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Deaf intermarriage does not increase the prevalence of deafness alleles

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Deaf intermarriage does not increase the prevalence of deafness alleles

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Abstract [299/300 words]

The idea that deaf intermarriage increases deafness was forcefully pushed in the late 19th century by Alexander Graham Bell, in proceedings published by the National Academy of Sciences. Bell's hypothesis was not supported by a 19th century study by Edward Allen Fay, which was funded by Bell's own organization, the Volta Bureau. The Fay study showed through an analysis of 4,471 deaf marriages that the chances of having deaf children did not increase significantly when both parents were deaf. In light of what appeared to be an increase in non-complementary pairings when a modern dataset of Gallaudet alumni was compared with the 19th century Fay dataset, Bell's argument has been resurrected in the published genetics literature that residential schools for the deaf, which concentrate signing deaf individuals, have promoted assortative mating based on language compatibility. A published report from a computer simulation posits that assortative mating could have increased the frequency of deafness alleles. Because this hypothesis, and the results of that computer simulation, contradict classical models of inbreeding introduced by Fisher and Wright, it is critically important that this hypothesis be thoroughly investigated. In this study, we used an established forward-time genetics simulator with parameters and measurements collected from the published literature. Compared to mathematical equations, simulations allowed for more complex modeling, were free of assumptions of parametricity, and captured ending distributions and variances. Our simulation results, whose median results matched predictions from mathematical equations, show that assortative mating modestly increases the incidence of phenotypically deaf individuals with this effect mostly completed by the third generation. Most importantly, our data show that assortative mating does not affect allelic frequency under reported conditions. We offer alternate explanations for the higher rate of non-complementary pairings measured in the contemporary Gallaudet alumni sample as compared to the Fay dataset.

Introduction

Alexander Graham Bell grew concerned and argued against the intermarriage of deaf individuals, stating that "a number of successive generations should result in the formation of a deaf variety of the human race [1]." The idea of the "deaf variety" of the human race coalesced during a period in American history where immigration was on the upswing and Darwinian rhetoric was being applied to different facets of American society, including education [2]. The residential schools, which sign language was used, often served as the linchpin for the deaf community. In the proceedings published by the National Academy of Sciences, Bell delineated the costs of educating deaf individuals and argued that the residential schools were an economic

burden to state governments funding the schools [1] (pp. 47-48). Because residential schools for the deaf drew a critical mass of deaf students, Bell sought to prohibit sign language use among deaf children and favored the oralism approach, in which deaf children used speech and lipreading [1] (p. 46). Students at residential schools for the deaf socialized, formed close bonds, and as adults joined organizations, clubs, and societies for the deaf, which Bell argued encouraged intermarriage among deaf people.

Essentially, Bell felt that the "social environment" in which deaf children interacted through school and community ties needed to be altered. Towards the end of the last chapter of the *Memoir*, Bell wrote: "The segregation of deaf-mutes, the use of the sign language, and the employment of deaf teachers produce an environment that is unfavorable to the cultivation of articulation and speech-reading, and that sometimes causes the disuse of speech by speaking pupils who are only deaf." [1] (p. 48). Following his address to the National Academy of Science, Bell conducted research on hereditary deafness on Martha's Vineyard in the late 1880s. Although he never understood the transmission of genetic deafness, Bell persisted in efforts to better understand its transmission [3,4]. To this end, he hired Edward Allen Fay, who was Vice-President at Gallaudet College and editor of the *American Annals of the Deaf*.

Bell's Volta Bureau funded Fay's landmark study of 4,471 deaf marriages. This study investigated the question of whether deaf intermarriage led to an increase in deafness. The Fay study [5] eventually concluded that deaf intermarriage did not much increase the chances of having deaf children. Bell disregarded Fay's results and nevertheless remained vocal in his beliefs that the ideal marriage was a marriage between a deaf and hearing person. As the wealthy inventor of the telephone, he was highly influential in the scientific community and in the nascent eugenics movement.

The results of Fay's study were not well understood at the time because they were published in 1898, before the rediscovery of Mendel's work [6] and the many discoveries in experimental and theoretical genetics that followed. In those days, the understanding of the heredity of deafness and heredity in general was based on observation, such as those by the otologist William Wilde in 1857, or by tallying summary statistics, which is what Fay did. Fay's work also preceded the population genetics model for inbreeding independently introduced by R.A. Fisher [7] and Sewall Wright [8] and more recently revisited by Crow and Felsenstein [9].

We now know that genetic deafness [OMIM 220290] accounts for approximately half of deafness in children and is caused by mutations in >100 mapped genes and a predicted another >200 genes [10]. Of these, deafness due to connexin 26 (*GJB2*) variant alleles [OMIM 121011] is by far the most common, accounting for slightly less than half of all genetic deafness, or roughly a quarter of congenital deafness [11]. Three *GJB2* frameshift variants account for nearly all *GJB2* deafness, and are associated with specific ethnic groups: 35delG in European ancestry, 167delT in Ashkenazi Jewish ancestry, and 235delC in Asian ancestry [12-14]. These three variants are inherited in an autosomal recessive fashion, and cause nonsyndromic deafness, meaning that there are no discernable physical characteristics other than deafness.

Most deaf intermarriage produces hearing children because of the complementation between the many recessive genes that cause deafness, and also because deafness is often acquired during life, which Fay [5] termed "adventitious," and may not have a proximate genetic cause. Further, we know from Fisher's [7] and Wright's [8] classical model that in a large population and in the absence of selective pressure, assortative mating increases the phenotypic expression of recessive alleles, but the allelic frequencies themselves do not change.

Several authors have resurrected Bell's original argument, pointing out that the concentration of signing deaf individuals in a residential environment over the past 200 years has led to assortative mating [15,16]. One work, in particular, shows through a computer simulation that assortative mating, augmented by relaxed selection, could increase both the incidence of phenotypic deafness as well as the prevalence of the commonest deafness alleles, i.e. the three *GJB2* deletions. This type of assortative mating has been termed "linguistic homogamy," in that it is driven by a strong preference for easy communication and linguistic compatibility between mates. This simulation is posited to explain results from a pedigree study by Arnos *et al*. [17] showing a higher rate of non-complementary pairings in a contemporary Gallaudet alumni dataset as compared with the original Fay dataset collected 100 years ago. This work has been well cited in the scientific literature, appearing in Online Mendelian Inheritance for Man [OMIM 121011]. Although the conclusion that linguistic homogamy would increase homozygosity and therefore the incidence of phenotypic deafness in subpopulations with intensive assortative mating is unsurprising because it remains consistent with Fisher's [7] and Wright's [8] classical model, this effect should be mostly complete within the first few generations. In addition, the second conclusion, that linguistic homogamy would also increase the prevalence of the deafness allele, is inconsistent with Fisher's and Wright's classical predictions.

The question of whether deaf intermarriage and deaf socialization affects the incidence of phenotypic deafness and the prevalence of deafness alleles is important because it has potentially profound implications for policy and funding decisions, such as popular support for funding of residential deaf education programs. Given the popularity of eugenics in fairly recent history, particularly in Germany and in Scandinavian countries, the ethically catastrophic impact of the eugenics movement on worldwide societies, and the recent introduction of gene-editing

technologies and discussion of their use in humans, it is critically important that this question and these conclusions are examined carefully using a variety of approaches.

In this study, we performed thousands of forward-time evolutionary simulations using a well-established package, which has been used to simulate assortative mating, to measure the expected change in phenotypic expression and also test the hypothesis that linguistic homogamy alone is sufficient to influence the gene pool [18,19]. We used measurements of allelic frequency and fitness collected over a century of research and reported in the contemporary literature. We used statistical analyses to compare not only median results, but also ending distributions. This approach allowed us to capture the variance in end results without underlying assumptions of parametricity. We further compared these results with mathematical modeling. Our simulation results remained consistent with classical predictions and mathematical models, affirming that linguistic homogamy modestly increases the incidence of homozygous deaf individuals which is mostly complete after the first two generations. However, linguistic homogamy does not affect allelic prevalence. Our simulations also affirm that homogamy affects allelic frequency synergistically with relative fitness, but when combined with the depressed relative fitness of deaf individuals, as has been uniformly reported in the literature, it depresses rather than increases the frequency of a deafness allele.

Throughout this paper, we use some antiquated and modern terms interchangeably: intermarriage, inbreeding, interbreeding, homogamy, linguistic homogamy, and assortative mating. Likewise, we also use the terms acquired deafness and adventitious deafness interchangeably. We did this to match the terms and contexts used by the original authors over a century of genetics research and societal change.

Results

We initially ran 5,000 simulations following parameters established elsewhere **[15]** as follows: the initial allelic frequency of the *GJB2* variant allele was set to 1.304%, as measured in European populations, and simulations were run over 20 generations (400 years), with a constant population size of 200,000 simulated individuals. At each generation, a proportion of simulated hearing individuals were randomly selected (of which a small proportion carried a single *GJB2* deletion), and given acquired deafness at a conservative rate of 0.8 per 10,000 simulated individuals, which is the measured frequency of deafness at birth **[20]**; the frequency of deafness at reproductive age is actually higher due to childhood diseases and other morbidities. Genetically deaf simulated individuals and simulated individuals with assigned acquired deafness were mated in the same pool. (This assumption of 0.8 per 10,000 is a lower limit and therefore pushes us in the direction of Type II error, resulting in more simulated non-complementary matings that occur in reality and therefore an overestimation of the effect of assortative mating). For our initial analysis, linguistic homogamy was set to 0% and 90% to create two datasets for endpoint comparison. The 90% assortative mating figure is based on Schein and Delk's **[21]** figure of 80-90%, is what was used elsewhere for simulations **[15]**, and is close to Fay's {Fay:*1898tr} uncorrected measure of 72.5%.

Under these parameters, after 20 generations (400 years), the median frequency of genetically deaf individuals increased by 22% relative to the simulations with no homogamy; 0.017% as compared to 0.0220%, which is statistically significant (Fig 1 and Table 1; $U = 5.8 \times 10^{6}$, $p < 10^{-308}$, 96% CI: 0.0125% to 0.0350%). This statistic was identical to the calculation of 0.0220% using equation (3) taken from Crow and Felsenstein [9] (Table 1) and described in Materials and Methods. Most of the change occurred within the first two generations. The frequency of the

GJB2 variant allele was 1.304% versus 1.306% after 20 generations, which is not statistically significant (Fig 1 and Table 1; $U = 1.2 \times 10^{7}$, $p = 0.94$). The inbreeding coefficient, F, was little different, 0 versus 0.00376, although this was significant ($U = 5.0 \times 10^{6}$, $p < 10^{-308}$). This increase in F was greatly attenuated by competition for mates between the small number of simulated genetically deaf individuals and the larger pool of simulated individuals with acquired deafness.

Table 1. Homogamy and reproductive fitness on the ending median frequencies of genetically deaf (*GJB2*) individuals and the deafness (*GJB2*) allele.

Deaf Individuals

Fitness	Homogamy 0%	30%	60%	90%
0.0	0.0105% (0.0050 - 0.0175%)	0.0105% (0.0055 - 0.0175%)	0.0105% (0.0055 - 0.0170%)	0.0105% (0.0050 - 0.0175
0.5	0.0130% (0.0070 - 0.0210%)	0.0135% (0.0070 - 0.0215%)	0.0135% (0.0075 - 0.0220%)	0.0140% (0.0075 - 0.0225
1.0	0.0170% (0.0100 - 0.0260%)	0.0180% (0.0105 - 0.0280%)	0.0195% (0.0110 - 0.0310%)	0.0220% (0.0125 - 0.0350
	0.0170%*	**0.0182%***	**0.0198%***	**0.0220%***
1.5	0.0220% (0.0135 - 0.0330%)	0.0260% (0.0155 - 0.0400%)	0.0345% (0.0190 - 0.0575%)	0.0770% (0.0310 - 0.2849
2.0	0.0305% (0.0195 - 0.0440%)	0.0445% (0.0265 - 0.0690%)	0.1485% (0.0565 - 0.4425%)	29.20% (3.43- 64.1%)

Allelic Frequency

Fitness	Homogamy 0%	30%	60%	90%
0.0	1.03% (0.908 - 1.16%)	1.03% (0.912 - 1.16%)	1.03% (0.910 - 1.16%)	1.03% (0.909 - 1.16%)
0.5	1.15% (1.02 - 1.30%)	1.15% (1.01 - 1.30%)	1.15% (1.01 - 1.29%)	1.14% (1.00 - 1.28%)
1.0	1.30% (1.15 - 1.47%)	1.30% (1.15 - 1.47%)	1.30% (1.15 - 1.47%)	1.31% (1.15 - 1.47%)
1.5	1.49% (1.31 - 1.70%)	1.52% (1.33 - 1.74%)	1.56% (1.35 - 1.81%)	1.70% (1.41 - 2.22%)
2.0	1.74% (1.52 - 2.00%)	1.86% (1.60 - 2.17%)	2.32% (1.78 - 3.41%)	36.4% (6.17 - 73.3%)

Values given are medians, with 96% credible intervals in parentheses. Values in bold and followed by an asterisk were calculated from a mathematical equation from Crow and Felsenstein as described in Materials and Methods. Simulations were run as described in Materials and Methods.

[Insert Fig 1 here]

We next ran simulations over a range of homogamies (Fig 2 and Table 1). The frequency of deafness increased proportionately to homogamy. Most of the change occurred in the first two generations. All differences in the frequency of deafness between each endpoint were highly significant with all $p < 10^{-40}$. The results also in close agreement with calculations using equation (3) from Crow and Felsenstein [9] (Table 1) and described in Materials and Methods. The allelic frequency, however, remained invariable regardless of the extent of homogamy, and no statistically significant difference was found between any of the endpoints.

[Insert Fig 2 here]

Synergistic Effects of Fitness And Homogamy on Allelic Frequency

Because homogamy increases the phenotypic expression of alleles, it would therefore modulate the effects of selective pressure upon those alleles. Nance and Kearsey {Nance:*2004jo} have argued that relaxed fitness would be necessary for increasing the numbers of deaf individuals. We therefore investigated this effect across a range of relative fitnesses and homogamies using our forward-time simulator.

The frequency of the *GJB2* variant allele was sensitive to relative fitness, which became particularly noticeable at or above fitnesses of 1.5 when combined with homogamy. (Fig 3 and Table 1).

[Insert Figure 3 here]

Discussion

In this study, we addressed the century-old debate about whether deaf intermarriage increases the phenotypic expression of genetic deafness. We also investigated a recent claim, based on

simulations, that assortative mating could increase the allelic frequency of the commonest deafness allele [15,16]. We ran forward-time computer simulations using the **SimuPOP** package, which has been used to simulate assortative mating, to test the hypothesis that linguistic homogamy alone would affect phenotypic deafness as well as allelic frequencies [18,19]. For each scenario, we aggregated the results of 5,000 simulations. We used statistical analyses to compare not only median results, but also ending distributions. We used this approach in addition to mathematical modeling because it allowed us to capture the variance in results without underlying assumptions of parametricity, and allowed us to easily set up the more complex scenario of introducing to the mating pool individuals with acquired deafness.

Our simulations confirm that 90% homogamy would increase the frequency of homozygous deaf individuals by 29% over 20 generations (96% CI: -26% to 105%). The simulations also confirmed that homogamy did not affect allelic frequency (Fig 1 and 2 and Table 1). Our simulation results are, unsurprisingly, consistent with predictions from the classical genetics model [9], with simulation results in nearly identical agreement with mathematical calculations using their equation (3).

Our simulation results also confirm that relative fitness impacts allelic frequencies. Because homogamy increases the expression of rare alleles, relative fitness acted synergistically with homogamy in our simulations to accelerate changes in allelic frequencies. In our simulations with well above-average relative fitness (1.5x and 2x), allelic frequencies increased. However, these results are not applicable to the worldwide deaf community today because there exists no sample from any population with above-average relative fitness for deaf individuals reported the literature. Instead, the literature uniformly reports depressed relative fitness, usually markedly so, ranging from 0.31 to 0.91; the highest measured fitness of 0.91, which is still depressed, was

from an educated American deaf sample from Gallaudet University [21-25]. Therefore, based on our simulations, the synergy of linguistic homogamy with depressed fitness should be expected to *constrain* the frequency of *GJB2* variant alleles to low levels (Fig 3 and Table 1).

Nance [15] forwarded a hypothesis that linguistic homogamy among early humans may have accelerated the evolution of human speech genes, particularly *FOXP2*, some 150,000 years ago, with the argument that improved language skills in early humans likely correlated with better cooperation, better survival and higher fitness; preferential mating among those with similar language capabilities would have increased the expression of these advantageous alleles and synergistically accelerated this evolution. This hypothesis is intriguing, and our simulation results agree with this hypothesis.

In 2008, Arnos and colleagues [17] studied contemporary pedigrees collected from Gallaudet University alumni, and compared them with pedigrees from Fay's study, which were ascertained from deaf institutions across the country. Segregation analysis comparing these two datasets showed that the proportion of non-complementary pairings were 4.2% in the 1801-1899 Fay dataset and 23% in the 2007 Gallaudet alumni dataset. Our simulation results show that homogamy among the larger deaf community is not a sufficient explanation for the large difference in non-complementary pairings when these two datasets are compared. Rather, we agree with the authors' deliberations that the reason may lie in the difference between how these two datasets were ascertained [17]. The original Fay dataset were ascertained from deaf institutions across the country, whereas the newer dataset were ascertained only from Gallaudet alumni. The Gallaudet dataset likely represents a special subpopulation. Gallaudet, established in 1864, is the world's only university for deaf students. Approximately 95% of its undergraduate student body are deaf. Today, Gallaudet attracts legacy students from multigenerational deaf

families, whose parents and, in some cases, grandparents also attended Gallaudet. While deaf individuals at the time of the original Fay dataset in 1890 were usually from hearing families and were themselves discouraged from marrying others from deaf families, there is a noted preference for contemporary individuals from deaf families both to attend Gallaudet and to pair with others from deaf families because of cultural and linguistic compatibility. Genetically deaf individuals with multigenerational pedigrees, concentrated into the Gallaudet community and directly seeking out one another, bypasses competition from those with acquired deafness, increases the odds of non-complementation, and accelerates the effects of assortative mating. However, (1) this is likely only happening within the Gallaudet community or other select communities that are enriched for multigenerational deaf families and should not reflect the genetic assortment of deaf individuals in the greater population; (2) the increase in phenotypic expression had already mostly occurred after the first three generations of intensive assortative mating and would be predicted to have tapered off already; and (3) regardless of the intensity of assortative mating, it has no effect on the prevalence of deafness alleles..

One intriguing possibility from intensive assortative mating is gametic phase disequilibrium [15]. In the case of connexin deafness, the *GJB6* gene [OMIM 604418] also resides on chromosome 13, a short 29 kb downstream from *GJB2*. There are two known *GJB6* deletion mutations and one missense mutation which are non-complementary with *GJB2* mutations and result in deafness in a digenic inheritance pattern. It is currently hypothesized that the molecular mechanism of this non-complementation is that the *GJB6* deletion causes down-regulation of *GJB2* expression, which may be the more proximal cause of deafness [26]. A rare recombination event in a deaf individual between these tightly linked genes could presumably translocate a *GJB2* and *GJB6* deletion into *cis*, which might create a dominant form of *GJB2/GJB6* digenic

nonsyndromic deafness. However, depending upon the molecular genetic mechanism, if the *GJB6* deletion downregulates *GJB2* in *cis*, these deletion mutations may be complementary in *cis* and the transmission would remain recessive.

We are left with the puzzling paradox of how the commonest *GJB2* variant alleles: 35delG, 167delT, and 235delC, have been measured at prevalences of between 1% and 4.4%, while measurements of fitness in deaf communities have been uniformly depressed [12-14,21-25]. One possibility is mutation-selection equilibrium: novel *GJB2* mutations are perhaps being introduced at the same rate that mutations in the gene pool are being eliminated. Evidence showing a mutational hotspot at *GJB2*, particularly for deletion mutations, would provide support for this hypothesis. A second, and intriguing possibility is that of heterotic balancing selection. Tran van Nhieu, Clair *et al.* have shown in tissue culture experiments that *Shigella flexneri* requires *GJB2* connexons for egression into the intestinal epithelia, raising the possibility that the three common *GJB2* deletions could confer resistance to dysentery [27]. Connexons are dimers of hexameric proteins made up of individual connexins; in individuals with *GJB2* deletions, *GJB2* is replaced by other connexons to form connexins which appear to retain normal function everywhere except for the cochlea. Dysentery has been endemic at least since the advent of urbanization, and resistance to this disease via altered connexons may have provided enough positive selection to bring the commonest *GJB2* mutations to their present frequencies.

We hope that this study can put to rest the century-long debate of whether deaf intermarriage increases deafness in the gene pool using simulations and drawing upon mathematical modeling, with measurements and parameters collated from the published literature – even though this debate continues to be the topic of published peer-reviewed papers in genetics. Our results unequivocally affirm the classical models introduced more than a century ago by Sewell Wright

and R.A. Fisher, and show that while deaf intermarriage had a small effect on the incidence of phenotypic deafness, this effect was mostly completed by the third generation of assortative mating. However, deaf intermarriage did not, and will not affect the prevalence of deafness alleles. Alexander Graham Bell's "deaf variety of the human race" will not happen under present conditions.

Materials and Methods

Code and Dataset

The code used in this study is publicly available from https://github.com/derekbraun/homogamy.git

Simulations

Simulations were performed using **`simuPOP 1.1.10.8`** which is a forward-time population genetics package, scriptable via Python, that has been used to simulate assortative mating [18,19]. Simulations were scripted with **`Python 3.7.4`** on a computer running **`macOS 10.14.6.`** Simulations were parallelized on a 16-core Intel Xeon workstation. It required 80 hours of CPU time to complete the final simulations shown in this manuscript. We modeled both homogamy and reproductive fitness using a non-monogamous mating scheme. Non-monogamous mating was chosen, after some experimentation with code, because this allowed for better stability in the final proportion of homogamy per generation given the small number of deaf individuals in the simulated population. Sexes were not assigned to individuals; this was decided, after some experimentation with code, because it reduced the influence of population size, for which we have no useful measurements; it simplified coding, and it sped up execution time.

After each generation, the following was calculated: the frequencies of the dominant and recessive alleles A and a; the frequencies of the homozygous dominant, heterozygous, and homozygous recessive genotypes AA, Aa, and aa; the number of individuals with each genotype; the number and frequency of deaf individuals (including acquired deafness); and the inbreeding coefficient (*F*) calculated as follows:

$$F = \begin{cases} 1 - \dfrac{P(Aa)}{2pq}, & P(Aa) \leq 2pq \\ 0, & otherwise \end{cases}$$

The frequency of deafness alleles from simulations were also compared to those calculated from equation (3) of Crow & Felsenstein [9]. The effective assortative mating fraction, *r*, was derived from the % homogamy and re-estimated after each generation by adjusting it by the size of the mating pool. This calculation matches the logic used in the forward simulation script which is that the mating pool size included non-genetic deafness at the initial rate of 0.8 per 10,000 individuals [20]. Therefore, initially and before assortative mating, q^2 individuals have genetic deafness due to connexin 26, and 0.008 - q^2 individuals have acquired deafness. At t_0, $R_t = q^2$, so the expression for the mating pool size, 0.008 - $q^2 + R_t$ simplifies to just 0.008. As assortative mating progresses in successive generations, R_t increases, and the mating pool size becomes slightly larger:

$$P(aa) = R_{t+1} = (1-r)\,q^2 + r\left[\frac{q^2 + R_t(p-q)}{1-R_t}\right],\ r = homogamy\%\left[\frac{R_t}{0.0008 - q^2 + R_t}\right]$$

Statistical Testing and Graphing

Statistical comparisons between datasets were performed using `SciPy 1.3.0`. We performed the Shapiro-Wilk test of normality on ending frequencies. Since these ending frequencies were often not normally distributed, and because we additionally wished to test for significant

differences in both medians and variances, we used nonparametric tests: the Mann-Whitney *U* test for two independent groups or the Kruskal-Wallis test for *k* independent groups. Significant Kruskal-Wallis *p*-values were followed by *post hoc* pairwise Mann-Whitney tests without Bonferroni correction, which is more sensitive than Dunn's test [28]. Figures were generated in Python using `matplotlib 3.1.1`.

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Figure 1. Effect over time of homogamy on the frequencies of genetically deaf individuals and a recessive deafness allele. Lines, from top to bottom: 98% interval, 75% quartile, median, 25% quartile, and 2% interval. To the right of each subplot is a violin plot showing the distribution of the endpoint data. The tips of the violins represent the extrema. The vertical lines within the violins show the 2% through 98% interval. The boxes within the violins show the first through third quartile. The cross-hatches show the medians. Simulations were run with relative fitness = 1.0 and other parameters as described in Materials and Methods.

Figure 2. Effect of homogamy on the frequencies of genetically deaf individuals and a recessive deafness allele. Violin plots show the distributions of the endpoint data after 20 generations. The tips of the violins represent the extrema. The vertical lines within the violins show the 2% through 98% interval. The boxes within the violins show the first through third quartile. The cross-hatches show the medians. Simulations were run with relative fitness = 1.0 and other parameters as described in Materials and Methods.

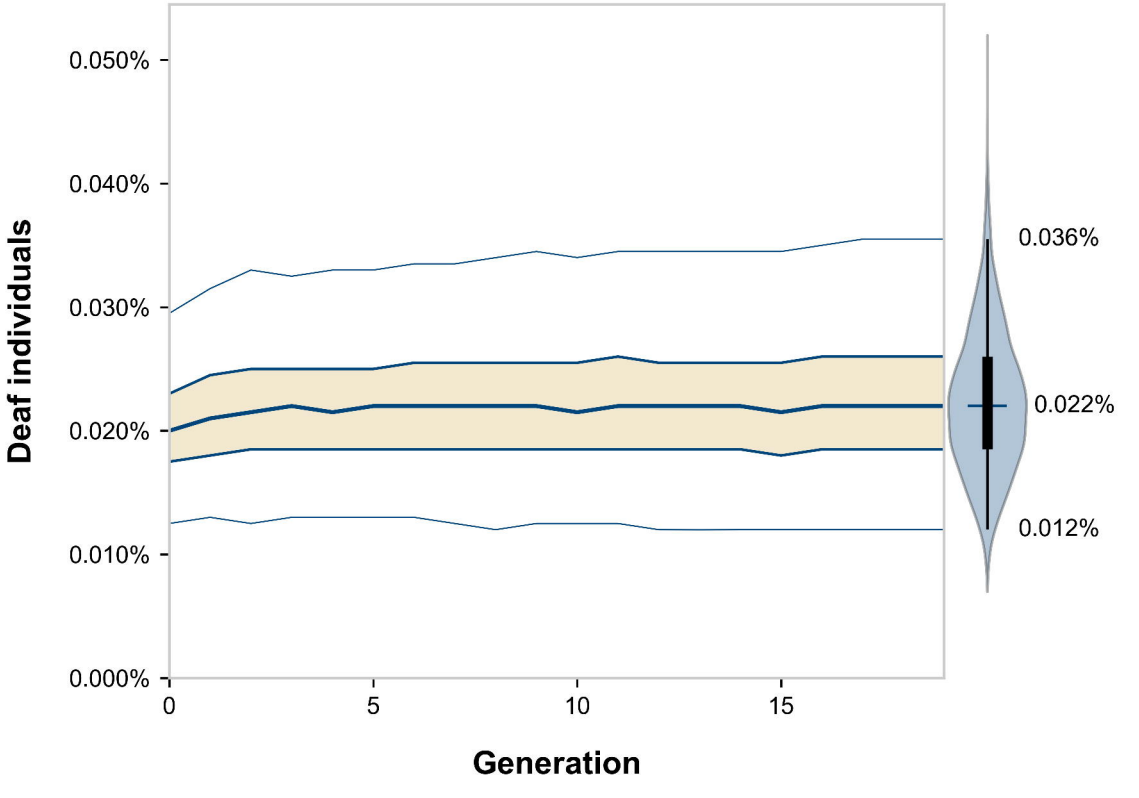
Figure 3. Synergy of homogamy and relative fitness on the frequencies of genetically deaf individuals and a recessive deafness allele. Right: no homogamy; left: 90% homogamy. Violin plots show the distributions of the endpoint data after 20 generations. The tips of the violins represent the extrema. The vertical lines within the violins show the 2% through 98% interval. The boxes within the violins show the first through third quartile. The cross-hatches show the medians.

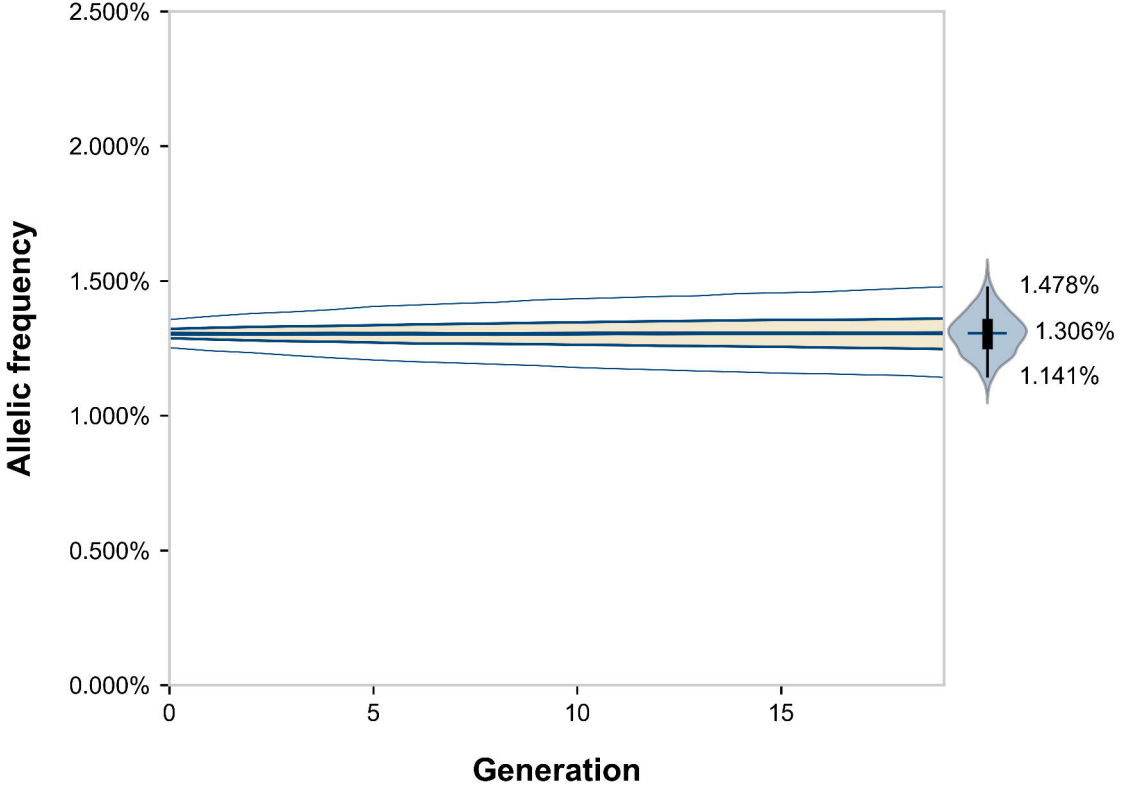
Deaf Individuals

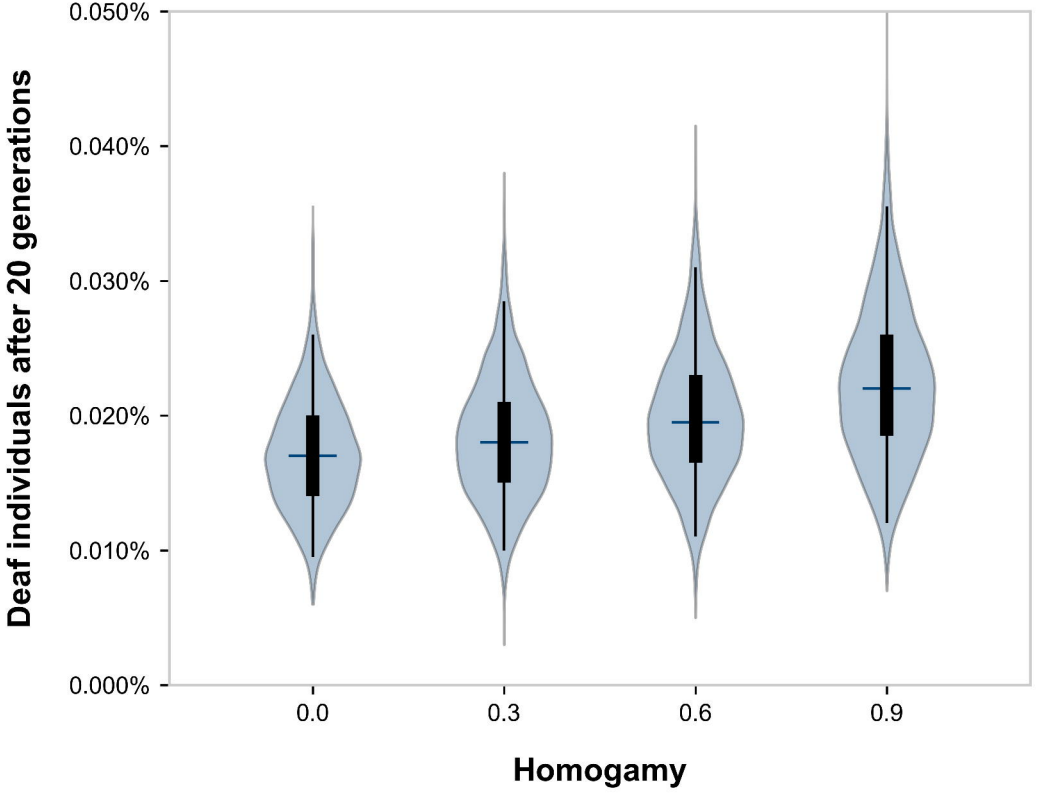
Fitness	Homogamy 0%	30%	60%	90%
0.0	0.0105% (0.0050 - 0.0175%)	0.0105% (0.0055 - 0.0175%)	0.0105% (0.0055 - 0.0170%)	0.0105% (0.0050 - 0.0175%)
0.5	0.0130% (0.0070 - 0.0210%)	0.0135% (0.0070 - 0.0215%)	0.0135% (0.0075 - 0.0220%)	0.0140% (0.0075 - 0.0225%)
1.0	0.0170% (0.0100 - 0.0260%)	0.0180% (0.0105 - 0.0280%)	0.0195% (0.0110 - 0.0310%)	0.0220% (0.0125 - 0.0350%)
	0.0170%*	**0.0182%***	**0.0198%***	**0.0220%***
1.5	0.0220% (0.0135 - 0.0330%)	0.0260% (0.0155 - 0.0400%)	0.0345% (0.0190 - 0.0575%)	0.0770% (0.0310 - 0.284%)
2.0	0.0305% (0.0195 - 0.0440%)	0.0445% (0.0265 - 0.0690%)	0.1485% (0.0565 - 0.4425%)	29.20% (3.43- 64.1%)

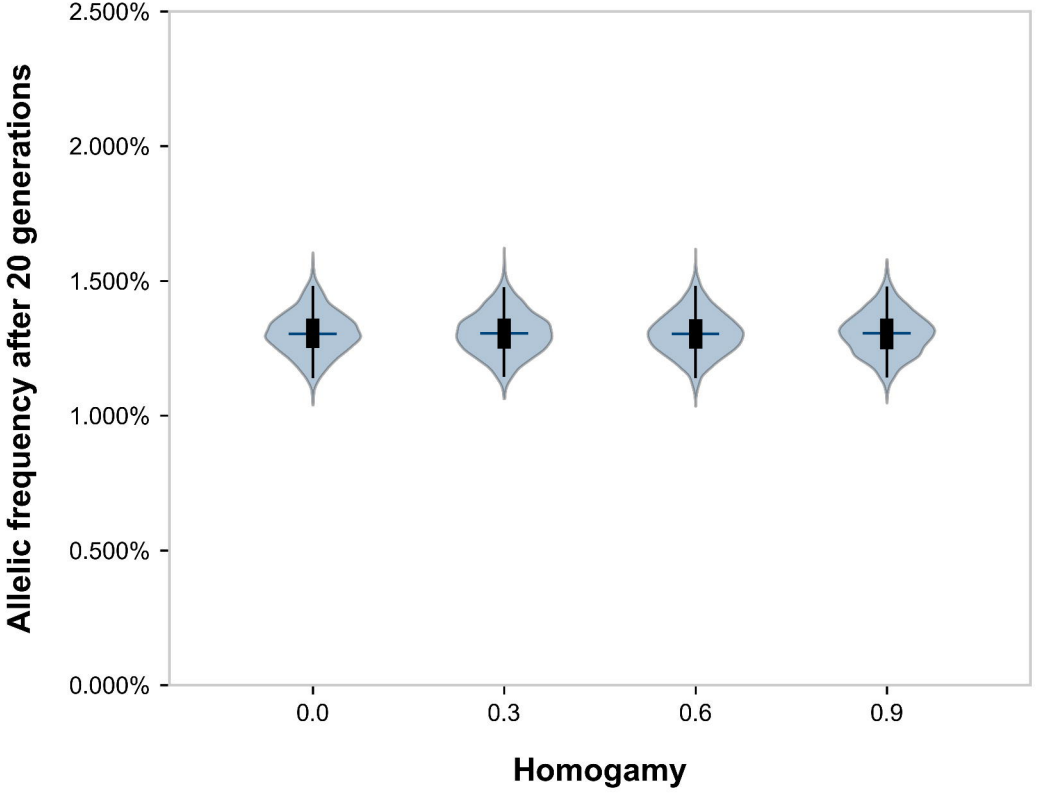
Allelic Frequency

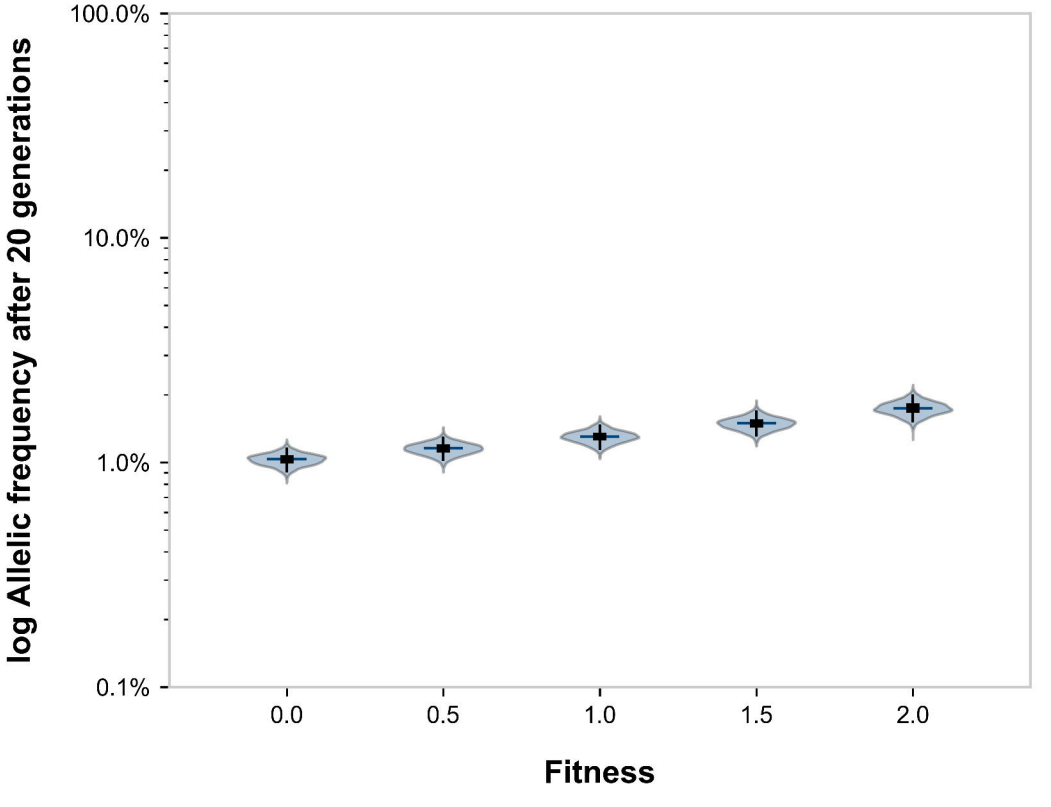
Fitness	Homogamy 0%	30%	60%	90%
0.0	1.03% (0.908 - 1.16%)	1.03% (0.912 - 1.16%)	1.03% (0.910 - 1.16%)	1.03% (0.909 - 1.16%)
0.5	1.15% (1.02 - 1.30%)	1.15% (1.01 - 1.30%)	1.15% (1.01 - 1.29%)	1.14% (1.00 - 1.28%)
1.0	1.30% (1.15 - 1.47%)	1.30% (1.15 - 1.47%)	1.30% (1.15 - 1.47%)	1.31% (1.15 - 1.47%)
1.5	1.49% (1.31 - 1.70%)	1.52% (1.33 - 1.74%)	1.56% (1.35 - 1.81%)	1.70% (1.41 - 2.22%)
2.0	1.74% (1.52 - 2.00%)	1.86% (1.60 - 2.17%)	2.32% (1.78 - 3.41%)	36.4% (6.17 - 73.3%)

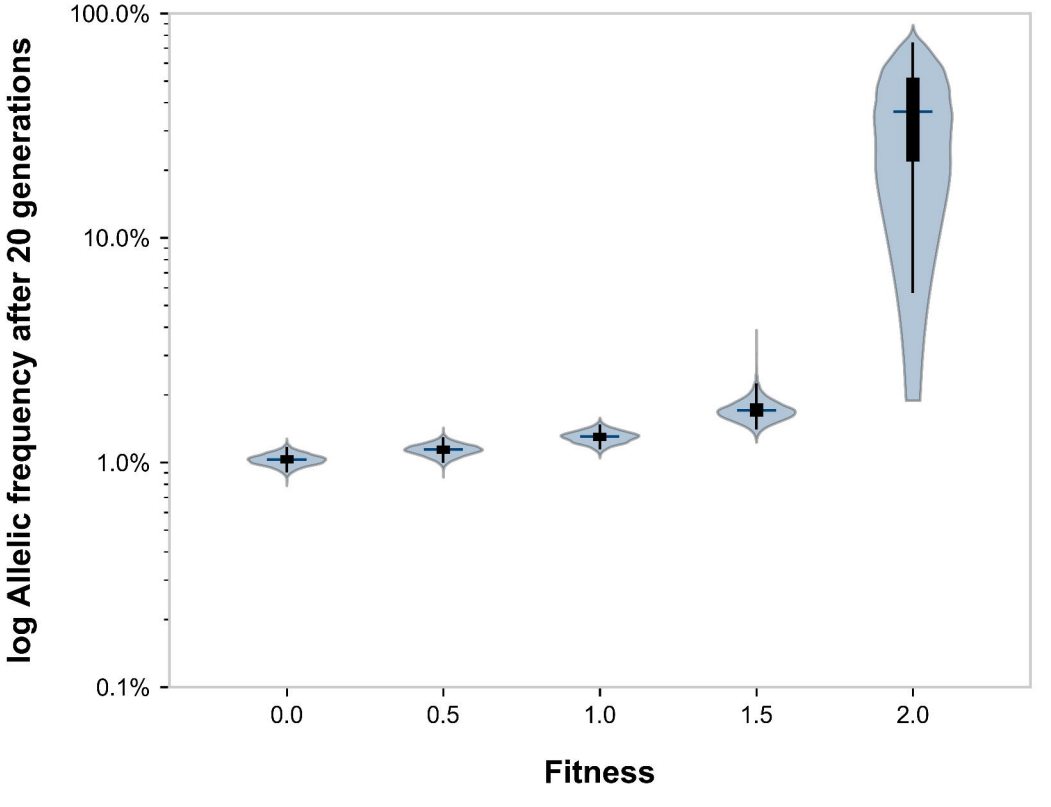

Deaf individuals
0.050%
0.040%
0.030%
0.020%
0.010%
0.000%
0
5
10
15
Generation
0.036%
0.022%
0.012%


2.500%
2.000%
1.500%
1.000%
0.500%
0.000%
Allelic frequency
0
5
10
15
Generation
1.478%
1.306%
1.141%


0.050%
0.040%
0.030%
0.020%
0.010%
0.000%
Deaf individuals after 20 generations
0.0
0.3
0.6
0.9
Homogamy


2.500%
2.000%
1.500%
1.000%
0.500%
0.000%
Allelic frequency after 20 generations
0.0
0.3
0.6
0.9
Homogamy


100.0%
10.0%
1.0%
0.1%
log Allelic frequency after 20 generations
0.0
0.5
1.0
1.5
2.0
Fitness


100.0%
10.0%
1.0%
0.1%
log Allelic frequency after 20 generations
0.0
0.5
1.0
1.5
2.0
Fitness