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Degeneration of the Y chromosome in evolutionary aging models

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Abstract. The Y chromosomes are genetically degenerated and do not recombine with their matching partners X. Recombination of XX pairs is pointed out as the key factor for the Y chromosome degeneration. However, there is an additional evolutionary force driving sex-chromosomes evolution. Here we show this mechanism by means of two different evolutionary models, in which sex chromosomes with non-recombining XX and XY pairs of chromosomes is considered. Our results show three curious effects. First, we observed that even when both XX and XY pairs of chromosomes do not recombine, the Y chromosomes still degenerate. Second, the accumulation of mutations on Y chromosomes followed a completely different pattern then those accumulated on X chromosomes. And third, the models may differ with respect to sexual proportion. These findings suggest that a more primeval mechanism rules the evolution of Y chromosomes due exclusively to the sex-chromosomes asymmetry itself, i.e., the fact that Y chromosomes never experience female bodies. Over aeons, natural selection favored X chromosomes spontaneously, even if at the very beginning of evolution, both XX and XY pairs of chromosomes did not recombine.

PACS. 87.23.Cc Population dynamics and ecological pattern formation – 87.23.Kg Dynamics of evolution – 05.10.Ln Monte Carlo methods

1 Introduction

Evolutionary aging models play an important role in studying evolution due to their successful ability to reproduce biological effects [1,2]. We are interested in studying two particular aging models in sex-chromosomes evolution background. The first one is the well known Penna model, which regards the individual's genome as having a discrete number of diseases [3,4]. The second was introduced by Heumann and Hötzel [5] and modified by Medeiros and Onody [6]. It associates the individual's genome to real numbers which represent survival probabilities. Hereafter they will be called Penna model and MHH model (modified Heumann-Hötzel model) for the sake of simplicity. We will deal with sexual versions of these models in the context of sex-chromosomes asymmetry.

Sex chromosomes have some very intriguing features, including the genetic degeneration of Y chromosomes and non-recombination of XY pairs [7–9]. In comparison to the X chromosomes, Y is poor in genes, it has less genes and it is full of repetitive sequences [10–12]. Suppression of recombination of XY pairs is pointed out as the main responsible for the Y chromosome degeneration [13–15]. We are interested, however, in studying sex-chromosomes evolution in the absence of recombination on both XX and XY pairs. The motivation for this work came out from the following intriguing question. If recombination was meant to be absent on both XY and XX pairs of chromosomes at the very beginning of evolution, would Y chromosomes still degenerate? The answer to this question, as we shall see, is surprisingly a conclusive yes. Sex chromosomes embody a very particular asymmetry: while Y chromosomes are forbidden to experience female bodies, the X chromosomes are free denizens of both sexes. The impact this asymmetry presents on Y chromosomes evolution is very profound.

2 Evolutionary aging models

Both models share some common evolutionary mechanisms. Distinctions arise mostly on the genome of the population, on mutations and on the mechanism of natural selection. So we will present the overall procedures, common to both models, emphasizing their differences on the appropriate occasion. Consider time evolution of diploid organisms, in which males consist of XY and females of XX pairs of chromosomes, just as in the ordinary human sex chromosomes. At each time step, the organisms follow some rules, such as reproduction, death due to natural selection and death when the maximum age k has

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been reached. For computational purposes an additional killing factor (Verhulst factor) is considered, which represents food and environmental restrictions. It kills an organism according to the probability $N(t)/N_{max}$, where $N(t)$ is the population size at time t and N_{max} is the maximum population size supported by the environment. The timescale used here is arbitrary.

Natural selection acts differently on each model, since the genomes structure of the organisms differ considerably. In Penna model, each chromosome consists of a number k of genes, where each gene can have one or none deleterious mutations. This is a chronological genome in the sense that each gene acts on a specific age of the organism. Once organisms are diploid, both chromosomes are read in parallel. If two corresponding genes have one mutation each, then a disease is accumulated in the organism lifetime, which means that we consider here the case where diseases are recessive (for more details, see the end of Sect. 4). Natural selection eliminates an organism when a number d of diseases is reached. In MHH model, the chromosomes also consist of k genes, and a probability value is associated to each gene. Likewise, this is a chronological genome and each gene value represents the survival probability of the organism due to natural selection at a specific age. Since organisms are diploid, both chromosomes ought to affect the organisms lifetime equally. Hence, the organisms will live at a specific age due to natural selection according to the averaged values of both corresponding genes.

Sexual reproduction starts at age i and ends at age f. A fertile female chooses randomly a fertile male to mate. They produce b offspring in that respective fertile age. One chromosome from the father and one from the mother are chosen with 50% of chance to produce the newborn genome. It is important to emphasize that both XX and XY pairs of chromosomes do not run any sort of recombination. Note that half of the births are from each sex. In Penna model, an integer number m of mutations is inserted on each of the baby's chromosomes. In MHH model, mutations occur on a fraction p of babies on a single gene of each chromosome. The survival probability of the mutated gene is modified by a real factor m', which means that the new value equals the old one multiplied by m'.

3 Simulations

We have performed a very large numerical simulation in order to assure that the stationary regime has been achieved on both models. In order to compare the degeneration of the chromosomes, we calculated a quantity that measures the overall accumulation of mutations for Penna model and the overall survival probability for MHH model, for each type of chromosome. Note that at the very beginning of the simulations all organisms are absolutely healthy, which means they have none deleterious mutations for Penna model and all the survival probabilities are equal to one for MHH model. In Penna model, we calculated the fraction of mutations on every X chromosomes and then averaged it over the total number of X chromosomes. The same calculation was performed with respect to the Y chromosomes. The averaged values from male and female X chromosomes happen to be equal, as expected. In MHH model, we calculated the mean survival probability for the k genes of each type of chromosome and then averaged it over the total number of the respective chromosome. Subtracting this value from unity we then obtain the mean mortality probability (or mean degeneration) for each type of chromosome. Therefore, we are able to compare the genetic degeneration of X and Y chromosomes on both models. It is important to remember that in the course of the simulations, mutations are treated equally on every chromosome. The results are shown in Figure 1 for both models.

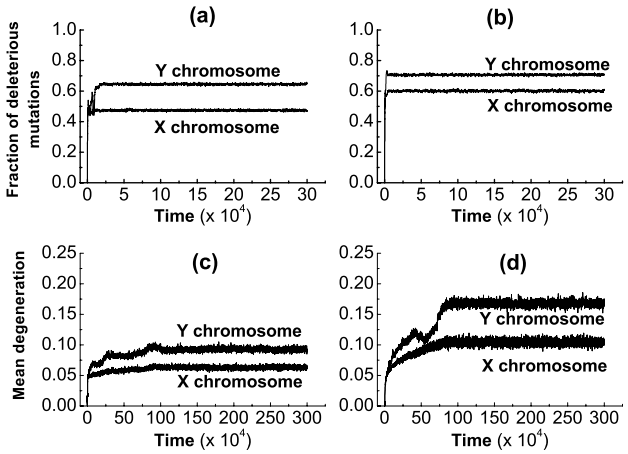

Fig. 1. Results from numerical simulations. For (a) and (b), the evolution of the mean fraction of deleterious mutation for X and Y chromosomes in Penna model. For (c) and (d), the evolution of the mean mortality probability for X and Y chromosomes in MHH model. The parameter values are: (a) $k = 15$, $i = 5$, $f = 10$, $b = 1.5$, $m = 1$, $d = 2$, $N_{max} = 600,000$; (b) The same as (a) except that $d = 3$; (c) $k = 15$, $i = 5$, $f = 10$, $b = 3$, $p = 0.1$, $N_{max} = 150,000$, m' is chosen randomly from the interval $[0.74, 1.01]$; (d) The same as (c), except that m' is chosen from $[0.95, 1.01]$.

The four graphics of Figure 1 lead to the same curious result: even though mutations did not favor any chromosome, the Y accumulated more mutations than the X chromosomes. These findings suggest that even in the absence of recombination on both XX and XY pairs of chromosomes there is an additional and spontaneous mechanism which leads Y chromosomes to their very degeneration. Other parameter values were exhaustively tested and led to this same degeneration.

Certainly this curious effect cries out for an explanation. Although we do not possess a rather analytical demonstration for this mechanism, we do have some quite satisfactory insights. Note that Y chromosomes travel exclusively within male lineages, whereas X chromosomes passes through both sexes. This is indeed a very subtle and important distinction. Consider, for instance, one very ill Y chromosome paired with a very healthy X chromosome. In order to eliminate this bad piece, one must expect to happen a random episode – fathers having no sons.

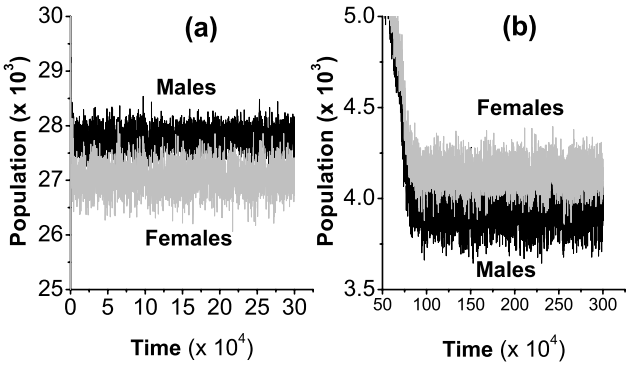

Fig. 2. Sexual predominance in: (a) Penna model, (b) MHH model. The number of male and female individuals is represented in black and gray, respectively. In the stationary regime we find the following mean values and standard deviations: (a) $(27,773 \pm 207)$ males (50.7%) and $(27,044 \pm 273)$ females (49.3%) (b)$(4,138 \pm 76)$ females (51.2%) and $(3,941 \pm 92)$ males (48.8%).

Consider now one very ill X chromosome paired with a very healthy Y chromosome. In order to eliminate this poor chromosome, we need another random episode - fathers having no daughters. Until this moment these situations are symmetrical and do not favor any type of chromosome. However, if we consider a very ill X chromosome paired with a very healthy X chromosome, an asymmetrical situation appears. This imperfect chromosome can be eliminated from the population even if these mothers have sons or daughters. The X chromosomes are more versatile in this sort of women (a healthy X paired with a poor X) because they can have offspring from both sexes and still not pass the mutated chromosome through generations. This distinction is not present on Y chromosomes. Over aeons of evolution this tiny distinction seemed to benefit X chromosomes, bringing huge far-reaching consequences for sex chromosomes.

Both models studied here are very likely except for their mechanisms of mutations and natural selection, which certainly play major importance on the evolution of chromosomes. Nevertheless, on both models the Y chromosome degeneration turned out to be inevitable, which suggests that there is an additional evolutionary force leading Y chromosomes to their very degeneration, not depending on a particular model.

4 Sexual predominance

It is also interesting to analyze the sexual proportion established on each model. Evidently we should expect an asymmetrical proportion between sexes, once the Y chromosomes accumulated more mutations than their partners X. One might naturally expect that women shall live more than men. This is quite true for MHH model but it is not for Penna model, as we can see from Figure 2.

We are facing at this very moment to a completely different behavior with respect to sexual proportion between those models. The female predominance in MHH model is clearly expected. It is natural to have most of deaths in male when Y chromosomes mortality probability is greater than the X chromosomes mortality. Therefore, it follows that the number of females will be larger.

Table 1. Pattern of mutations accumulated on each type of chromosome for each age group on Penna model. Standard deviations are less than 1% of their corresponding mean values.

age	Females first X chromosomes	Females second X chromosomes	Males X chromosomes	Males Y chromosomes
1	0.50	0.51	0.51	1.00
2	0.57	0.58	0.58	1.00
3	1.00	1.00	1.00	0.21
4	0.75	0.73	0.73	0.32
5	0.52	0.53	0.53	1.00
6	0.68	0.67	0.66	0.41
7	0.50	0.52	0.52	1.00
8	0.65	0.66	0.66	1.00
9	1.00	1.00	1.00	0.64
10	1.00	1.00	1.00	1.00

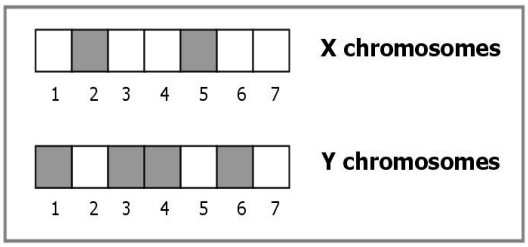

Fig. 3. Pattern of mutations accumulated on X and Y chromosomes for a typical population on Penna model. White squares hold for ages with no mutations and gray squares represents ages with a mutation.

A more careful discussion over the population of Penna model is needed. In order to fully understand this male prevalence in Penna model it is very useful to compute the mean fraction of mutations per age on the whole population for each type of chromosome. We calculated for each age the mean fraction of mutations within the respective chromosome for all organisms. Our results are given in Table 1 for a particular set of parameters. Other parameter values led to very similar patterns. We can see from Table 1 that the X chromosomes followed the same pattern of mutations, while Y chromosomes presented a very different configuration. More precisely, when the mean fraction of mutations is high at a specific age for X chromosomes it is low for Y chromosomes and vice versa.

The different pattern of mutations accumulated on Y chromosomes holds the explanation for male predominance in Penna model, as we shall see through an example. Consider, for instance, such a population where Y chromosomes embody more mutations than X chromosomes, with alternated mutations, like the one illustrated on Figure 3. We can realize that a typical woman will carry two diseases during her lifetime, while a typical man will be unharmed during his life. Although Y chromosomes carry

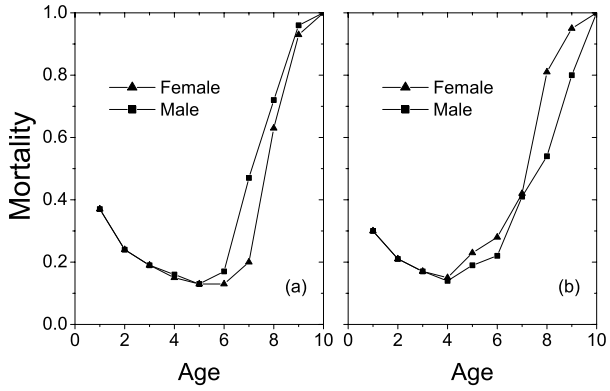

Fig. 4. (a) Mortality per age in the MHH model. Parameters: $k = 10$, $b = 3$, $i = 5$, $f = 10$, $p = 0.1$, $N_{max} = 150,000$, $m' \in [0.82, 1.01]$. (b) Mortality per age in the Penna model. Parameters: $k = 10$, $b = 3$, $i = 5$, $f = 10$, $m = 1$, $N_{max} = 100,000$, $d = 4$.

more mutations, male are favored due to their alternated pattern of mutations with respect to X chromosomes, built up during evolution. We notice that this is the first time these two evolutionary models have exhibited different results, since up to now they have agreed in a series of phenomena, such as catastrophic senescence, Gompertz law, among others [6].

Our results for MHH and Penna models can be corroborated by determining their respective mortalities rate per age $\mu(a) = 1 - \frac{N(a+1)}{N(a)}$, where $N(a)$ is the number of individuals (time averaged in the steady regime) at age a. Figure 4 shows us, unambiguously, that the male's mortality is bigger than female's mortality in the MHH model while, for the Penna model, the situation is the other way round.

Last but not least, it is important to analyze what happens with the degeneration of the Y chromosome if there are dominant positions in the genome. Although they represent less than 10% of a real genome [16], they can change the level or intensity of the Y chromosome degeneration. In the Penna model, we have a dominant position if, in a fixed (pre-chosen) location of the genome, it is enough to have *only one* allele mutated in order to count it for the threshold d. In the MHH model, such a dominant position is taking into account by choosing the allele with the smaller survival probability. For both models, we have verified that the Y chromosome degeneration *decreases* as we *augment* the number of dominant positions dp. In Table 2, we present the Penna model pattern of mutations when the number of dominant positions are $dp = 2$ and $dp = 10$, in the latter case (extremely improbable), the Y chromosome degeneration fades away.

Finally, it is interesting to measure the dependence of the average age of the population with increasing fertility. Table 3 shows the average age of the population, $\frac{\sum_a aN(a)}{\sum_a N(a)}$, for males and females against fertility.

Surprisingly, the average age of the population is a decreasing function of the fertility. This reminds the behavior found by Hwang, Krapivsky and Redner [17] when they measured the average age of the population against life expectancy.

Table 2. Pattern of mutations accumulated on male's X and Y chromosomes when the number of dominant positions are 2 (selected at ages 3 and 6) and 10. In the latter case, the ages 9 and 10 disappear.

age	dp=2 X chromosomes	dp=2 Y chromosomes	dp=10 X chromosomes	dp=10 Y chromosomes
1	0.66	0.36	0.27	0.27
2	0.70	0.35	0.27	0.27
3	1.00	1.00	1.00	1.00
4	0.48	0.62	0.27	0.27
5	0.43	1.00	0.28	0.28
6	1.00	1.00	1.00	1.00
7	0.65	1.00	1.00	1.00
8	1.00	0.97	1.00	1.00
9	1.00	1.00	0.00	0.00
10	1.00	1.00	0.00	0.00

Table 3. Dependence of the average age population with fertility in the Penna model.

Fertility	Female	Male
1.5	3.79	3.96
3.0	3.29	3.45
5.0	2.93	3.01

5 Discussion

An important feature of our results is that it is robust. Although the space of the parameters is very high, we have scanned a reasonable number of them. The tests ranged over the intensity of mutations, reproduction interval, and fertility. For Penna model: $k = 15$; $d = 2, 3, 4$; $(i, f) = (5, 10), (7, 10)$; $b = 1.5, 3.0$. For MHH model: $k = 15$; $(i, f) = (5, 10), (7, 10)$; $p = 0.1, 0.2$; $b = 1.5, 3.0$; $m' \in [0.61..0.97, 1.01]$. All parameters values confirmed the Y chromosome degeneration, as shown in Figure 1, as well as the sexual predominance of Figure 2. The asymmetry embodied in sex chromosomes is more imperative than any biological parameter, such as intensity of mutation, fertility, reproduction interval, whatsoever.

In summary, we studied two types of evolutionary models in the context of sex-chromosomes evolution with non-recombining XX and XY pairs of chromosomes. Mutations were treated equally on each type of chromosome. Although mutations did not favor any chromosome or any sex, the Y chromosomes accumulated more mutations than the X chromosomes on both models. Our results lead us to conclude that natural selection favors X chromosomes and harms Y chromosomes spontaneously, even in the absence of recombination on both XX and XY pairs of chromosomes. There is an evolutionary force which leads Y chromosomes to accumulate more diseases then X chromosomes in a straightforward manner. This

force is a direct consequence of the asymmetry present on sex-chromosomes. We believe this spontaneous degeneration mechanism was present in sex-chromosomes evolution since the very first Y chromosome appeared on Earth, not depending if those primeval chromosomes did or did not recombine during the first moments of evolution.

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