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ORIGINAL PAPER

Sympatric speciation as intrinsic property of the expanding population

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Abstract Sympatric speciation is still debatable, though some well documented empirical data that support it already exist. Our computer modeling reveals that sympatric speciation is an intrinsic property of the expanding populations with differentiated inbreeding—higher at the edges and lower inside the territory. At the edges of expanding populations, the probability of forming deleterious phenotypes by placing two defective alleles in the corresponding loci is relatively high even with low genetic load. Thus, the winning strategy is to use rather the complementary haplotypes to form zygotes. This strategy leads to a very fast sympatric speciation and specific distribution of recombination activity along the chromosomes—higher at the subtelomeric regions (close to the ends of chromosomes) and lower in the middle of chromosomes, which is also observed in all human chromosomes (excluding Y).

Keywords Monte Carlo simulation · Sympatric speciation · Recombination · Genome evolution

Introduction

The allopatric speciation assuming that new species emerge from the original one if a fraction of its populations is separated by geographical, physical or biological barriers is a well known and commonly accepted phenomenon. But the emergence of a new species inside the older one on the same territory without any barriers, called sympatric speciation, is debatable since Ernst Mayr, who was rather skeptical about the possibility of speciation in such conditions (Mayr 1942; Jiggins 2006). Nevertheless, some empirical evidences (Barluenga et al. 2006; Bunje et al. 2007) and theoretical models that address the problems showed the possibility of speciation in sympatry (Doebeli and Dieckmann 2003; Luz-Burgoa et al. 2006; Schwämmle et al. 2006; Stauffer et al. 2006). Computer simulations reveal that organisms living in small, highly inbreeding populations use a very specific strategy of reproduction; the genomes of the offspring are formed of the complementary haplotypes (Zawierta et al. 2007). On the other hand, the decreased frequency of crossover or uneven distribution of recombination spots along the chromosomes facilitates generating two complementary sets of haplotypes in the genetic pool of population (Bońkowska et al. 2007). Thus, the inbreeding coefficient, which is a measure of how genetically related, on average, are organisms in the population and intragenomic recombination rate co-operate in the choice of the proper strategy of reproduction. In the large panmictic populations with high intragenomic recombination rate, the best strategy is the purifying, Darwinian selection. In small populations or under high inbreeding, even without physical barriers, the forming of the offspring genomes from the complementary haplotypes prevails. Two independently evolving populations form different complementary sets of haplotypes which do not fit to each other and such populations cannot form surviving hybrids; thus, such populations could be considered as two species (Łaszkiewicz et al. 2003). The strategy of reproduction based on the complementary haplotypes could be even more efficient if the system of haplotype recognition exist. We discuss the possibility that in nature, the Major Histocompatibility Complex (MHC) genes plays such a

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role because similar or identical MHC alleles in partners diminish the chance of creating stable partnerships, their mating (Yamazaki et al. 1976; Potts et al. 1991; Wedekind et al. 1995; Ober et al. 1997; Jacob et al. 2002; Santos et al. 2005; Garver-Apgar et al. 2006) and survival of their offspring (Ober et al. 1998; Fernandez et al. 1999). It is also possible that Olfactory Receptor genes (OR) have a role in the mating preference. Some of them are physically linked to the MHC, which may suggest some functional association with genes of the complex (Ehlers et al. 2000; Younger et al. 2001). The other example of controlling the intragenomic recombination is hybridogenesis (Som and Reyer 2006). It is a specific strategy of reproduction of so-called "complex species"; two species can form the population of hybrids, which can reproduce by cross-breeding with parental species or by inbreeding inside the hybrid population. The characteristic feature of hybridogenesis is the total switching off the recombination between parental haplotypes in the hybrids during the gametogenesis process. Thus, the fraction of hybrids in this complex system is a parameter directly controlling the intragenomic recombination rate.

Model

All simulations were performed on a square lattice of size 1,000 × 1,000. Each place on the lattice can be occupied by only one individual. Each individual is represented by two bitstrings (haplotypes) 64 bits long. Two bits, located at the corresponding positions (loci) in the bitstrings, correspond to two alleles of the same gene in the real haplotypes of the diploid genome. Bits set to 0 represent wild (correct) alleles while bits set to 1 represent defective alleles. All defective alleles are recessive which means that two bits at the same position have to be set to 1 to determine the defective phenotypic trait. To reproduce, an individual produces a gamete by copying its two haplotypes, introducing one mutation into a randomly chosen locus of each copy of haplotypes and crossing-over between the two new haplotypes at a randomly chosen point with probability R. Mutation changes a bit set to 0 into bit 1. If the bit chosen for mutation is already set to 1, it stays 1—there are no reversions. An individual which has produced a gamete looks for a partner at a distance no larger than "D" [in a square $(2D + 1) \times (2D + 1)$ with an individual in its center]. If succeeds—the partner produces a gamete in the same way as described above and both gametes form a diploid genome of their offspring. A newborn is located at the distance no larger than "d" of the first parent. Since any place on the lattice can be occupied by only one individual, if there is no free location, the offspring is not born. If in the newborn genome at any locus both alleles are set to 1, a newborn dies (each deleterious phenotype is lethal). During one iteration or Monte Carlo step (MCs), all individuals are tested for the possibility of reproduction. At the end of each step, the individuals die randomly with probability 0.02 leaving free space for the newborns of the next iteration. Computer simulation starts with two ideal individuals (all bits set for 0 in both haplotypes) placed in the middle of the lattice.

In the model, only three parameters vary:

- R—recombination rate, the probability of crossing-over between two copies of haplotypes of parent,
- D—distance for looking for a partner for reproduction, and
- d—distance for placing a newborn.

Results and discussion

Expansion rate of populations

We have analyzed the rate of population expansion under the conditions described in the Section "Model". Each simulation was performed with different frequency of crossover. All other parameters were constant—individuals looked for partners inside the distance $D = 2$ and placed newborns in the free place at the distance no larger than $d = 2$ from the first parent (maximum 23 partners to choose if a newborn is going to be born). To measure the expansion rate of populations, we have counted the number of individuals in populations after different numbers of MCs (different times of evolution). We have found a nonlinear relation between the expansion rate of population and crossover rate. The expansion is the slowest for recombination rate close to 0.5 and increases in both with the increase of the recombination rate and with its decrease (results are shown in Fig. 1). The minimum expansion rate close to probability of recombination 0.5 under our conditions of simulations divides the space of evolution parameters into two regions with different winning evolution strategies. The fate of populations depends on the inbreeding coefficient and they face two extremely different possibilities. First, populations are subject to the purifying selection, i.e., elimination of haplotypes with the highest number of defective alleles when the intragenomic recombination rate is high and the inbreeding coefficient is low (large, crossbreeding, panmictic populations). The second strategy is more advantageous in small populations with high inbreeding coefficient and low intragenomic recombination rate or uneven distributed recombination spots (Zawierta et al. 2007). In such conditions, the winning strategy is to switch on the possibility of generating complementing haplotypes. Let us imagine a genome of

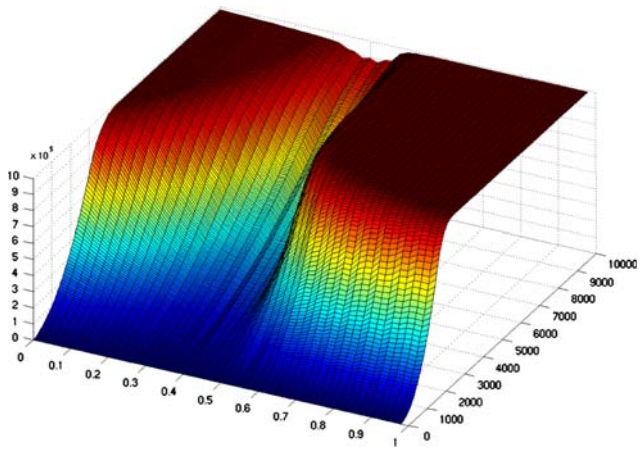

Fig. 1 Expansion rate of populations. *X-axis*—crossover rate, *Y-axis*—time of evolution in Monte Carlo steps, *Z-axis*—number of individuals in the population

1,000 loci (not extremely large) where all mutations are recessive and lethal in homozygous state (when both alleles in the same locus are defective); then, if only 2.2% of loci (on average) in one haplotype are randomly mutated, the probability of generating the lethal configuration of a zygote is close to 0.5. But if we consider that haplotypes complement each other, all 1,000 loci could be heterozygous and the fraction of defective alleles might be 50%, which means 500 defective genes in each haplotype on average. If there are only two different haplotypes that complement each other in the genetic pool of crossbreeding population, the probability of generating the healthy zygote is still 0.5. If there is no complementation and all defective alleles are randomly distributed, the probability of zygote survival is extremely low. It has been recently shown (Zawierta et al. 2007; Bońkowska et al. 2007) that in small populations the strategy of complementing haplotypes prevails.

In fact, it is not exactly the size of population which directly determines the strategy of genome evolution but the inbreeding. In the computer models, the total size of population determines the inbreeding because populations in the models usually are panmictic; any individual can freely choose any partner from the whole population. In nature, large populations are not panmictic in such a sense—the sexual contacts are usually restricted to much smaller, though overlapping, groups of organisms (Hoffman et al. 2007). In our model, we introduced these restrictions by the distance D within which partner can be found and by the distance d where the offspring can be placed.

Sympatric speciation

In the model of evolution on lattices—like in nature—at the edges of the expanding populations, inbreeding is higher than inside (pioneers live in small groups) which increases the possibility of meeting two identical haplotypes or chromosomes in one zygote (like two bitstrings 10001, 10001). This promotes the strategy of "looking for complementary haplotypes" (like bitstrings 10001 and 01110). In complementary pairs, haplotypes "fit" each other and produce heterozygous loci. Nevertheless, this strategy produces specific sequences of defective alleles in haplotypes. Groups of organisms evolving under the regime of high inbreeding may produce different configurations of these defects in the evolving haplotypes. Such groups of organisms may emerge as new species with no possibility of generating hybrid offspring that would survive.

We have tested such an evolution in our model. To show the emerging species, we have colored the individuals according to their haplotypes. Since our computer produces "only" 2^{24} (more than 16 million) different colors, we have used only the central 24 bits of haplotypes (bits from 21 to 44 of the total 64 bits in each haplotype) for coloring individuals. We have transformed these fragments into numbers. Each haplotype in the genome was represented by one such a number and we have ascribed a specific color only to the higher number that represents the individual genome. The distribution of "colored individuals" for crossover rate $R = 0.1$, $D = 5$ and $d = 5$ is shown in Fig. 2; see also: http://www.smorfland.uni.wroc.pl/sympatry/ for

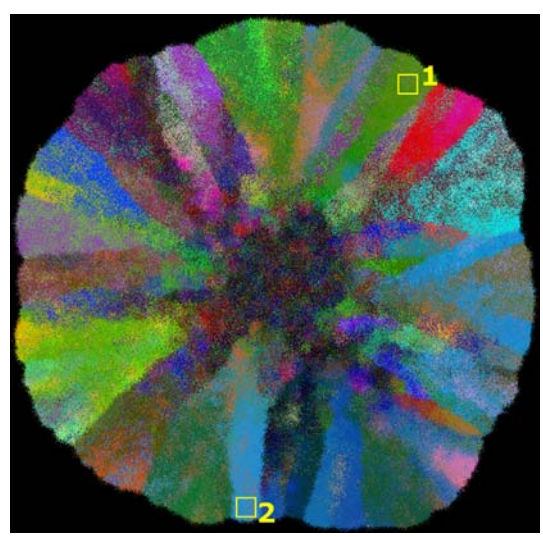

Fig. 2 Genetic diversification of expanding population after 1,400 MCs of evolution. The capacity of the whole "territory"—1,000,000 individuals, crossover rate 0.1, $D = 5$, $d = 5$, *different colors* represent haplotypes with different sequences of defective genes (see text for more explanation). *Large spots of the same colors* mean that the region is occupied by individuals with the same genotype. Note, the edges of population are irregular; expansion is slower at places where two colors meet. At these regions more hybrids are produced, they are dying

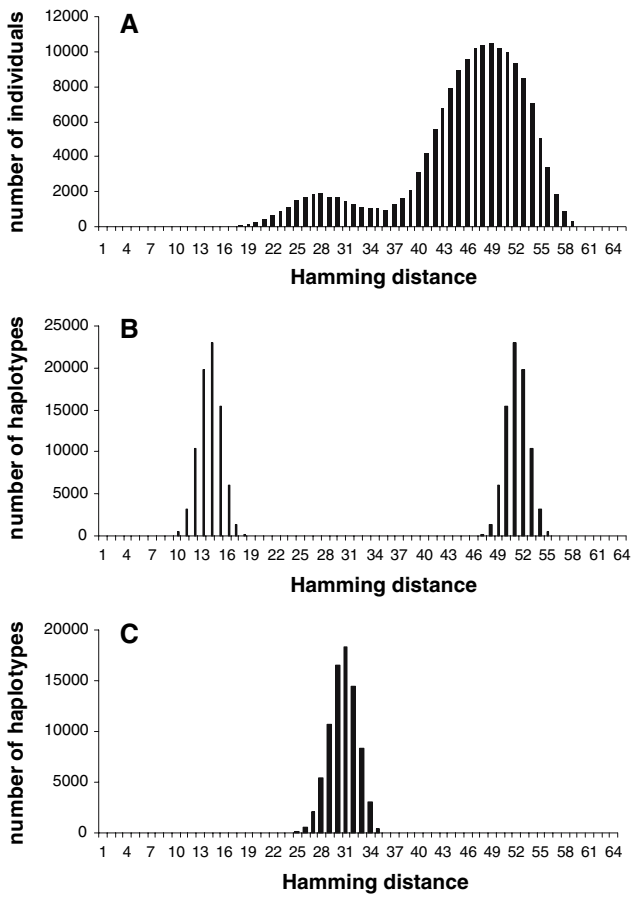

Fig. 3 The Hamming distances between haplotypes of different sets of individuals. The Hamming distance corresponds to the number of heterozygous loci if we consider that two compared haplotypes form a diploid genome; **a** distribution of numbers of heterozygous loci in the genomes of all individuals in the population; **b** the distances between haplotypes of one "species" measured between all haplotypes found on the area marked by a *square* 1 in Fig. 2 (the results indicate that all haplotypes of one species form two complementary sets); **c** the distances between haplotypes of two different species (analyzed regions marked in the Fig. 2 by *squares* 1 and 2)

more examples of populations evolving under different regimes of inbreeding and intragenomic recombination rate.

Again, the evolution starts with two ideal individuals placed in the middle of the lattice. The capacity of the whole lattice is 1,000,000 and the edges of the lattice were reached by the expanding population after about 1,400 MCs. One can see radiative speciation represented by radially located groups of individuals of the same colors. It needs to be stressed that there are no physical borders or any other barriers that would disturb the expansion of individuals. Nevertheless, sharp demarcations between "species" emerge because of high mortality of hybrids; individuals at the demarcation space where two species meet are allowed to crossbreed, but the hybrids start dying.

Genetic differences between subpopulations

To show the differences between the sets of individuals that belong to different species, we have analyzed the Hamming distances between haplotypes of different species. The Hamming distance is a sum of all corresponding loci which have different values of bits (0,1 or 1,0) in the two compared haplotypes. If the compared haplotypes belong to the same genome, the Hamming distance represents the number of heterozygous loci. Results are shown in Fig. 3. Figure 3a shows the distribution of the number of heterozygous loci in the genomes of the whole population. The distribution is bimodal. We can see two classes of genomes: one class has a moderate number of defective genes (maximum in the diagram of distribution—28 heterozygous loci corresponding to 14 defective alleles per haplotype) and the second one has a much higher number of defects (50 heterozygous loci corresponding to 25 defective alleles per haplotype on average). These distributions suggest that the population is not uniform. The first part of population is under purifying selection and the second one is using rather complementary strategy. Figure 3b shows the distances between haplotypes of one "species" measured between all haplotypes found on the area marked by one square in Fig. 2. These results indicate that all haplotypes of one species form two complementary sets. Distances inside each set are small (left part of the diagram) and between the two sets are large (right part of diagram). This right part of diagram corresponds to distribution of numbers of heterozygous loci in the genomes. Figure 3c shows the distances between haplotypes of two different species (analyzed regions marked in Fig. 2 by two squares). In such a case, the division for two peaks is not seen and the distances look as if the defective genes were distributed randomly. These comparisons explain why two different "species", even if they neighbor, cannot form hybrids that would survive. Figure 4 shows the average number of heterozygous loci in genomes versus the distance from the center of the expanding population. One can notice that the average number of heterozygous loci in the center is lower than at the edges of expanding population, which means that the purifying selection keeps the number of defective genes low in the center of the territory where the inbreeding is lower, whereas the strategy for complementary haplotypes prevails at the edges of expanding populations (compare with Fig. 2 and Fig. 3a).

All the results described above show that high inbreeding and relatively low recombination rate lead to speciation even if the population lives in a uniform environment without any geographical or physical barriers. The reproduction potential at the borders, where two "species" meet, is diminished because individuals are involved in ineffective sexual behavior; the probability of hybrid's

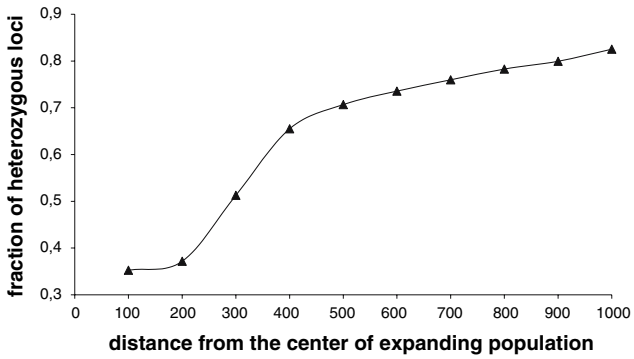

Fig. 4 The average number of heterozygous loci in a genome versus the distance from the center of the expanding population. The number of heterozygous loci is lower in the center of territory where purifying selection eliminates the defective alleles and higher at the edges where complementary strategy prevails (compare with Fig. 2)

survival in these regions is very low. It is also easy to predict that the reproductive potential of inbreeding populations could increase if any pre-zygotic or early post-zygotic mechanism of isolation were to develop. To lower the evolutionary costs, the function of haplotype recognition could be set as early as possible in the reproduction process at the levels of sexual preferences, gamete recognition or early embryo abortion. Such recognition before the information exchange is exploited even in bacteria. Some conjugative plasmids encode an entry exclusion system which informs both donor and acceptor cells that a physically possible process of the information exchange would be ineffective because the plasmids are probably identical (Lederberg et al. 1952; Novick 1987). Many authors suggest that in case of higher animals, including humans, the MHC plays such a role in determining the sexual preferences (Yamazaki et al. 1976; Potts et al. 1991; Wedekind et al. 1995; Ober et al. 1997; Jacob et al. 2002; Santos et al. 2005; Garver-Apgar et al. 2006). The interplay of embryo and maternal MHC haplotypes can also be responsible for post-zygotic isolation that influences the development of fetus (Ober et al. 1998; Fernandez et al. 1999). There are some data indicating that some groups of genes belonging to MHC, located on different chromosomes, are not inherited independently (Ehlers et al. 2000; Trowsdale 2001; Younger et al. 2001; Hiby et al. 2004; Gendzekhadze et al. 2006; Yawata et al. 2006), which suggests gamete preselection or zygotic selection. Other studies suggest that the largest family of human genes—OR genes—could be also involved in the gamete preselection (Ziegler et al. 2002; Fukuda et al. 2004; Spehr et al. 2006). Big clusters of these genes are located on almost every human chromosome (excluding chromosomes 20 and Y) (Glusman et al. 2001). These genes are expressed in different tissues, including testis during spermatogenesis (Younger et al. 2001; Feldmesser et al. 2006). One cluster of OR genes is linked to MHC locus and can participate in the gamete preselection process through cooperation with MHC (Ziegler et al. 2002). If we assume that these genes are involved in the haplotypes recognition, then the process of reproduction in the small inbreeding groups would be more efficient—it would avoid pairing the same haplotypes increasing the chance of forming zygote of complementary haplotypes, simultaneously increasing the probability of species emergence. Recently, Pękalski (2007) has shown in the computer simulations that it could be important for population survival if individuals tolerated only phenotypically significantly different sexual partners. Our model predicts another phenomenon, which could be called back speciation, observed also in nature (Seehausen 2006). Individuals which were forced to use the "complementing" strategy of reproduction during some period of their evolution can switch to the purifying selection and eliminate the surplus of defective alleles. The other possibility of back speciation assumes that the purifying selection could generate the winning population from the pool of surviving hybrids (data of simulations not shown).

Distribution of the recombination probability along the chromosomes

One can argue that our observation have been done for low intragenomic recombination rate. In fact, in our simulations, the genetic distance between genes is of the same order as in the human genome (six genes per 1 cM on average; centiMorgan is a unit of genetic distance with probability of recombination inside = 1%). The model predicts that even if the recombination events are evenly distributed along the chromosome, the highest probability of markers' separation would be observed for the most distant genes (located at the opposite ends of bitstrings). Since the complementary strategy depends on the interplay of intragenomic recombination and inbreeding, the probability of acceptation of the recombination events by selection should be higher at the ends of chromosomes and lower in the middle parts. We have considered the possibility recombination event being accepted when the gamete produced after such recombination formed a surviving zygote. We have analyzed the frequency of the recombination acceptance that depends on the position on chromosome under different inbreeding (depending on the distance to the center of the lattice).

In Fig. 5 we have shown the results of analysis of the distribution of accepted recombination events along the virtual chromosomes after simulations and along the 6th human chromosome (data download from http://www.hapmap.org/) (The International HapMap Consortium 2003). In this figure, *x*-axis represents position on chromosome normalized to 1, while *y*-axis represents the

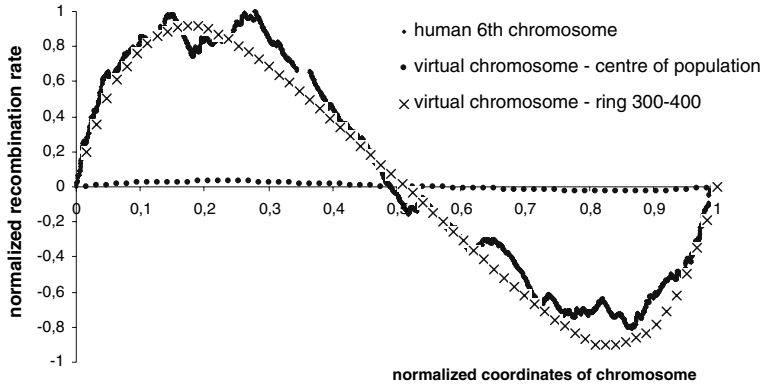

Fig. 5 The detrended cumulative plot of the distribution of accepted recombinations along the chromosomes. *Dense points* (look like a *bold line*)—human 6th chromosome, *x*—virtual chromosome of individuals occupying in Fig. 2 ring in-between diameters 400–500; *bold points*—virtual chromosomes in the central part of population (diameter = 100). *Increasing parts of plots* represent higher recombination rate than average, *decreasing parts* show the regions where the recombination rate is lower than average

normalized, cumulated recombination frequencies, counted from the beginning of chromosome, diminished by the value expected in this region under assumption that the accepted crossover events are evenly distributed along the chromosome. Thus, the increasing parts of plots correspond to the relatively high recombination rate while decreasing parts correspond to the regions of chromosomes where recombination rate is lower than average for this chromosome. In both cases—the human 6th chromosome and the virtual chromosome—the subtelomeric regions characterize with higher probability of acceptation the recombination event than internal parts of chromosomes. We have obtained the same results of recombination rate analysis by detrended cumulative walks for all human chromosomes (excluding Y), which is in agreement with observations of other authors (Payseur and Nachman 2000; Kong et al. 2002; Cheung et al. 2007). Corresponding genome analysis of individuals occupying the center of the territory shows the evenly distributed recombination events along the chromosome (bold points distributed in the small range of *y*-axis values). The results of simulations suggest that the uneven distribution of recombinations in human chromosomes would be the result of relatively high inbreeding of human populations at least in the past. Since the bias of recombination distribution is growing toward the edges of expanding populations (results not shown), it would be interesting to perform such analyzes in genomes of small, highly inbred populations. The model also predicts that species living in conditions where higher inbreeding is expected (in the model, lower distances for looking for partners and placing the offspring) should evolve under lower intragenomic recombination rate. If we assume that rats and mice are more inbred species than humans, it could explain why crossover rate in rats' and mice' genomes is significantly lower (Jensen-Seaman et al. 2004).

Supporting online materials

Some additional results of simulations under different parameters of intragenomic recombination rate and inbreeding coefficient are available on request from the corresponding author or at our Web site: http://www.smorfland.uni.wroc.pl/sympatry/.

Conclusions

Low recombination rate and high inbreeding lead to specific strategy of genome evolution with uneven distribution of accepted recombination events inside genomes. This strategy is connected with high probability of generation the complementing sets of haplotypes. Thus, sympatric speciation is an intrinsic property of highly inbred populations, i.e., after catastrophes or at the edges of the expanding populations.

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