolecular). *Shaded circles* contain complete mitochondrial information, i.e., are master circles, and *hatched circles* (*circles 9, 10, 12,* and *13*) are duplicated-deleted circles.

(circles 4 and 5). Furthermore, one from each pair of subgenomic circles (circles 2 and 4 for example) can recombine via their shared sequence ('a') to generate a new master circle (circle 9). This new master circle (circle 9) contains a duplicated sequence ('a') and lacks a sequence ('c') in comparison with the initial master circle (circle 1). This model proposed two rare recombination events to generate the four subgenomic circles and a frequent recombination event between two of them to generate the new master circle. Fauron et al. (1995a) independently developed a similar model. They considered one pair of repeats which recombines actively (for example repeat 1) and a second pair which recombines infrequently. Intermolecular recombination in a pairwise manner between any two of the subgenomes (circles 2, 3, 4, and 5) will create new master circles with a duplication and a deletion compared to the initial master circle.

We decided to simulate these duplication-deletion events using a computer model of mitochondrial genome replication-recombination that we have been described previously (Albert et al. 1996). Our model includes three different levels of selection:

1. Intermolecular selection: molecules with a higher density of replication origins replicate faster than others.
2. Intermitochondrial selection: mitochondrial growth and division depend on the mitochondrion containing a full set of genetic information.
3. Intercellular selection: cell growth and division are proportional to the total mitochondrial function in the cell.

Using this model, we investigated the dynamics of deletion/duplication, and in particular three parameters:

1. The effect of varying the rate of recombination of the two pairs of direct repeats involved

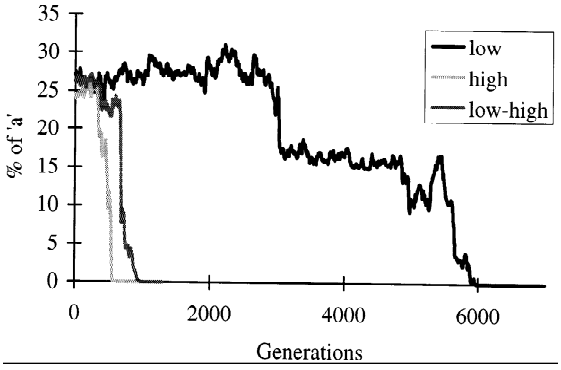

Fig. 2. Influence of the recombination rates on the dynamics of deletion-duplication events. The three simulations presented have the same parameters except for the recombination rates. The graphs show the frequency of sequence '*a*' as a percentage of total sequences. *Low:* the recombination rates of the two sets of repeats are equal and low. *Low-high:* the recombination rate of one set of repeats is low and that of the other set, high. *High:* the recombination rates of the two sets of repeats are equal and high. The sequence '*a*' is lost after 550 generations in *high,* 900 in *low-high,* and *5,800* in *low.* During the first 300 generations the mt selection pressure was the same for all sequences, but subsequently there was no selection against the loss of sequence '*a.*'

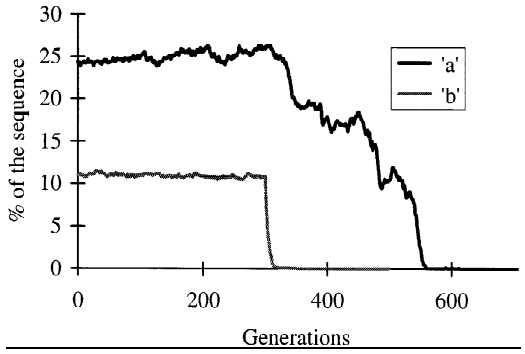

Fig. 3. Dynamics of deletion of different types of sequences. Two examples of simulations are shown; one shows the deletion of the sequence '*a*' and the other one the deletion of the sequence '*b.*' The graphs indicate the frequency of sequence '*a*' or '*b,*' respectively, as a percentage of total sequences. During the first 300 generations the mt selection pressure was the same for all sequences, but subsequently there was no selection against the loss of sequence '*a*' or '*b,*' respectively.

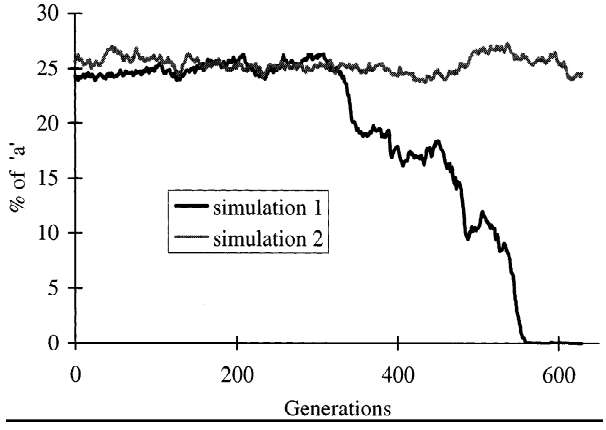

Fig. 4. Deletion of a sequence is possible only when there is no selection pressure against its loss. Two examples are given. In simulation *1* there was selection pressure against the loss of sequence '*a*' throughout the course of the simulation, whereas in simulation *2* the selection for sequence '*a*' was removed after the first 300 generations. The graphs show the frequency of sequence '*a*' as a percentage of total sequences.

2. The effect of varying the location of the sequence which is deleted with respect to the replication origin
3. The effect of varying the selection pressure on the sequence which is deleted

In the deletion-duplication models described above, Small et al. (1989) and Fauron et al. (1995b) invoke rare recombination events across at least one of the pairs of repeats involved. Our simulations show that it is not necessary to have low recombination rates to get deletion-duplication events; in fact, whatever the recombination rates, a sequence not necessary for mitochondrial function can be lost. However, when both sets of repeats recombine frequently, the sequence is lost very rapidly (Fig. 2). The instability of the starting genome in this case suggests that such a configuration, if it ever arose in vivo, would be short-lived. This probably explains why the natural events observed to date generally involve short, rarely recombining repeats. Furthermore, our simulations show that the third recombination event (postulated by Small et al. 1989 to explain the generation of a new master circle) is unnecessary for the maintenance of the new genome.

The dynamics of the appearance of the deletion-duplication event is linked to the configuration of the starting genome. When the sequence becomes unnecessary, the sequence 'b' opposite to the origin of replication is lost faster than the sequence 'a' or 'c,' adjacent to the origin (Fig. 3). This can be easily explained; when the sequence 'b' is lost the origin of replication is duplicated, and then the mitochondrial genome is composed of highly replicative molecules (circles 2, 5, 6, 12, 14 of Fig. 1). The other molecules are lost. In this case, there is no conflict between the intermolecular selection which favors the molecules which replicate rapidly and the intermitochondrial and intercellular selection which favors the presence of a complete set of information. However, the deletion of the sequence 'a' or 'c' involves the loss of the circles which replicate faster than the others (circles having more replication origins per unit size). Therefore, the intermolecular selection is in opposition with the intermitochondrial and intercellular selection.

The power of the selection processes in our simulations is exemplified by the fact that in our model a sequence can only be lost if the sequence becomes unnecessary for the mitochondria (Fig. 4) (this can occur, for example, if the function of a mitochondrial gene is usurped by a nuclear gene, e.g., *coxII,* reviewed in Fau-

ron et al. 1995b). Thus the recombination events are not responsible per se for the apparent deletion-duplications; rather the determining factor is the selection pressure (or lack of it) on the sequence to be deleted.

Conclusion

Our computer model faithfully reproduces coupled duplication-deletion events, a common class of rearrangement in plant mitochondrial genomes. When two direct repeats are involved, the loss of a sequence is always associated with the duplication of another one. Our dynamic simulations allow us to add some new information to the previously proposed hypotheses and confirm that selection pressure on the deleted sequence is the determining factor. A sequence which becomes unnecessary for mitochondrial function can be lost whatever the recombination rates across the flanking repeats. By observing the dynamics of deletion-duplication events, it is possible that indications about the location of replication origins could be obtained.

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