

RESEARCH

A simple strategy for managing many recessive disorders in a dairy cattle breeding program

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Abstract

Background: High-density single nucleotide polymorphism genotypes have recently been used to identify a number of novel recessives that adversely affect fertility in dairy cattle. Current methods for mate allocation do not use that information, and it will be increasingly difficult to manage matings when a large number of recessives must be managed.

Results: A simple, sequential mate allocation method that constrains inbreeding and accounts for the economic effects of Mendelian disorders was developed and compared with random mating, truncation selection, and Pryce's method of constraining genomic inbreeding for several different scenarios, including 6 hypothetical alleles and 12 recessives currently segregating in the US Holstein population. Pryce's method and the modified Pryce's method showed similar ability to reduce allele frequency, particularly for loci with frequencies greater than 0.30. The modified Pryce's method may outperform Pryce's method for low-frequency alleles with small economic values. Cumulative genetic gain for the selection objective was slightly higher using Pryce's method, but rates of inbreeding were similar across methods.

Conclusions: The proposed method appears to reduce minor allele frequencies for recessives with low frequencies faster than other methods, and can be used to maintain or increase the frequency of desirable recessives. It can easily be implemented in software for mate allocation, and the code used in this study is freely available as a reference implementation.

Keywords: dairy cattle; genetic selection; mating programs; recessive disorders

Introduction

Recessive disorders have been present in livestock populations since modern animal breeding programs began, and hundreds are known to exist [1]. While lethal recessives were present in livestock populations long before the dawn of modern animal breeding, increased levels of inbreeding and bottlenecks due to the differential use of parents have made it far more likely that offspring carrying two copies of rare alleles will result from those matings. In the past, test matings were used to identify recessive disorders [2], but not all recessives were identified before the carrier bull sired many daughters (e.g., BLAD [3], CVM [4], and DUMPS [5]).

Genomic tools have enabled the detection of many new recessives that have deleterious effects on fertility [6], many of which have effects early in gestation and could

not previously be distinguished from failed breedings. As the number of recessives continues to grow, new tools are needed to consider that information when making mating decisions. However, current mate allocation tools do not consider carrier status when bulls and cows are paired. When there are only a few recessives in a population it is easy to monitor individuals to avoid carrier-to-carrier matings, but that is considerably more difficult, or even impossible, when there are many harmful defects segregating in a population.

Pryce et al. [7] recently proposed a simple method for controlling the rate of increase in genomic inbreeding by penalizing parent averages (PA) for matings that produce inbred offspring. After PA are adjusted, the bull that will produce the highest PA when mated to a cow is selected in a sequential manner, and the number of matings permitted for each bull is constrained to prevent one bull from being mated all cows. This method is straightforward to program, and effectively constrains genomic inbreeding at reasonable levels. The objective of this research was to extend Pryce's method to include information about recessives in order to simultaneously account for a large number of Mendelian disorders when allocating mates in dairy cattle breeding schemes.

Data

Base population

Base population cows had true breeding values (TBV) for lifetime net merit (NM\$) that were randomly sampled from a normal distribution with a mean of \$0 and a standard deviation of \$200, which is similar to the genetic SD of lifetime net merit (NM\$, [8]). Bull TBV were sampled from a normal distribution with a mean of \$300 (+1.5 genetic SD of NM\$) and a standard deviation of \$200. An animal's carrier status for each recessive was constructed by randomly sampling sire and dam alleles using the minor allele frequencies (MAF) shown in Table 1. Recessives were assumed to be independent of one another, as though each locus was located on a different chromosome. A sex ratio of 0.5 was used, and base population animals were assigned a birth year from -9 to 0 (bulls) or -4 to 0 (cows) by sampling from a uniform distribution.

The base population in each scenario included 350 bulls and 35,000 cows distributed over 200 herds, and the population was permitted to grow to a maximum of 500 bulls and 100,000 cows over the 20 generations simulated. Bulls were permitted a maximum of 5,000 matings per generation, and in the truncation selection scheme described later in this section only the top 10% of bulls based on TBV were retained for use as mates.

Descendants

The TBV for new calves were created by taking the parent average (PA) and adding a Mendelian sampling term computed as a random variate from a standard normal distribution ($\sim N(0,1)$) multiplied by the additive genetic SD of NM\$ (\$200). Sex was assigned randomly with a 50:50 sex ratio. For each recessive in the scenario, an allele was sampled at random from each parent and used to construct the progeny genotype. If the recessive was lethal, an affected (aa) calf was created and marked as dead. Calves were born in the same herd as their dams, and cows did not move between herds.

Allele frequencies for lethal recessives were updated each generation using the formulae of Van Doormaal and Kistemaker [9]:

$$f_{dom} = \frac{1 - q^2}{p^2 + 2pq} \quad (1)$$

$$f_{het} = \frac{2pq}{p^2 + 2pq} \quad (2)$$

where p and q are the frequencies of the major and minor alleles, respectively. Allele frequencies for non-lethal recessives were updated using standard equations [10].

Mating schemes

Four systems of mating, referred to hereafter as schemes, were simulated: random mating, truncation selection, the scheme proposed by Pryce et al. [7], and a modified version of Pryce's scheme that accounts for recessive alleles. In the random mating scheme, bulls were mated randomly to cows, with a user-specified limit on the maximum number of matings permitted for each bull. In the truncation selection scheme, the top 10% of the bulls, based on TBV, were randomly mated to the cow population. Both lethal (e.g., DUMPS) and non-lethal (e.g., red coat color) recessives were included in the simulations.

In the Pryce scheme, matings were assigned as follows. First, a matrix of parent averages, B_0 , was constructed with rows corresponding to bulls and columns corresponding to cows. The elements of B_0 were computed as:

$$B_{ij} = 0.5 \times (TBV_i + TBV_j) - \lambda F_{ij}$$

where TBV_i is the TBV for NM\$ of bull i , TBV_j is the TBV for NM\$ of cow j , λ is the inbreeding depression (\$) associated with a 1% increase in inbreeding, and F_{ij} is the pedigree coefficient of inbreeding of the calf resulting from mating bull i to cow j . A value of \$12 was used for λ [11].

In the fourth scheme, recessives were accounted for by adjusting the elements of B_{ij} to account for the recessives carried by the parents as:

$$B_{ij}^* = B_{ij} - \sum_{r=1}^{n_r} [P(aa)_r \times v_r]$$

where n_r is the number of recessives in a scenario, B_{ij}^* is the PA adjusted for all recessives in a scenario, $P(aa)_r$ is the probability of producing an affected calf for recessive r , and v_r is the economic value of recessive r . $P(aa)$ will be either 0.25, for a mating of two carriers, or 1, for a mating of two affected animals. Non-lethal recessives were entered into the simulation with an economic value of either 0 or a negative number (which increases the PA). The recessives used in each scenario are described in Table 1, which includes the minor allele frequency and the economic value assigned to each.

Once the matrix of PA is constructed, a matrix of matings, M , is used to allocate bulls to cows. An element, M_{ij} , is set to 1 if the corresponding value of B_{ij} is the greatest value in column j (that bull produces the largest PA of any bull available

for mating to cow j), and all of the other elements of column j are set to 0. If the sum of the elements of row i is less than the maximum number of permitted matings for that bull then the mating can be allocated. Otherwise, the bull with the next-highest value of B_{ij} in the column is selected, and so-on, until each column has one and only one element in it with a value of 1.

Animals were culled each generation. Bulls were culled first for age, with a maximum age of 10 years, and then on TBV (lowest-ranking animals culled first) to maintain a maximum population size. Cows were first culled for age, with a maximum age of 5 years. After age-related culling, animals were culled involuntarily. Finally, cows were culled at random to maintain population size, if necessary. The time (generation) and reason for culling was added to each record, and records for dead bulls and cows were moved from live to dead animal lists. Animals were not culled based on carrier status.

Recessive scenarios

Several scenarios were used to characterize the performance of the proposed method, where the term scenario is used to refer to one or more recessives studied together.

Holstein recessives

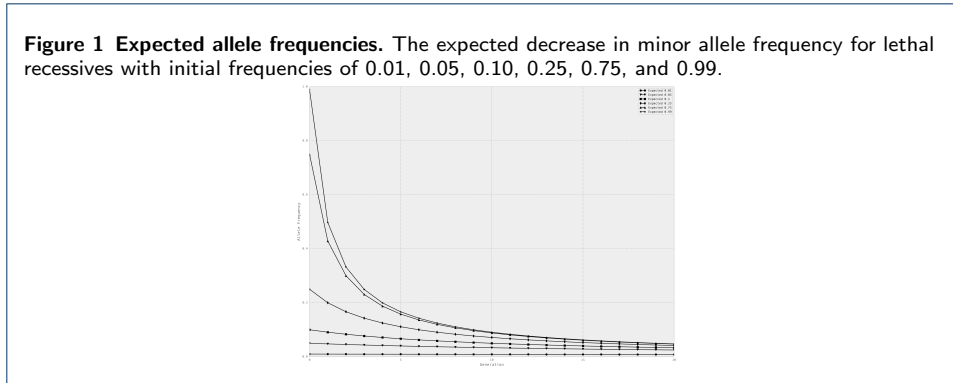
Twelve recessives currently segregating in the US Holstein population were grouped together in order to determine how the modified Pryce method will perform in a commercial livestock population: bovine leukocyte adhesion deficiency (BLAD), brachyspina, complex vertebral malformation (CVM), deficiency of uridine monophosphate synthase (DUMPS), Holstein haplotypes 1 through 5 (HH1–HH5), horned, mulefoot, and red coat color). Three scenarios that used the 12 Holstein recessives, but which differed in the economic value assigned to each locus, were used to determine the sensitivity of matings to different prices. In the normal scenario, prices were assigned based on the effect of the recessive and the timing of occurrence. For example, early embryonic lethals (e.g., HH1–HH5) were assumed to have smaller costs than those that result in late-term abortions or stillbirths (e.g., BLAD, brachyspina, mulefoot). In the zero-cost scenario all economic values were set to \$0. In the high-cost scenario the prices used for the normal scenario were multiplied by 3. Allele frequencies for the 12 recessives were taken from [12].

Hypothetical recessives

The effect of initial allele frequency on response to selection under each strategy was examined using six scenarios, each of which included a single locus at low (0.01), medium (0.50), or high (0.90) frequency with either a low (\$20) or high (\$200) cost. In addition, a seventh scenario that included all of the hypothetical loci was examined.

Horned and other high-frequency non-lethal recessives

Not every recessive in a livestock population is lethal to homozygotes, one example being the horned locus in cattle. Because the horned condition in cattle is due to the action of a recessive allele [13], although it has a very high frequency, it was included in the simulation in place of polled with an allele frequency of $1 - 0.0071 = 0.9929$.



Based on the work of Widmar et al. [14], who calculated average expected costs for dehorning and polled genetics of \$11.79 and \$10.73, respectively, a value of \$40 was assumed for horned (recall that a positive value reduces the PA in the modified Pryce method). In addition, a second scenario assuming an extreme value of \$400 was simulated.

Analysis

Results were averaged over each of the 10 replicates for each scenario. Observed changes in allele frequency were compared against expectations, where the expected allele frequency in each generation for lethals was calculated using an equation derived from Van Doormaal and Kistemaker [9]:

$$p_t = \frac{p_{t-1}^2 + p_{t-1}q_{t-1}}{2p_{t-1}^2 + p_{t-1}q_{t-1}} \quad (3)$$

$$q_t = \frac{p_{t-1}q_{t-1}}{2p_{t-1}^2 + p_{t-1}q_{t-1}} \quad (4)$$

where p_t is the frequency of the major allele at time t , q_t is the frequency of the minor allele at time t , and t is the time in generations (ranging from 1 to 20). The minor allele frequency at time 0 was the value used in each scenario for each recessive, and the major allele frequency was calculated by subtracting the minor allele frequency from 1 (Figure 2). Expected allele frequencies for non-lethals was calculated based on Hardy-Weinberg proportions as:

$$p_t = p_{t-1}^2 + p_{t-1}q_{t-1} \quad (5)$$

$$q_t = q_{t-1}^2 + p_{t-1}q_{t-1} \quad (6)$$

For each recessive in each scenario, as well as for the expected frequencies, allele frequencies were regressed on generation using a linear model as implemented in the Python module Statsmodels version 0.5.0 ([15]; <http://statsmodels.sourceforge.net/>). For a given recessive, the slopes were extracted from the regression results and a two-sample t -test assuming unequal variances was used to compare the coefficients against each other, as well as against the expected frequencies. A Bonferroni adjustment was used to correct for multiple comparisons.

Computing environment

Simulations were carried out using programs written in Python 2.7.6 (<http://www.python.org/>) as packaged in the Anaconda 2.0.0 distribution (Continuum Analytics, Austin, TX). Results were analysed in IPython 2.1.0 notebooks (<http://ipython.org/notebook.html>) using pandas 0.13.1 [16] and visualized using matplotlib 1.3.1 [17]. The programs used to conduct the simulations, resulting data files, and notebooks used for data analysis are available in a GitHub repository (<https://github.com/wintermind/multiple-recessives>). All programs in the repository are in the public domain. INBUPGF90 version 1.27 [18] was used to compute coefficients of inbreeding for the Pryce scenario, and is available for download from the University of Georgia (<http://nce.ads.uga.edu/wiki/doku.php?id=readme.inbupgf90>).

All simulations were performed on a Pogo Linux Atlas 1205 (Pogo Linux, Inc., Redmond, WA) computer with an 8-core AMD Opteron 6328 processor with a clock speed of 3.2 GHz, 64 GB of DDR3 1600 MHz RAM, and 64-bit CentOS Linux EL6 (Red Hat, Inc., Raleigh, NC). Data analysis and visualization were performed on a MacBook Pro with two Intel Core i7 processors running at 2.9 GHz, 8 GB of DDR3 1600 MHz RAM, and Mac OS X 10.7.5 (Apple Inc., Cupertino, CA).

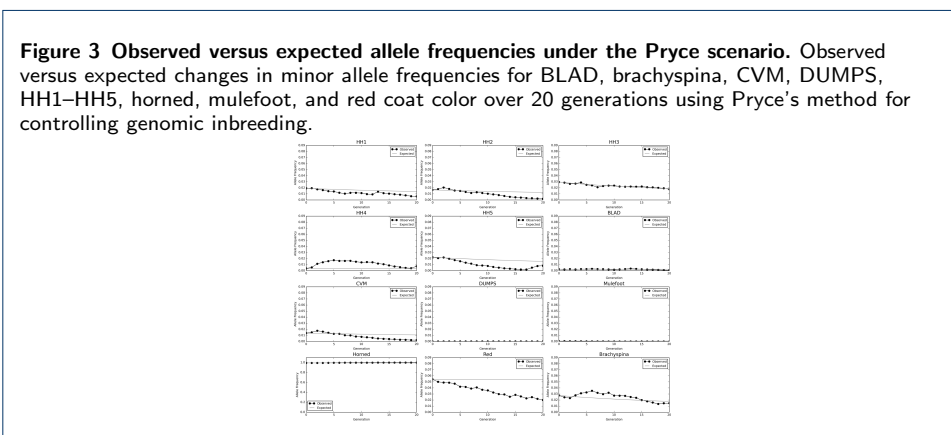
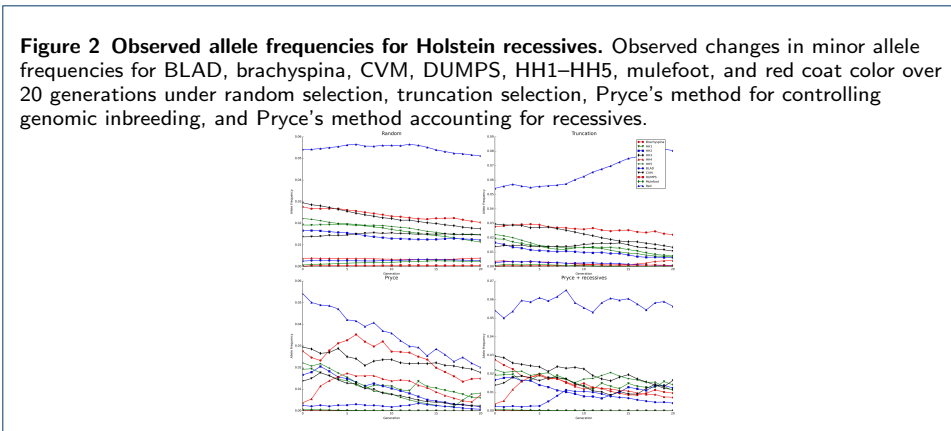
Results and Discussion

Holstein recessives

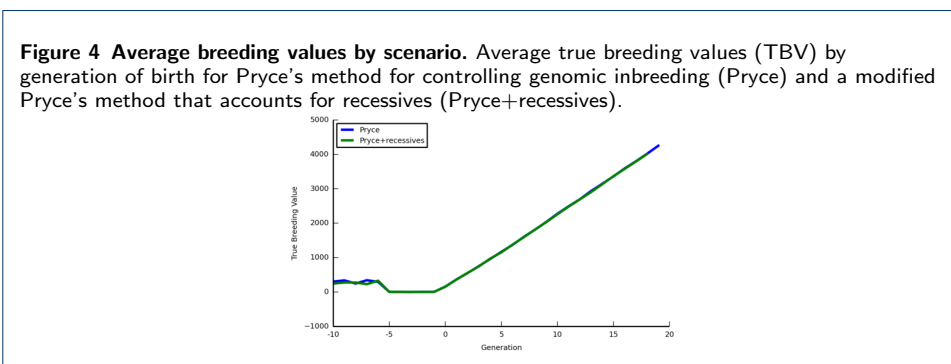
Normal costs

Observed allele frequency changes for 11 of the 12 recessives from the four mating schemes are shown in Figure 3. Horned is not shown because the allele frequency remained above 99% in all 4 schemes, and its inclusion in the plot obscured the changes in alleles at low frequency. The frequency of the 10 lethals generally decreased over time in all scenarios. The frequencies of HH2, HH4, HH5, CVM, and red decreased significantly faster ($P < 0.05$ after a Bonferroni correction) under Pryce's method than under the modified Pryce's method, while the frequency of HH3 decreased faster under the latter scenario. Several allele frequencies decreased at a faster rate than expected under the Pryce's (Figure 4) and modified Pryce's (data not shown) schemes. A clear advantage of the modified Pryce approach is that it maintains the frequency of desirable recessives, such as red coat color, in the population. In the Pryce scheme, the frequency of red decreased over time because there is no mechanism in that scenario to balance undesirable economic effects of inbreeding against the desirable economic value of some recessives. In the modified Pryce scheme the positive economic value of red coat color offsets the inbreeding penalty and maintains a relatively constant gene frequency over time.

Average TBV for the total merit index under selection were similar among the schemes over time, as shown in Figure 5. The difference between cows in generation 20 of the two schemes was \$288, \$4,298 versus \$4,010 for Pryce and modified Pryce, respectively. Bulls in generation 20 differed by only \$165 on average (\$4,178 versus \$4,013). These differences are relatively small when compared to the overall genetic gain in the population, which averaged approximately \$200 per generation. The decrease in TBV after the first 5 generations of selections is due to the mating of bulls to the first generation of calves produced, which have lower TBV than the

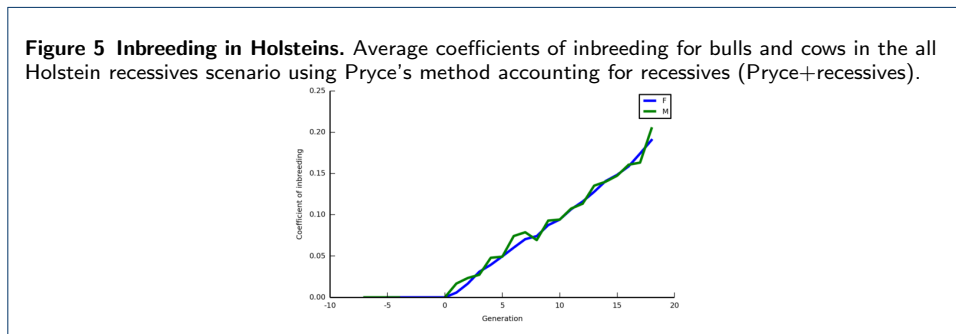


bulls and bull dams simulated as the base population, and includes all animals, including calves that died and cows and bulls that were culled without producing any offspring.



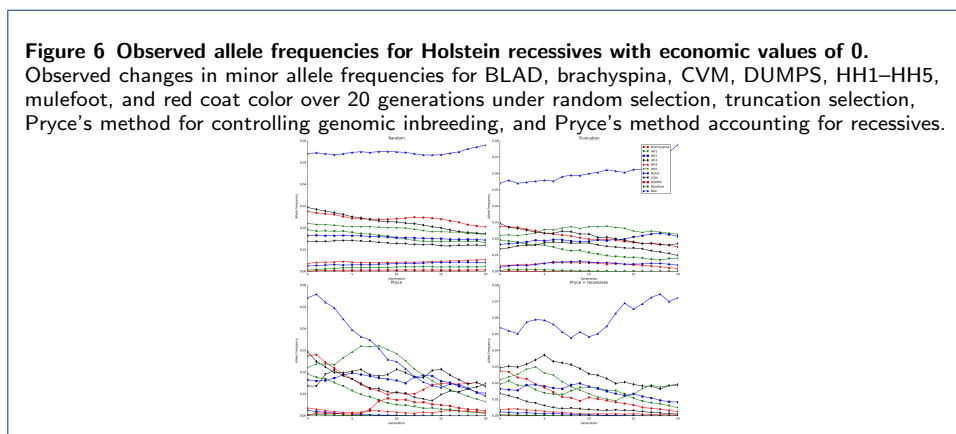
Average coefficients of inbreeding by generation for cows and bulls are shown in Figure 6 for the all Holstein recessives scenario using the modified Pryce’s method for mate assignment. Inbreeding increased by approximately 2% per year in both the cow and bull populations. The increase was constant in cows, but more variable in bulls, which reflects the small number of bulls relative to cows, as well as changes in the bull portfolio available over time. The same general pattern was observed across all scenarios and mate allocation schemes (data not shown). A value of $\lambda = \$12$

was used based on the work of Smith et al. [11], which is higher than the AUS\$5.00 value used by Pryce et al. [7], but dairy production in the US and Australia also differ substantially.

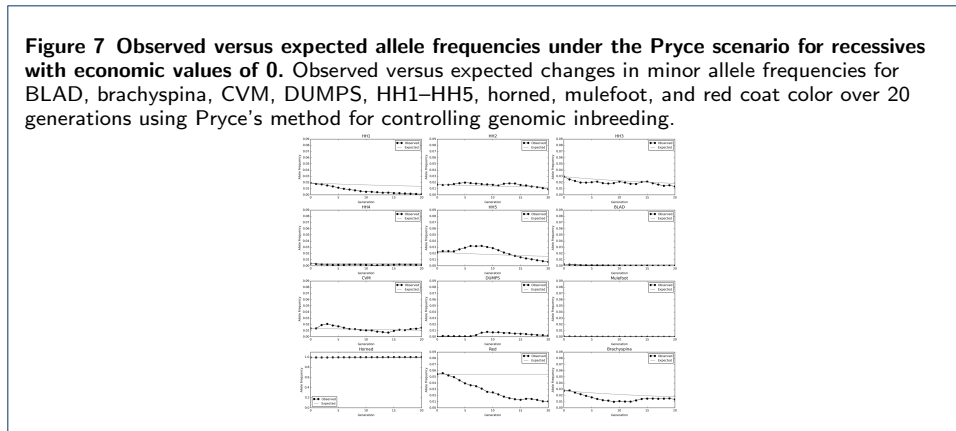


Zero costs

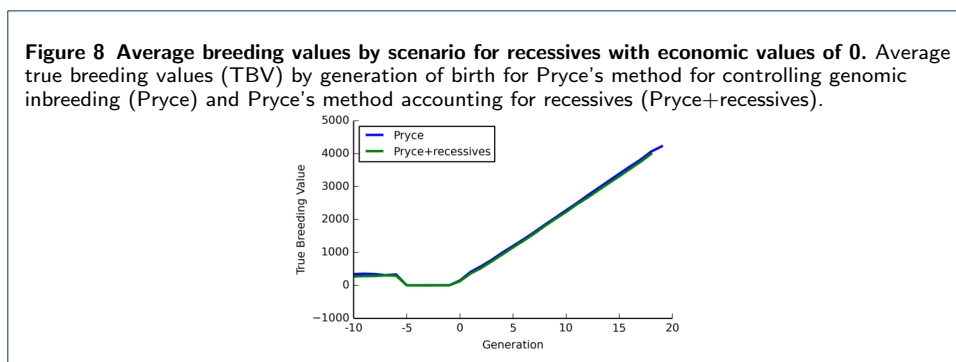
The scenario in which all recessives have an economic value of \$0 is equivalent to assuming that all recessives have equivalent values and changes over time should be driven principally by allele frequencies, with similar trends expected for the Pryce and modified Pryce schemes. The observed allele frequency changes in Figure 7 show trends similar to those noted in the normal price scenario (Figure 3), with the lethals generally decreasing in frequency over time in all scenarios. Minor allele frequencies decreased faster in the Pryce and modified Pryce schemes than under random mating or truncation selection, and the rates were significantly faster than expectations for all traits but red coat color ($P < 0.05$). The frequencies of brachyspina, HH3, HH4, and horned decreased significantly faster in the modified Pryce scheme, while red decreased faster using Pryce’s method. The rates of change of the other recessives did not differ. In both schemes, there was generally good correspondence between the observed and expected changes for each recessive, as shown in Figure 8 for Pryce’s method.



In generation 20, average TBV were \$235 higher for bulls and \$226 higher for cows under the Pryce scenario than the modified Pryce scenario (Figure 9). The difference was larger for bulls than under normal pricing, and slightly smaller for



cows. In generation 0, both populations had almost identical average TBV, so these differences represent the cumulative effect of a slightly higher genetic trend under the Pryce scenario, probably because matings of carrier cows to high genetic merit bulls were not penalized for the economic consequences of producing affected calves.



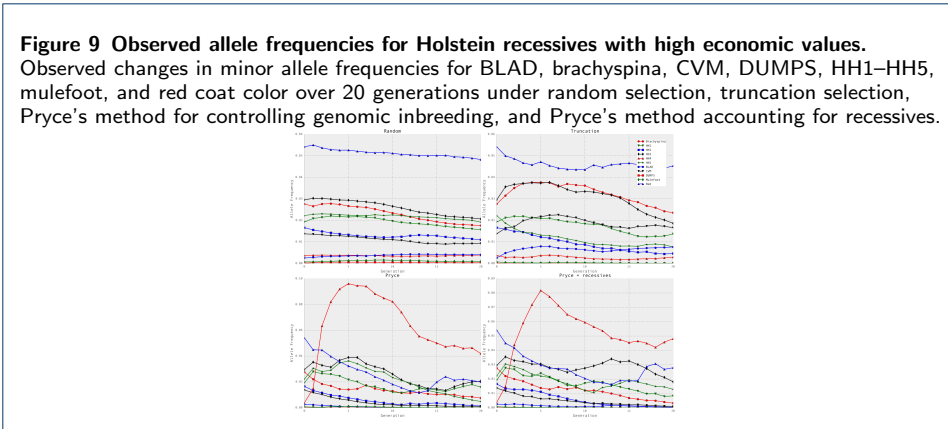
High costs

In this scenario, the economic value of each recessive was increased by a factor of 3 over the base scenario. The observed allele frequencies shown in Figure 10 show a surprising and unexpected increase in the frequency of HH4 under both the Pryce and modified Pryce schemes, but not under the random mating or truncation selection cases. There was also a rapid decreases in the frequency of BLAD and brachyspina, both with economic values of \$450 in this scenario, relative to the other two mate allocation methods. The extreme value placed on BLAD and brachyspina relative to HH4 may have resulted in more selection against the former two recessives than the latter. It is possible that a method such as linear programming, which has previously been applied to mate allocation (e.g., [19, 20]) would do a better job of preventing such a rapid increase in the frequency of a lethal.

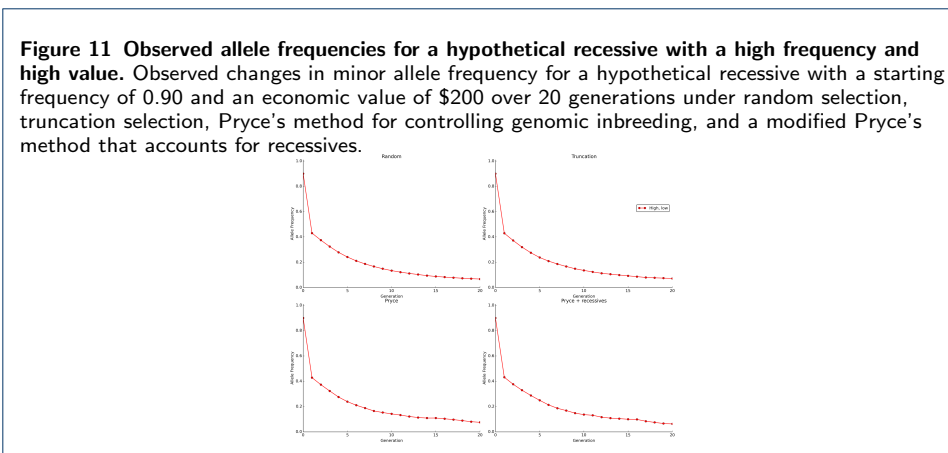
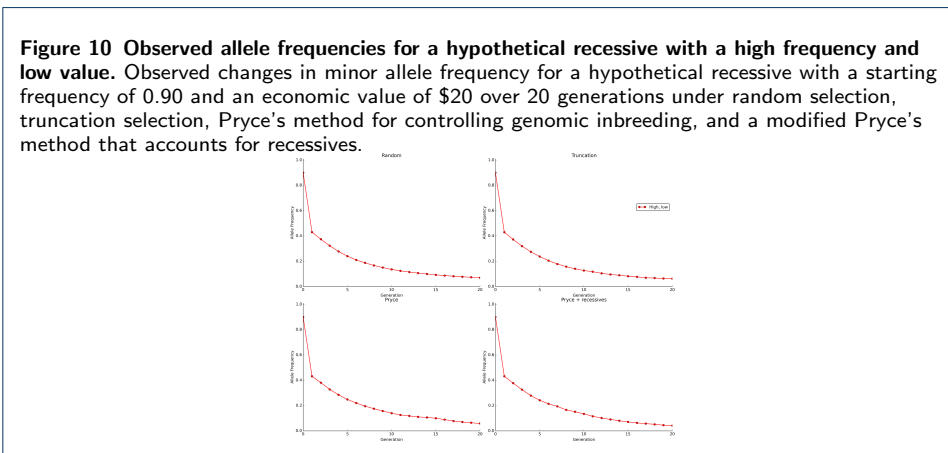
Hypothetical recessives

High frequency, lethal recessives

The rate of allele frequency change was similar for both the low (\$20) and high (\$200) value scenarios (Figures 11 and 12, respectively). This suggests that at



minor allele frequency the change from generation to generation is driven principally by allele frequencies, not by economic value. The fit of the observed to expected allele frequency changes was very good in both scenarios (data not shown).

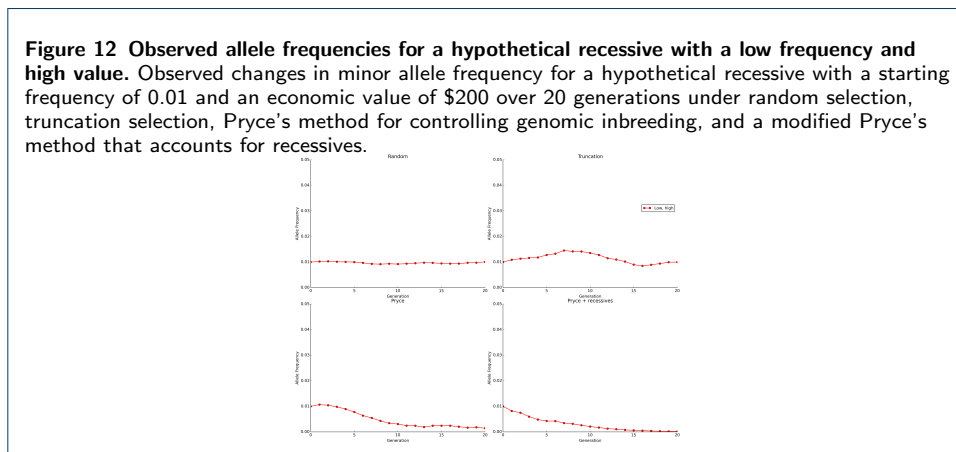


Medium frequency, lethal recessives

Results for a minor allele with an initial frequency of 0.50 and an economic value of either \$20 or \$200 were very similar to those for the previous section. The economic values were again dwarfed by the allele frequency, and a different mate allocation strategy will be needed to decrease the allele frequency more quickly.

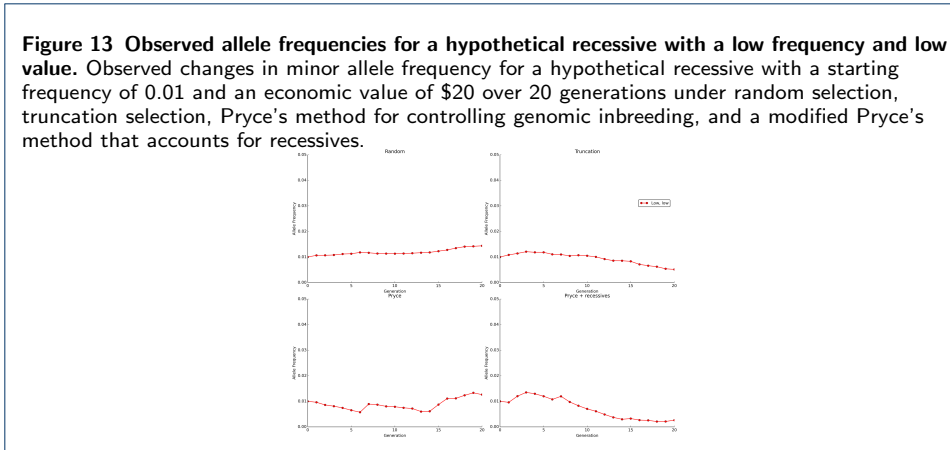
Low frequency, lethal recessives

The two low-frequency scenarios discussed in this section are perhaps the most representative of the deleterious recessives seen most commonly in livestock populations [12], that is, harmful alleles with low frequencies (<0.05). Both the Pryce and modified Pryce methods are successful at decreasing the allele frequency over time when the value of the recessive is high (Figure 13), and they do so more quickly than expected (data not shown). However, the modified Pryce’s method appears to be much more effective than random mating, truncation selection, or Pryce’s method schemes at lowering the allele frequency when the economic value of the recessive is low (Figure 14). It is not clear why the modified Pryce’s method performed so much better than Pryce’s method in the latter scenario because, at low allele frequency, the only way to increase the frequency of the minor allele is either through inbreeding, or the spread of a *de novo* mutation by a popular sire. While mutation is included in the simulation, each replicate uses a different seed for the random number generator, so new mutations are not expected to arise at the same time across different runs of the program.

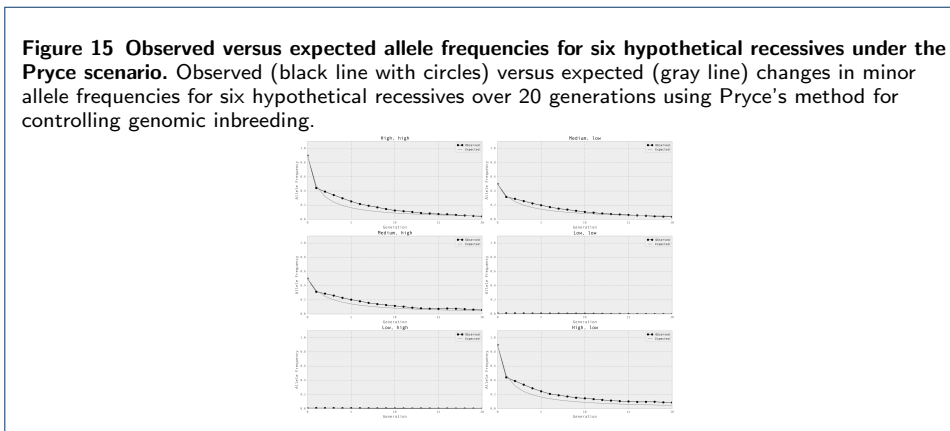
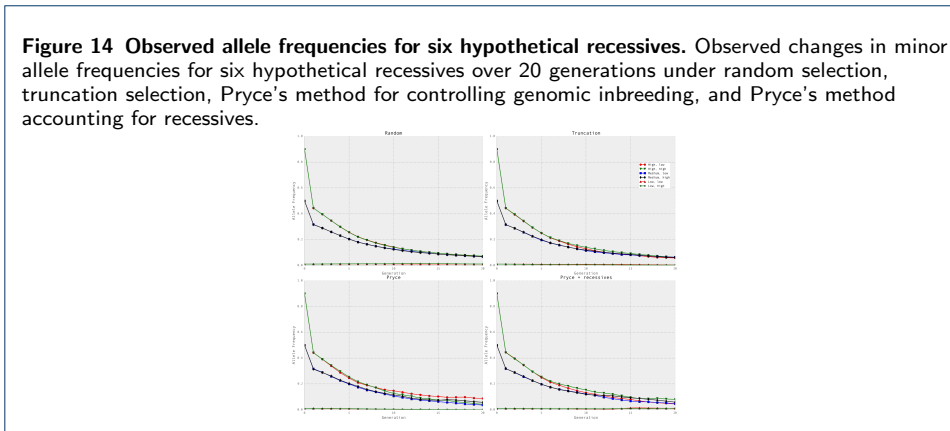


Six hypothetical, lethal recessives

The change in allele frequencies over time are shown in Figure 15, and all four systems of mate allocation produce similar results. Pryce’s method and the modified Pryce’s method do produce slightly lower frequencies for some of the alleles that had high or medium initial frequencies, but there was no apparent pattern based on frequency of economic value. The observed allele frequencies shown in Figure 16 show a much better fit to the theoretically predicted values than in the scenarios based on the actual Holstein recessives, but that is expected when alleles have initial frequencies greater than 0.20.



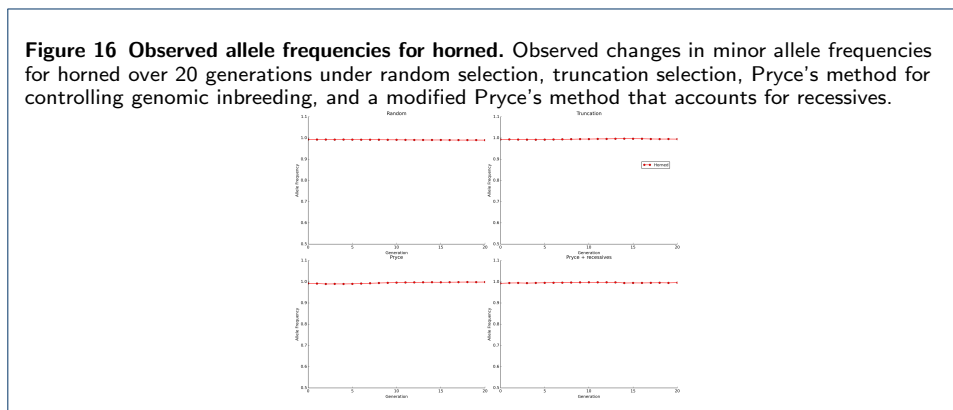
There was no apparent difference between the change in allele frequencies over time even though there was a tenfold difference between the high- (\$200) and low-valued (\$20) recessives. When the minor allele frequency is relatively high, almost all of the potential mate pairs in the population will have their parent averages reduced, so there is no more pressure on one recessive than another.



Horned and other high-frequency non-lethal recessives

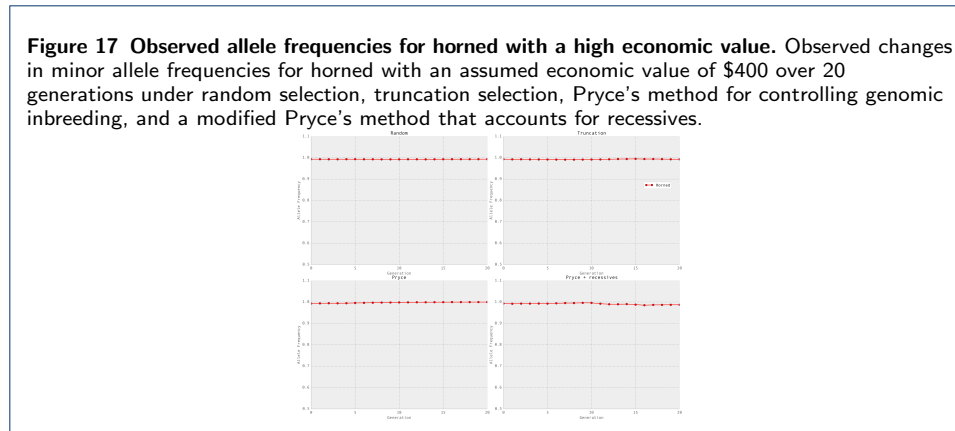
The horned allele is present at a frequency greater than 99% in the US Holstein population, and there is increasing interest in reducing its frequency to improve animal welfare. Spurlock et al. [21] recently studied three breeding schemes for increasing the frequency of polled animals, concluding that it is possible to substantially increase the number of polled animals in the population over a reasonable time horizon. One of the key challenges is that there are few polled bulls, but the addition of a haplotype test for polled to the US genomic evaluation program will make it easier to identify heterozygous animals for mating. A scenario including only the horned recessive was simulated to determine if the modified Pryce’s scheme is an effective tool for increasing the frequency of polled animals in the population.

Including horned with a value of \$40 was not effective in reducing the minor allele frequency, as can be seen in Figure 17. This is probably because the frequency of the polled allele is so low that carriers were unlikely to be one of the top-ranked bulls by TBV, and even if one was, the simulation included a limit of 5,000 matings per bull per generation. That limited a single bull to only being mated to 5% of the cow population in a generation. A second horned scenario in which the economic value was increased from \$40 to \$400 was run to determine if a higher cost would increase the rate of change. The second scenario was also unsuccessful in changing the frequency of horned (Figure 18. These results are consistent with the results from scenarios that included 12 Holstein recessives described above, in which there was not appreciable change in the frequency of horned. A more sophisticated approach for selecting mate pairs that will either produce polled offspring or heterozygotes, such as one of the schemes described by Spurlock et al. [21] or the use of tools for non-meiotic allele introgression [22], will be needed to effectively increase the frequency of polled (decrease the frequency of horned) cows in the national dairy herd.



Mating schemes

As expected, there was negligible genetic trend under the random mating scheme except in scenarios in which lethals had initial minor allele frequencies greater than 20%, which suggests that the simulation was performing reasonably. The results from the truncation selection scheme were generally similar to the Pryce’s and modified Pryce’s schemes for lethals, and to random mating for non-lethal recessives.



This is reasonable because the allele frequency of the lethals is expected to decrease over time even if no additional selection pressure is imposed, and the threshold that retains the top 10% of bulls for breeding ensures that genetic trend is positive. The truncation selection scheme loosely resembles current mating strategies used on large commercial dairies in North America.

Mate allocation

Mate allocation, the process of selecting mating pairs from a population of female and some portfolio of males, has a long history in animal breeding programs in both general ([19, 23–25]) and trait-specific ([26]) applications. Many artificial insemination firms provide mate allocation to their customers as part of their services, but the algorithms used are usually very simple. In 2012, Pryce et al. [7] proposed the use of a simple sequential method that maximizes the parent average of a mating after adjusting for any inbreeding of the offspring, subject to constraints on the number of matings per bull per generation, and showed that their method effectively constrains inbreeding when genomic relationships are used. More recently, [20] showed that rates of genetic gain can be further increased when genomic relationships are used and matings are allocated using linear programming to simultaneously account for all desired constraints. The modified Pryce's method proposed in this paper uses a sequential allocation method that also accounts for the economic effect of recessives in the population. This may be a more practical approach to account for recessives than to include them in selection indices because of the difficulty of obtaining the marginal cost of a recessive independent of all other costs already accounted for by the other traits in the index, although the possibility of double-counting costs remains.

An advantage of the modified Pryce method over Pryce's original method is that the former can be used to maintain the frequency of desirable recessives, such as red coat color, in the population. There are other recessives, such as slick hair coat [27], that are segregating in some lines of Holstein that are desirable to producers in sub-tropical regions, and the modified Pryce's method could be used to increase the frequency of that allele in the general population.

Pryce's method and the modified Pryce's method described in this paper also suffer from order-dependence, that is, if the cows are reordered before bulls are

allocated the mate pairs change. This is probably not a serious problem if the elite bulls in the population have similar breeding values, but could be important if there is a small group of, for example, elite young genomic bulls that have much higher breeding values than other active bulls. The use of linear programming rather than sequential allocation of mate pairs would eliminate this problem, at the cost of some added complexity in the implementation phase.

Integration with on-farm systems

As of 25 August 2014 there were 722,093 genotypes in the National Dairy Database maintained by the Council on Dairy Cattle Breeding (Reynoldsburg, OH, USA), of which 555,981 were from females (https://www.cdcb.us/Genotype/cur_freq.html). There is considerable interest from the farmers who have invested in those data in using them to make optimal management and breeding decisions. Initial research focused on increased genetic gains from the use of genomic information for early culling decisions [28], but there also is interest in using those data with integrated on-farm decision support systems. Gaddis [29] has showed that genotype information may have value in predicting changes in health status, and it seems reasonable to assume that similar approaches can be used to make decisions about what animals to breed based on fertility status, or what animals to dry-off or cull based on predicted future performance. The modified Pryce's method described in this paper can easily be integrated into existing herd management and mate planning software, where it could be used to better inform culling decisions or identify matings that should be avoided. In the case of some haplotypes, such as A2 beta-casein and polled, this may be a useful tool for increasing allele frequencies without sacrificing substantial cumulative genetic gain.

Conclusions

A modified version of Pryce's method [7] that accounts for the economic effects of recessive conditions was developed and compared with random mating, truncation selection, and Pryce's method for several different scenarios, including hypothetical alleles as well as 12 recessives currently segregating in the US Holstein population. The new method appears to reduce minor allele frequencies for recessives with low frequencies faster than other strategies, including Pryce's method, and can be used to maintain or increase the frequency of desirable recessives. The method can easily be implemented in software used for mate allocation, and the code used in this study is freely available for use as a reference implementation.

Competing interests

The author declares that he has no competing interests.

Author's contributions

JBC designed the study, wrote the simulations, analyzed the data, and prepared the manuscript.

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Tables

Table 1 Properties of the recessives included in each scenario simulated.

Group	Scenario ¹	N ²	Recessives					
			Frequency	Value (\$) ³	Name	Lethal		
Holstein	All recessives	12	0.0276	150	Brachyspina	Yes		
			0.0192	40	HH1	Yes		
			0.0166	40	HH2	Yes		
			0.0295	40	HH3	Yes		
			0.0037	40	HH4	Yes		
			0.0222	40	HH5	Yes		
			0.0025	150	BLAD	Yes		
			0.0137	70	CVM	Yes		
			0.0001	40	DUMPS	Yes		
			0.0007	150	Mulefoot	Yes		
			0.9929	40	Horned	No		
			0.0542	-20	Red coat color	No		
			All recessives, zero cost	12	As above, but all recessives have a value of \$0.			
			All recessives, high cost	12	0.0276	450	Brachyspina	Yes
			0.0192	120	HH1	Yes		
			0.0166	120	HH2	Yes		
			0.0295	120	HH3	Yes		
			0.0037	120	HH4	Yes		
			0.0222	120	HH5	Yes		
			0.0025	450	BLAD	Yes		
		0.0137	210	CVM	Yes			
		0.0001	120	DUMPS	Yes			
		0.0007	450	Mulefoot	Yes			
		0.9929	120	Horned	No			
		0.0542	-60	Red coat color	No			
Hypothetical	High frequency, low value	1	0.90	20	High, low	Yes		
	High frequency, high value	1	0.90	200	High, high	Yes		
	Medium frequency, low value	1	0.50	20	Medium, low	Yes		
	Medium frequency, high value	1	0.50	200	Medium, high	Yes		
	Low frequency, low value	1	0.01	20	Low, low	Yes		
	Low frequency, high value	1	0.01	200	Low, high	Yes		
	All recessives	6	As above.					
Horned	Horned, market value	1	0.9929	40	Horned	No		
	Horned, high value	1	0.9929	400	Horned	No		

¹The specific scenario simulated for each trait or group of traits.

²The number of recessives in the scenario.

³Positive values are undesirable and negative values are desirable.