ABSTRACT: Changes in maintenance energy requirements and in feed efficiency have been achieved by divergent selection for heat loss in mice in 3 replicates, creating high heat loss, high maintenance (MH) and low heat loss, low maintenance (ML) lines and an unselected control (MC). However, feed intake has mainly been measured in mature animals and not during growth or reproduction. Additionally, there is evidence that reducing maintenance energy will increase fat content, an undesirable result. To evaluate if selection has altered body composition and lifecycle feed intake, mating pairs were continuously mated and maintained for up to 1 yr unless culled. Offspring pairs were sampled from each line at each parity and maintained from 21 to 49 d of age. Feed intake was recorded for mating pairs throughout the year and on offspring pairs. Body weight was recorded on all animals at culling as well as percent fat, total fat, and total lean, measured by dual X-ray densitometry. Average daily gain was also recorded for offspring. Energy partitioning was achieved using 2 approaches: Approach I regressed energy intake of the pair on sum of daily metabolic weight and total gain to obtain maintenance ($b_m$) and growth ($b_g$) coefficients for each line, replicate, feeding period, and sex (offspring pairs only); Approach II calculated $b_m$ for each pair assuming constant energy values for lean and fat gain. Energy coefficients and body composition traits were evaluated for effect of selection (MH vs. ML) and asymmetry of selection ([MH + ML]/2 vs. MC). Both MC mating and offspring pairs tended to have greater BW than the average of the selection lines ($P < 0.08$). Males of offspring pairs weighed more than females ($P < 0.01$), while females of mating pairs weighed more than males ($P < 0.01$). Line was insignificant ($P > 0.15$) for body composition traits. Using Approach I, MH mice had a greater $b_m$ than ML mice for mating pairs ($P = 0.03$) but not offspring pairs ($P = 0.50$). For Approach II, MH had a greater $b_m$ than ML mice for both mating ($P = 0.03$) and offspring pairs ($P = 0.01$). The effect of selection for heat loss on body composition was smaller than previously reported and unlikely to outweigh the benefit of reduced feed intake, which was shown to be maintained throughout an entire lifecycle that included reproducing animals. Additionally, the reduction in energy intake seems primarily due to reduced maintenance energy costs, validating the success of the selection procedure.

**Key words:** body composition, feed efficiency, heat loss, maintenance energy, mice


INTRODUCTION

Maintenance energy requirements represent the largest input cost for all livestock species as a majority of ME intake must meet these requirements. Reducing maintenance energy requirements independent of growth or other outputs (reproduction, growth, etc.) could greatly reduce feed intake and improve feed efficiency. Heat loss can be used to select for reduced maintenance energy requirements as energy that is consumed and not stored is released as heat, and this trait has previously been shown to exhibit genetic variation. Due to economic and management advantages, mice provide a useful model for livestock species to evaluate maintenance energy.

Nielsen et al. (1997b) demonstrated that selection response in maintenance energy requirements can be achieved by initiating divergent selection for heat loss in mice measured via direct calorimetry to create a
high heat loss, high maintenance (MH) line and a low heat loss, low maintenance (ML) line as well as an unselected control (MC). Selection over a total of 25 generations has resulted in a 55.7% divergence (McDonald and Nielsen, 2007). A correlated reduction in feed intake has been reported in the ML line when compared to the MH line (a 34% difference), and selection lines do not differ in BW (McDonald and Nielsen, 2007; Nielsen et al., 1997a). However, there is evidence that ML mice have a higher percentage of body fat than MH mice (a 5.6% difference), an undesirable effect in livestock species (Kgwatalala and Nielsen, 2004; Nielsen et al., 1997a). Previous research in these lines has focused on young, mature mice (9 to 14 wk of age) and has not followed performance throughout an entire lifecycle, including continuously reproductive animals.

The objective of this study was to use these mouse lines to imitate a livestock system and determine if changing maintenance energy requirements affects body composition of young and adult mice and if improved feed efficiency of ML mice is maintained throughout an entire lifecycle.

### MATERIALS AND METHODS

#### Experimental Animals

All animal procedures were approved by the University of Nebraska – Lincoln Institutional Animal Care and Use Committee. Animals used in this study were sampled from lines of mice divergently selected for heat loss (MH = high, ML = low, and MC = control) and have been previously described by Nielsen et al. (1997b). Briefly, heat loss per unit of metabolic BW (kcal·kg\(^{-0.75}\)·d\(^{-1}\)) was measured on individual males 9 to 11 wk of age by placing them in direct calorimeters for 15 h overnight. Selection occurred in 3 replicates, creating 9 independent lines. Initial selection lasted for 16 generations, and then selection was relaxed for 26 generations, although independence of the lines was maintained. Selection was then resumed for 9 generations, based on the same selection criteria and lines have been maintained independently since, although no active selection has occurred. In the present study, which is part of a larger study on lifecycle efficiency of these lines, 21 mating pairs were selected from each line × replicate combination from generation 70, resulting in 189 total pairs of mice. Pairs were cohabitated (continuously mated) in plastic cages at 7 wk of age and maintained together for the duration of the study, unless culled, as described later. Data were collected from mating pairs and selected offspring produced throughout the experiment, which lasted 1 yr unless culled due to illness, death, or poor reproductive performance. Rooms housing animals were subjected to a 12:12 h light:dark cycle and ambient temperature was maintained at 23.5 ± 1.0°C.

#### Data Collection – Mating Pairs

Within each line × replicate combination, pairs were randomly separated into 3 groups of 7 pairs each for weekly feed intake measurements from weaning of 1 litter to weaning of the next (feeding periods). Feed intake was measured on group 1 animals from cohabitation until weaning of their first litter (period 1), group 2 animals were measured from weaning of parity 1 to weaning of parity 2 (period 2), group 3 animals from weaning of parity 2 to weaning of parity 3 (period 3), and then data collection returned to group 1 animals (period 4), etc. Feed intake measurements continued in this rotational matter for the year of the study or until pairs were culled, so that feed intake was measured on one-third of the animals at any given feeding period. If the litter died before weaning, feed intake measurements were terminated when mortality was observed. Body weights of each individual in the mating pair were measured at the beginning and end of the feed intake measurement period.

Pairs had ad libitum access to pelleted feed (Teklad diet 2019: 19% crude protein, 9.0% crude fat, 2.6% crude fiber, and 3.3 kcal of ME/g; Harlan Teklad, Madison, WI) in hanging wire baskets with weighted lids to minimize feed wastage. Consumption was measured by weekly feed disappearance.

Pairs were culled due to death or illness of either member, no first parity by 42 d cohabitation, 2 consecutive litters with none born alive, 3 consecutive litters with none weaned, 42 d between parities, or if the average size of the most recent 2 litters is less than half the average of the first 3 litters. Reproductive performance data were collected and relevant to the current study, weaning weights of the litter were collected for all mating pairs at every parity. Upon culling, a final BW (g) was recorded for each individual of a mating pair, and individuals were euthanized by CO\(_2\) asphyxiation. Body composition was measured on each individual of the mating pair at culling, except those culled for death or illness, as fat and protein content of those carcasses would be biased. Body composition was measured by dual X-ray densitometry (PIXImus; LUNAR Corporation, Madison, WI), which measures bone mineral density and percent fat (PF), which can be used to calculate total fat (TF) mass (g fat mass excluding lean and bone content), and total lean (TL; g lean mass excluding fat and bone content). In a pilot study on a subset of 22 animals, the correlation between dual X-ray prediction of body composition and chemical ether extraction measurements for percent fat was 0.88. Other studies comparing results from dual X-ray densitometry and chemical methods of measuring body composition have reported higher correlations and accuracy when measuring more animals with a greater range of BW (Brommage, 2003).
Data Collection – Offspring

Offspring were sampled at weaning (21 d) for data collection based on the group assigned to their parents, and animals identified for data collection followed a rotation in a similar manner to feeding period measurements of mating pairs. Offspring born in parity 1 were sampled from group 1 mating pairs to measure feed intake and postweaning growth, offspring born in parity 2 were sampled from group 2 mating pairs, offspring born in parity 3 were sampled from group 3 mating pairs, and offspring sampling returned to group 1 mating pairs for parity 4. This rotation continued until culling of the mating pair. Two offspring of the same sex were selected from each available mating pair (4 male pairs and 3 female pairs, from the 7 parent mating pairs) for full feed intake and growth data collection (full data [FD]), and the remaining pups of the opposite sex were kept to measure growth measurements only (reduced data [RD]). If a mating pair in the group scheduled for data collection had been culled, an even male to female ratio was maintained when sampling from the remaining mating pairs. Full data pups were housed together as a pair, and the RD pups were housed together with a maximum of 5 pups per cage.

Full data offspring pairs had ad libitum access to a powdered feed (Teklad diet 2018: 18.6% crude protein, 6.2% crude fat, 3.5% crude fiber, and 3.1 kcal of ME/g; Harlan Teklad) in glass jars with wire inserts to minimize feed wastage. Feed intake was measured weekly by feed disappearance from 21 to 49 d of age (28 d of measurements). Offspring on RD collection had ad libitum access to a pelleted diet (Teklad diet 2020X: 19.1% crude protein, 6.5% crude fat, 2.7% crude fiber, and 3.1 kcal of ME/g; Harlan Teklad). Different diets were used for multiple reasons. Offspring require diets with a lower ME content than mating pairs as they are not pregnant or lactating. For the FD animals, a powdered diet was used to reduce measurement error and the 2018 diet was more suitable as a powdered diet. In a pilot study, there was no difference in feed intake, growth, and percent fat between mice fed a pelleted or powdered diet (P = 0.97, P = 0.58, and P = 0.15, respectively); therefore, the difference in methods between mating pair and offspring should not bias measurements.

Body weight was measured on FD cages as a pair at the beginning of data collection and divided by 2 to estimate individual 21-d weights. Individual BW were taken at 49 d and used to calculate total gain and individual ADG ([49 d BW – 21 d BW]/28 d). Offspring in RD cages were weighed on a cage basis at 21 and 49 d and divided by the total number of pups in the cage to estimate individual weights. These weights were used to calculate total gain and ADG identically to the FD cages. Average daily gain was measured on an individual basis rather than a cage basis to implement more accurate partitioning of feed intake, as described later. Offspring from the FD cages were also analyzed for body composition by dual X-ray densitometry, and PF, TF (g), and TL (g) were recorded for each individual.

Body Composition Analysis

Body composition was analyzed using the GLIMMIX procedure of SAS 9.3 (SAS Inst. Inc., Cary, NC). All variables for both mating and offspring pairs were analyzed using the same model:

\[ y_{ijkl} = \text{line} + \text{sex} + \text{rep} + \text{line} \times \text{sex} + \text{line} \times \text{rep} + \text{sex} \times \text{rep} + \text{line} \times \text{sex} \times \text{rep} + e_{ijkl} \]

in which \( y_{ijkl} \) is the body composition trait recorded for each individual (PF, TF, or TL), line is the fixed effect of line (MH, ML, or MC), sex is the fixed effect of the sex (male or female), and rep is the random effect of replicate (1, 2, or 3). For all traits, orthogonal contrasts were used to test for selection response (MH vs. ML) or asymmetry of response ([MH + ML]/2 vs. MC).

Estimation of Maintenance Energy Costs

Maintenance energy costs for mating pairs and offspring pairs were obtained using similar methods. Total feed intake for each pair (mating pair or pair of offspring under FD collection) was calculated by summing weekly feed intake for each period the pair was undergoing feed intake measurements. The sum was converted to ME by multiplying total feed (g) by 3.3 kcal/g for mating pairs and 3.1 kcal/g for offspring pairs (ME value provided by feed manufacturer). Offspring noted for feed wastage and with a high ME intake to BW gain ratio (consuming more than 1,500 kcal while losing more than 10 g) were removed from the dataset (8 MH, 6 MC, and 1 ML removed). Other mouse studies have suggested that selection could result in increased feed wastage; however, relatively few animals were removed in this study, and therefore this possibility was not further examined in this population (Hastings et al., 1997). The sum of daily metabolic BW (\( \Sigma \text{BW}^{0.75} \); kg) was calculated for each individual by the following method:

\[ \Sigma \text{BW}^{0.75} = \text{integral of daily metabolic BW} = (1.75 \times \text{ADG})^{-1} \times [(\text{BW}0 + 28 \times \text{ADG})^{1.75} – \text{BW}0^{1.75}], \]

in which \( \text{BW}0 \) is the BW of the individual at the beginning of feed intake data collection and ADG is the ADG over the feeding period. The \( \Sigma \text{BW}^{0.75} \) values for each individual in a mating or offspring pair were summed to obtain the total sum of daily metabolic weights on a cage basis.
Partitioning of total ME intake was then achieved by 2 approaches used by Eggert and Nielsen (2006). In Approach I, energy was partitioned into components for maintenance and growth. Coefficients for maintenance \( b_m \): kcal-kg\(^{-0.75}\).d\(^{-1}\) and growth \( b_g \): kcal/g were estimated for each replicate, line, and period combination using the following regression model in the REG procedure of SAS 9.3 (SAS Inst. Inc.):

\[
ME \text{ intake} = b_m (\Sigma BW^{0.75}) + b_g (\text{total gain}) + b_w (\text{weaning weight}) + \text{error},
\]

in which ME intake is measured in kilocalories, total gain \((g)\) for each cage was calculated as the sum of the ADG of each individual in the mating or offspring pair multiplied by the number of days under feed intake data collection, and weaning weight is measured in grams.

The coefficient for weaning weight was only present in analysis of mating pairs and is the weight of the litter produced by the mating pair in that specific replicate, line, and period combination. Coefficients were produced for each line × replicate × period (mating pairs) or line × replicate × sex × parity (offspring) combination. Consecutive feeding periods were combined into 3 total periods (TP; TP A: feeding periods 1 through 3, TP B: feeding periods 4 through 6, and TP C: feeding periods >7) to ensure sufficient numbers within each line × replicate × TP grouping to accurately estimate coefficients.

In Approach II, maintenance coefficients were calculated for each pair, assuming costs for lean and fat deposition are constant amongst lines. Values for energy costs for lean \((b_\ell)\) and fat \((b_f)\) deposition of 2.9 and 12.8 kcal/g, respectively, were obtained from the literature (Pullar and Webster, 1977). The value for lean was derived from the value for protein gain reported (11.4 kcal/g), assuming lean is 25% protein and 75% water. The \( b_m \) was then calculated for each individual as

\[
b_m = \frac{\text{energy intake} - b_f(\text{fat}) + b_\ell(\text{lean})}{\Sigma BW^{0.75}},
\]

in which fat and lean were measured in grams.

Fat gain and lean gain were obtained from the dual X-ray densitometry measurements taken at culling and were the sum of individual gains for each individual in a mating or offspring pair. For mating pairs, culling occurred at variable times and body composition was only measured at culling. Therefore, percentage of lean and fat was considered constant and used to estimate carcass composition at earlier feeding periods by multiplying percent fat by the total gain in each feeding period and then subtracting the fat gain from total gain to obtain lean gain.

Coefficients were then treated as a dependent variable and analyzed using the GLIMMIX procedure to evaluate differences due to line or sex, in the case of offspring. For Approach I, the following model was used for mating pairs:

\[
y_{ijkl} = \text{line}_i + \text{TP}_j + \text{line} \times \text{TP}_j + \text{rep}_k + \text{line} \times \text{rep}_k + \text{line} \times \text{sex}_k + \text{line} \times \text{rep} \times \text{sex}_k + \text{line} \times \text{sex} \times \text{pair}_i + e_{ijkl},
\]

in which \( y_{ijkl} \) is the \( b_m \) or \( b_g \), line \( i \) is the fixed effect of line (MH, ML, or MC), TP \( j \) is the fixed effect of the measurement period (A, B, or C), and \( \text{rep}_k \) is the random effect of replicate (1, 2, or 3).

For coefficients estimated for offspring under Approach I, the following model was used:

\[
y_{ijkl} = \text{line}_i + \text{sex}_j + \text{rep}_k + \text{line} \times \text{rep}_j + \text{line} \times \text{sex}_k + \text{line} \times \text{rep} \times \text{sex}_j + \text{line} \times \text{sex} \times \text{pair}_i + e_{ijkl},
\]

in which \( y_{ijkl} \) is the \( b_m \) or \( b_g \), line \( i \) is the fixed effect of line (MH, ML, or MC), sex \( j \) is the fixed effect of the sex of the offspring pair (male or female), and \( \text{rep}_k \) is the random effect of replicate (1, 2, or 3).

Because of the incomplete nature of data collection (e.g., group 1 had a data point at feeding period 1, 4, 7, and 10, but intake was not recorded during other feeding periods), feeding period was redefined again for Approach II. Similar to the analysis for Approach I, feeding periods were again grouped into TP. Feeding periods 1 through 3 were grouped and designated TP A, feeding periods 4 through 6 were designated TP B, feeding periods 7 through 9 were designated TP C, and feeding periods 10 through 12 were designated TP D. This conversion ensured that each mating pair had a feed intake measurement during each period until that mating pair was culled and created a balanced data set. For Approach II, the following model was used to analyze coefficients for mating pairs:

\[
y_{ijkl} = \text{line}_i + \text{TP}_j + \text{line} \times \text{TP}_j + \text{rep}_k + \text{line} \times \text{rep}_k + \text{line} \times \text{sex}_k + \text{line} \times \text{rep} \times \text{sex}_j + \text{line} \times \text{sex} \times \text{pair}_i + e_{ijkl},
\]

in which \( y_{ijkl} \) is the \( b_m \) or \( b_g \), line \( i \) is the fixed effect of line (MH, ML, or MC), sex \( j \) is the fixed effect of the sex of the mating pair (male or female), and \( \text{rep}_k \) is the random effect of replicate (1, 2, or 3).

An autoregressive variance component structure was chosen based on Aikake information criterion corrected for finite sample size (Burnham and Anderson, 2002).

For offspring, the following model was used to analyze coefficients obtained from Approach II:

\[
y_{ijkl} = \text{line}_i + \text{sex}_j + \text{rep}_k + \text{line} \times \text{rep}_j + \text{line} \times \text{sex}_k + \text{line} \times \text{rep} \times \text{sex}_j + \text{line} \times \text{sex} \times \text{pair}_i + e_{ijkl},
\]
in which $y_{ijkl}$ is the $b_m$ or $b_g$, $line_j$ is the fixed effect of line (MH, ML, or MC), $sex_i$ is the fixed effect of the sex of the offspring pair (male or female), and $rep_k$ is the random effect of replicate (1, 2, or 3).

For all models, orthogonal contrasts were used to test for selection response (MH vs. ML) or asymmetry of response ([MH + ML]/2 vs. MC).

### RESULTS AND DISCUSSION

#### Body Composition

Body composition results are shown in Table 1 (matting pairs) and Table 2 (offspring pairs). There were no differences between lines in TL, TF, or PF for matting pairs ($P = 0.54$, $P = 0.15$, and $P = 0.77$, respectively). Sex was significant for TL ($P = 0.02$) where females had more total lean content; however, sex did not have an effect on any other body composition trait. The increase in TL in females was most likely related to in greater BW of females. Numerically, MC had the greatest TF, TL, and PF of the lines, mostly due to the greater overall BW of these animals.

No differences were detected due to line for TF, TL, and PF in offspring ($P = 0.24$, $P = 0.24$, and $P = 0.58$, respectively). Sex was significant for all 3 traits ($P < 0.01$ for TF, $P < 0.01$ for TL, and $P = 0.03$ for PF). Males had greater amounts of TF and TL; however, females had a greater PF. Nielsen et al. (1997a) showed ML mice to have a greater percent fat than MH mice, although the differences were numerically small (16.9 vs. 16.0%), while Moody et al. (1997) found ML mice to have a greater percent fat than MH mice (a difference of 6.77% fat between lines). Kwatalala and Nielsen (2004) found a slightly greater difference in fat percentage, with ML at 16.32% and MH at 14.45%, averaged across 3 different environmental temperatures. In all of these studies, measurements were taken at similar ages (9 to 14 wk), while age of mating pairs at analysis would range (15 to 55 wk) in the current study. This does not account for the lack of difference in offspring pairs, which were all 49 d of age when measured. It seems that differences in percent fat are less extreme when considering an entire life cycle.

Other studies have observed higher fat content in mice selected for improved feed efficiency, which can be related to the current study. Hastings et al. (1997) achieved divergence for maintenance energy requirements by selecting mice for food intake corrected by phenotypic regression on mean BW at maturity. Authors found the low intake line to be 2.4 to 7.2% fatter than the high intake line, a much greater difference than what was reported in the current study although similar to some previous work in these heat loss lines (Bünger et al., 1998; Hastings et al., 1997; Moody et al., 1997).

Residual feed intake has been proposed a selection criterion that more accurately isolates maintenance energy requirements than traditional measures of feed efficiency. Barea et al. (2010) demonstrated that pigs selected for low residual feed intake had reduced heat production and thus lower maintenance energy requirements. A subsequent study on these lines found a tendency for a positive genetic correlation between residual feed intake and backfat and negative correlations with dressing percent and lean meat content (%), indicating that pigs with higher maintenance energy requirements may have a higher fat content, which contradicts the hypothesis that lower maintenance animals have a higher fat content, but reflects the lack of differences in body composition seen in this study (Gilbert et al., 2007). However, it should be noted that calculation of residual feed intake in the French pig study accounted for backfat and may prevent an increase in fat content with lower maintenance requirements than selection for reduced maintenance energy requirements alone. Richardson et al. (2001) also found evidence of increased fat content with increased residual feed intake after a single generation of selection in beef cattle.

### Table 1. Body composition of mating pairs by line$^{1}$ and sex$^{2}$

<table>
<thead>
<tr>
<th>Item</th>
<th>Percent fat, %</th>
<th>Total fat, g</th>
<th>Total lean, g</th>
</tr>
</thead>
<tbody>
<tr>
<td>MC</td>
<td>23.52 ± 2.05</td>
<td>9.68 ± 0.99</td>
<td>20.84 ± 1.36</td>
</tr>
<tr>
<td>MH</td>
<td>21.53 ± 2.06</td>
<td>8.49 ± 0.99</td>
<td>23.19 ± 1.36</td>
</tr>
<tr>
<td>ML</td>
<td>19.85 ± 2.06</td>
<td>5.15 ± 0.99</td>
<td>24.70 ± 1.36</td>
</tr>
</tbody>
</table>

Sex

<table>
<thead>
<tr>
<th>Item</th>
<th>Percent fat, %</th>
<th>Total fat, g</th>
<th>Total lean, g</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>21.60 ± 1.34</td>
<td>8.67 ± 0.67</td>
<td>30.39 ± 1.36</td>
</tr>
<tr>
<td>M</td>
<td>23.50 ± 1.33</td>
<td>9.88 ± 0.67</td>
<td>33.68 ± 1.36</td>
</tr>
</tbody>
</table>

$^{1}$MH = high heat loss selection; ML = low heat loss selection; MC = unselected control. $^{2}$F = female; M = male.

### Table 2. Body composition and growth of offspring pairs by line$^{1}$ and sex$^{2}$

<table>
<thead>
<tr>
<th>Item</th>
<th>Percent fat, %</th>
<th>Total fat, g</th>
<th>Total lean, g</th>
<th>ADG, g/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>MC</td>
<td>12.54 ± 0.45</td>
<td>3.33 ± 0.13</td>
<td>16.21 ± 0.56</td>
<td>0.70 ± 0.45</td>
</tr>
<tr>
<td>MH</td>
<td>12.01 ± 0.46</td>
<td>3.02 ± 0.14</td>
<td>19.05 ± 0.56</td>
<td>0.61 ± 0.45</td>
</tr>
<tr>
<td>ML</td>
<td>12.62 ± 0.45</td>
<td>3.14 ± 0.14</td>
<td>19.48 ± 0.56</td>
<td>0.56 ± 0.45</td>
</tr>
</tbody>
</table>

Sex

<table>
<thead>
<tr>
<th>Item</th>
<th>Percent fat, %</th>
<th>Total fat, g</th>
<th>Total lean, g</th>
<th>ADG, g/d</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>12.92 ± 0.35</td>
<td>2.92 ± 0.11</td>
<td>19.55 ± 0.44</td>
<td>0.47 ± 0.45</td>
</tr>
<tr>
<td>M</td>
<td>11.86 ± 0.34</td>
<td>3.41 ± 0.11</td>
<td>25.19 ± 0.44</td>
<td>0.70 ± 0.45</td>
</tr>
</tbody>
</table>

$^{1}$MH = high heat loss selection; ML = low heat loss selection; MC = unselected control. $^{2}$F = female; M = male.
**Final Body Weight**

Differences between lines in final BW of mating pairs tended toward significance ($P = 0.08$), and there was significant evidence of asymmetry of selection ($P = 0.04$) because the MC mice weighed more than the average of the selection lines (Fig. 1). Sex was highly significant ($P < 0.01$), with females weighing more than males at culling (44.2 ± 0.81 vs. 40.6 ± 0.81 g). Kgwatalala and Nielsen (2004) observed higher BW in males compared to females from this population; however, mice were 9 wk of age or younger in that study and females were not reproducing. There was no significant line × sex interaction ($P = 0.20$).

Selection effect of final BW of offspring was not significant ($P = 0.17$); however, there was a tendency towards asymmetry ($P = 0.07$), with MC mice again being heavier (Fig. 1). Sex was again highly significant ($P < 0.01$); however, in this case, males were heavier than females (31.3 ± 0.54 vs. 24.7 ± 0.54). Again, the line × sex interaction was insignificant ($P = 0.48$). This is in agreement with the results seen by Kgwatalala and Nielsen (2004). Average daily gain (Table 2) was not different due to line ($P = 0.49$); however, males gained more per day than females ($P < 0.01$). Similar results in growth across lines were also reported in other studies using these lines (Kgwatalala and Nielsen, 2004; Murphy et al., 2013).

In lines of mice selected for feed intake adjusted for BW, Hastings et al. (1997) did not observe a strong relationship between selection and BW, although the high line did tend to have 7 to 11% greater BW averaged over 3 generations of selection. However, there were no significant differences in BW at 70 or 98 d of age in 10-wk-old males sample from the 29th or 30th generation of selection. Control animals were of intermediate BW at 70 d of age and heavier than both the high and low line at 98 d of age, although the difference was not significant. Conversely, MC mice have consistently been reported as heavier in previous studies of the populations described in the current study (Kgwatalala and Nielsen, 2004; McDonald and Nielsen, 2007; Murphy et al., 2013).

After a single generation of selection for residual feed intake in beef cattle, which one would expect to be similar to selection for maintenance energy requirements, there were no differences between animals from the high and low line (Richardson et al., 2001). However, the correlated response in BW to selection for residual feed intake in pigs was inconsistent with results observed in the current study. In pigs, high residual feed intake animals also had greater BW than low residual feed intake animals after 6 wk, despite having similar weaning weights (Barea et al., 2010).

The higher female BW observed in mating but not offspring pairs is likely due to the fact that these females were reproductively active and produced multiple parities. Increased female growth with multiple parities has been observed in several mouse studies (Brien and Hill, 1986; Rebholz et al., 2012). In lines of mice with the lit/lit mutation, which is believed to reduce production of growth hormone, growth rates and mature body size are substantially decreased compared to normal mice. Female lit/lit mice subjected to repeated pregnancies were able to overcome this effect and achieved greater growth rates than heterozygous mice (Beamer and Eicher, 1976). Both lit/lit mice and heterozygous mice subjected to repeated pregnancies grew more than unmated controls, indicating that changes in growth hormone levels during pregnancy (among other hormonal changes) cause increased growth in females. Brien and Hill (1986) measured female growth across multiple parities in several lines selected for different criteria and showed variation between these lines. Variation in growth rates of older, unmated males and females in the MH and ML lines has not been studied. However, due to the nature of the lifecycle evaluation that was the ultimate goal of the present experiment, it could not be accurately analyzed in the current study.
Table 3. Energy coefficients by line for mating pairs using 2 approaches

<table>
<thead>
<tr>
<th>Line</th>
<th>Approach I</th>
<th>Approach II</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$b_m^{3,4}$</td>
<td>$b_m^3$</td>
</tr>
<tr>
<td></td>
<td>$b_m^{3,4}$</td>
<td>$b_g^{3,4}$</td>
</tr>
<tr>
<td>MC</td>
<td>161.39 ± 11.49</td>
<td>2.40 ± 1.96</td>
</tr>
<tr>
<td>MH</td>
<td>183.14 ± 11.49</td>
<td>0.97 ± 1.96</td>
</tr>
<tr>
<td>ML</td>
<td>157.83 ± 11.49</td>
<td>1.19 ± 1.96</td>
</tr>
</tbody>
</table>

1MH = high heat loss selection; ML = low heat loss selection; MC = unselected control.

2Approach I simultaneously estimated maintenance and gain costs; Approach II assumed common costs for lean and fat gain and estimated maintenance costs.

3$b_m$ = maintenance coefficient (kcal·kg$^{-0.75} ·\text{d}^{-1}$); $b_g$ = growth coefficient (kcal/g).

4Significant response to selection ($P < 0.05$), evaluated using orthogonal contrasts (MH – ML).

Life-Cycle Feed Intake

Energy coefficients for mating pairs are reported in Table 3. In Approach I for mating pairs, line tended to have an effect on $b_m$ ($P = 0.06$) but was insignificant for $b_g$ ($P = 0.86$). For $b_m$, there was evidence of a selection response ($P = 0.03$) but no evidence of asymmetry of selection ($P = 0.24$). Feeding period was insignificant for $b_m$ and tended to be significant for $b_g$ ($P = 0.11$ and $P = 0.06$, respectively). Mating pairs of line MH consumed about 16% more for maintenance (kcal·kg$^{-0.75} ·\text{d}^{-1}$) than ML pairs, and MC animals were intermediate. In Approach II, line had a significant effect on $b_m$ ($P = 0.03$) due to a significant selection response ($P = 0.01$). Similar to Approach I, MH mice consumed 20% kcal·kg$^{-0.75} ·\text{d}^{-1}$ more for maintenance than ML mice, and MC mice were intermediate. Overall, the reduced feed intake for maintenance seen in younger animals from these lines is maintained in mature, reproducing mice. Gilbert et al. (2012) also found that pigs selected for reduced residual feed intake produced dams with lower daily feed intake and residual feed intake as dams during gestation and lactation. Using values from Approach II for a 40 g male and 44 g female, MC pairs would consume 308.9 g, MH would consume 358.24 g, and ML would consume 298.6 g of feed for maintenance over a 28-d period.

Energy coefficients for offspring pairs are reported in Table 4. For offspring, both $b_m$ and $b_g$ were not different across lines ($P = 0.50$ and $P = 0.98$, respectively) using Approach I although MH mice did consume 7% more feed than ML mice. Sex was also insignificant for both traits ($P = 0.80$ for $b_m$ and $P = 0.45$ for $b_g$). However, under Approach II, line was significant ($P = 0.01$) and females tended to have a greater $b_m$ than males (a 6% difference; $P = 0.06$). There was a significant response to selection ($P < 0.01$) and a tendency for asymmetry of response ($P = 0.06$). Mice of line MH consumed 16% more for maintenance (kcal·kg$^{-0.75} ·\text{d}^{-1}$) than ML mice, and MC mice were intermediate but more similar to ML mice. Using Approach II values and starting with 11.0-g males, 2 MC males would consume 268.0 g, 2 MH males would consume 295.8 g, and 2 ML males would consume 261.8 g of feed over a 28-d period. Starting with 10.9-g females, 2 MC females would consume 246.8 g, 2 MH females would consume 272.8 g, and 2 ML females would consume 236.8 g of feed over a 28-d period.

Table 4. Energy coefficients by line for offspring pairs using 2 approaches

<table>
<thead>
<tr>
<th>Item</th>
<th>Approach I</th>
<th>Approach II</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$b_m^4$</td>
<td>$b_g^4$</td>
</tr>
<tr>
<td></td>
<td>$b_m^{4,5,6}$</td>
<td></td>
</tr>
<tr>
<td>Line</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MC</td>
<td>254.19 ± 22.48</td>
<td>1.31 ± 2.30</td>
</tr>
<tr>
<td>MH</td>
<td>271.03 ± 22.48</td>
<td>1.49 ± 2.30</td>
</tr>
<tr>
<td>ML</td>
<td>237.13 ± 22.48</td>
<td>1.82 ± 2.30</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>249.95 ± 21.91</td>
<td>4.27 ± 1.41</td>
</tr>
<tr>
<td>M</td>
<td>258.29 ± 21.91</td>
<td>1.55 ± 1.41</td>
</tr>
</tbody>
</table>

1MH = high heat loss selection; ML = low heat loss selection; MC = unselected control.

2F = female; M = male.

3Approach I simultaneously estimated maintenance and gain costs; Approach II assumed common costs for lean and fat gain and estimated maintenance costs.

4$b_m$ = maintenance coefficient (kcal·kg$^{-0.75} ·\text{d}^{-1}$); $b_g$ = growth coefficient (kcal/g).

5Significant response to selection ($P < 0.05$), evaluated using orthogonal contrasts (MH – ML).

6Significant difference due to sex ($P < 0.05$).
was analyzed as grams of feed intake per unit BW (or BW raised to the 0.75 power) rather than kilocalories of ME and not as coefficients calculated by regression as in this study. Additionally, in previous studies animals on feed intake were housed individually rather than as pairs. Individual animals would presumably require more energy to maintain body temperature than those housed as a pair. Furthermore, due to the fact that this study is part of a larger, lifetime efficiency study, feed intake measurements were done on a cage basis. In the case of mating pairs, cages included mature animals of both sexes as well as the litter produced, which would begin consuming feed as they approached weaning age. Measurements on a cage basis clearly do not facilitate partitioning feed intake amongst all the animals in the cage but do provide input values for a lifetime efficiency evaluation that is mostly focused on total consumption of all animals in the system at any given life stage.

Other studies in mice have shown that lower heat production is associated with reduced feed intake or improved feed efficiency (Archer and Pitchford, 1996; Hastings et al., 1997; Selman et al., 2001). Hughes and Pitchford (2004) measured feed intake in mice selected for postweaning net feed intake (a similar trait to residual feed intake) throughout pregnancy and lactation to determine the effect of these processes on feed intake divergence. Divergence was maintained during pregnancy but lines converged for 2-wk period in early lactation, immediately following parturition. This convergence could be occurring for MH and ML mice and could partially explain the smaller difference in feed intake observed in the current study compared to previous studies using these lines. Low heat production is also associated with reduced residual feed intake in chickens and beef cattle (Gabarrou et al., 1998; Luiting et al., 1991; Nkrunmah et al., 2006). Barea et al. (2010) selected for high and low residual feed intake in swine and observed reduced total and fasting heat production in the low line.

The underlying cause of the differences in maintenance energy requirements between MH and ML lines has been previously studied. Differences in activity levels were determined to account for 11.5% of the differences in heat loss and 17 to 36% of the difference in feed intake between lines, with MH mice being more active (Mousel et al., 2001; Sojka et al., 2013). Differences in mitochondrial efficiency have also been found to be partially responsible for divergence in heat production, mainly due to increased uncoupling during electron transport in MH mice (McDonald et al., 2009; Murphy et al., 2013).

Implications

Selection for reduced heat loss to reduce maintenance energy requirements has been previously shown to improve feed efficiency in mice. In this study, the reduced energy intake was confirmed in postweaning offspring and also shown to be maintained in older, mating individuals. Therefore, the reduced maintenance energy requirement and resulting improved feed efficiency is maintained throughout all life stages. However, this study did not confirm higher fat content of low maintenance animals seen in previous studies of these populations. Therefore, reducing maintenance energy requirements may not negatively affect body composition and selection should result in animals with improved feed efficiency throughout their entire life cycle. Integration of these results with reproductive performance and longevity is necessary to determine the overall effect of changing maintenance energy requirements on lifetime efficiency.

LITERATURE CITED


