Inheritance of litter size at birth in the Brazilian grass mouse (Akodon cursor, Sigmodontinae, Rodentia)

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Summary

By means of complex segregation analysis we studied the inheritance of litter size in two large pedigrees of captive-bred colonies of the Brazilian grass mouse Akodon cursor. Genetic analysis has revealed a highly significant influence of genetic factors on the variation of litter size (heritability, \( h^2 \)), was estimated as 0.44). The inheritance followed the classical polygene model: neither the major-gene model nor the polygene with unequal contribution model described the data significantly better.

1. Introduction

Analysis of genetic and environmental factors controlling variation of life history traits in natural populations is essential to understanding their evolution. However, little is known about the quantitative genetics of natural populations. A study of genetic control requires trait measurements on many individuals of known parentage (Falconer & MacKay, 1996; Lynch & Walsh, 1997). Natural populations rarely provide this opportunity. Although several new methods of parentity testing have recently been developed and applied to field studies (Slate et al., 1999; Kruuk et al., 2000; Merila & Sheldon, 2000; Kingsolver et al., 2001), the progress in unravelling the structure of variation in quantitative traits is rather slow. The problem is that natural populations are always under the strong influence of many random and systematic environmental effects. It is impossible to control the environmental variables in the field and therefore it is hard to assess the genetic architecture of the traits.

This problem can be solved in a laboratory experiment. When we put representatives of natural populations in a controlled environment and breed them in captivity we may estimate the genetic structure of the traits. Weigensberg & Roff (1996) demonstrated that laboratory estimates of heritability provide reasonable estimates of both the magnitude and the significance of heritabilities in nature.

In this study we use this approach to analyse the genetic control of one of the most important life history traits – litter size – in a captive-bred colony of the Brazilian grass mouse Akodon cursor, Winge, 1887 (Sigmodontinae, Rodentia).

Inheritance of litter size has been extensively studied in various laboratory and farm animals (Maizul Islam & Hill, 1976; Eklund & Bradford, 1977; Land, 1978; Falconer, 1989; Eisen & Johnson, 1981; Montgomery et al., 1994). It has been shown that litter size is genetically variable in outbred strains. It can be gradually increased or decreased by direct or correlated selection. These findings have been interpreted as an indication of additive polygenic control of this trait. However, the heritability (\( h^2 \)) of litter size was found to be very low. In laboratory and farm animals studied so far \( h^2 \) varied from 0 to 20% (Falconer, 1989). This low heritability might result from strong artificial selection for an increase in the litter size (that was applied for economic reasons in both livestock and laboratory animals). It may also reflect the consequence of strong natural selection that has reduced an additive component of genetic varia-
bility for litter size in the natural populations from which the founders of farm and laboratory animals came.

A study of heritability of this trait in animals that were recently introduced into the laboratory and have not been affected by selection in captivity may give us a more accurate estimate of the genetic variability of litter size in natural populations.

2. Materials and methods

(i) Materials

*Akodon cursor* is a small rodent that is widely distributed in grassland areas of South America from Central Brazil to Northern Argentina. The founders of the captive-bred populations were isolated from natural populations of this species from Central–Eastern Brazil.

One pedigree (Fig. 1a) was established by crossing animals captured at Sumidouro, State Rio de Janeiro (22°03'S, 42°41'W) in 1989. Since then and until 1995 the stock was maintained at the Institute of Tropical Medicine (Rio de Janeiro). Additional founders were captured during 1989–1993 at the same locality and introduced into the pedigree. There were 34 founders and 115 non-founders involved in the crosses. A total of 79 dams and 70 sires produced 171 litters. There were 50 dams that were mated with only 1 sire, 16 were mated with 2 sires and 13 with 3 or more. In turn, the number of sires mated with 1, 2 and 3 or more dams was 42, 13 and 15, respectively.

The other pedigree (Fig. 1b) originated from two parental couples. The founders were captured in the vicinity of Juiz de Fora, State Minas Gerais (21°58'S, 43°19'W) in 1994. Since then and until 1996 the pedigree was maintained as an isolated stock at the Institute of Biology of the Federal University of Rio de Janeiro. A total of 32 sires and 31 dams in 38 parental couples produced 151 litters. In this pedigree only 7 dams were crossed with more than 1 sire while 6 sires were mated with more than one dam.

Both stocks were maintained in the same laboratory conditions, under a natural daylight cycle. Litter size was scored at birth as the number of live-born offspring. The body mass of the dams was scored on the day of delivery.

Both pedigrees contained multiple loops. Some of the loops were inbred. However, close inbreeding (crosses between relatives of the first degree) was rare: only 2 dams in the Sumidouro pedigree resulted from such a cross and had an inbreeding coefficient 0.25. In this pedigree there were 18 inbred dams participating in reproduction with an average coefficient of in-breeding equal to 0.022. In the Juiz de Fora pedigree, despite a limited number of founders, there were only 6 inbred dams with an average inbreeding coefficient 0.024.

![Fig. 1. Pedigrees of female grass mice Akodon cursor whose litter size was analysed. (a) Pedigree derived from founders captured at Sumidouro, State Rio de Janeiro. (b) Pedigree derived from founders captured at Juiz de Fora, State Minas Gerais. Open squares, male; open circles, female; filled circles, inbred female. There were 4 more females (not shown) that were introduced into the Sumidouro colony from the natural population at the final stage of colony formation.](https://doi.org/10.1017/S0016672302005724)
(ii) Segregation analysis

We performed complex segregation analysis using a mixed model of major-gene and polygene inheritance. Three mathematical components form the basis of complex segregation analysis: the penetrance function, the gene frequency distribution and the transmission probabilities distribution. The mixed model of inheritance assumes that a quantitative trait is under control of a major gene, a large number of additive genetic factors and environmental factors (Morton & MacLean, 1974). The effects of these components (major-genic, polygenic and environmental) are considered to be independent of each other. Additional covariates might be included in the model as independent factors via regression. Thus, under the mixed model the value of the quantitative trait $y_i$ of some $i$th individual may be expressed as

$$y_i = \mu + p_{g_i} + G_i + \sum b_j x_{ij} + e_i,$$

where $\mu$ is the general baseline mean, $p_{g_i}$ is the impact from the major gene, $G_i$ is the impact from the polygenic component, $e_i$ is the random effect of environment, $x_{ij}$ is the value of the $j$th covariate and $b_j$ is the coefficient of regression of $y$ on the $j$th covariate.

It is assumed that the random environmental effects are distributed normally with mean zero and variance $\sigma^2_e$.

Assuming a diallelic (Q and q) autosomal major gene, the contribution of the major-genic component may be described through the additive contribution $A$ and dominance deviation $D$ (Falconer, 1989). In this the term $p_{g_i}$ equals $A$, $D$ and $-A$ for major genotypes QQ, Qq and qq, respectively. The frequency distribution of major genotypes in the population can be described by the population frequency of the q allele ($p_q$) under the assumption of panmixia and Hardy–Weinberg equilibrium.

For each triplet of major genotypes, $g, g_d$ and $g_s$, the model provides a probability $Pr(g/g_d,g_s)$ that parents of genotypes $g_d$ and $g_s$ produce an offspring of genotype $g$. In the case of a diallelic major gene this probability distribution is described via three transmission probabilities $\tau$, i.e. probabilities of transfer of allele Q to offspring from a parent with genotype QQ, Qq or qq. With Mendelian transmission of the gene, the $\tau$ values must be 1, 0.5 and 0 for QQ, Qq and qq, respectively.

The distribution of the polygene in a pedigree consisting of $N$ members follows an $N$-variate normal distribution with mean zero and a variance–covariance matrix which is determined by the variance of polygenes in the population ($\sigma^2_g$) and the coefficients of kinship within pairs of individuals in the pedigree (Fisher, 1918; Lange et al., 1976).

Thus, in our study the mixed model of inheritance was expressed via parameters \(p_q, \mu, A, D, \tau_{QQ}, \tau_{Qq}, \tau_{qq}, \sigma^2_g, \sigma^2_e\).

The estimates of genetic parameters were obtained using the maximum likelihood method (Kendall & Stewart, 1951). Hypotheses were tested by the likelihood ratio test in a hierarchical manner. Twice the negative of the natural logarithm of the likelihood ratio is asymptotically distributed as $\chi^2$ with degrees of freedom equal to the difference in number of independent parameters of the two models under comparison (Neyman & Pearson, 1928).

To check the major-gene hypothesis we compared five genetic models:

1. sporadic model: the variation of the trait is assumed to be entirely due to non-genetic variation;
2. polygene model: the major-gene component is excluded;
3. mixed model: the transmission probabilities of the major gene are fixed at Mendelian values and all other parameters are estimated;
4. arbitrary transmission probabilities model: the least restricted model (all parameters are estimated); and
5. equal transmission probabilities model: the restriction $\tau_{QQ} = \tau_{Qq} = \tau_{qq}$ is imposed on the model.

First, we tested for significance of genetic components of the variation by comparing model (3) with model (1). Then we checked whether there was a Mendelian gene that made a major contribution to the variation of the trait. According to Elston & Stewart (1971), Morton & MacLean (1974), Demenais et al. (1986) and Lynch & Walsh (1997), the major-gene hypothesis is accepted if:

- model (3) is significantly better than model (2),
- model (3) does not differ significantly from model (4),
- model (4) is significantly better than model (5).

We have previously mentioned that the pedigrees under analysis contained many loops (see Fig. 1). The computation of the exact likelihood for a large pedigree with multiple loops is unaffordable in terms of computing power. Several methods for likelihood approximation have been developed (Guo & Thompson, 1994; Stricker et al., 1995, 1996; Wang et al., 1996). We adopted the approximation approach under which the loops were cut-extended by introducing artificial phenocopies of some individuals in a pedigree, then the likelihood was computed conditional on the likelihood of the phenocopies (Stricker et al., 1996; Wang et al., 1996).

The computation of the exact likelihood of the extended pedigrees under the mixed model is feasible only in the case when the major-gene component is excluded from the model (Hasstedt, 1991; Sham, 1992).
1998). To calculate the likelihood of the extended pedigrees under the complete mixed model, some approximate methods have been developed (Hasstedt, 1982, 1991; Fernando et al., 1994; Lange, 1997). We used the hypergeometric approximation (Cannings et al., 1978; Lange, 1997) and the finite polygene model (Fernando et al., 1994; Stricker et al., 1995).

We used a modified version of MAIA software, which we have designed for complex segregation analysis under the mixed model (Aulchenko, 2000). The ‘pure polygene’ model with excluded major-gene component was studied by exact methods using FISHER software (Lange, 1988).

3. Results

We carried out statistical and genetic analysis of each pedigree separately. There was no significant difference between the pedigrees in litter size: one-way ANOVA gave $F_{1,285}$-ratio = 0.225 ($P > 0.6$). By the use of FISHER we also compared (i) the heterogeneity model, where each pedigree was described by its grand mean, effects of fixed factors (parity, season, body mass of female), heritability and total variance with (ii) the homogeneity model assuming that these parameters are equal in the two pedigrees. The two likelihoods coming from these models were remarkably close ($-305.379$ and $-306.758$, respectively; $\chi^2_{df=1} = 2.758$, $P > 0.8$). Therefore we pooled the data from the pedigrees.

(i) Statistical analysis

The mean litter size in the pooled sample was $4.273 \pm 1.709$. The distribution of the litter size deviated significantly from a normal distribution: a non-parametric Kolmogorov–Smirnov test gave $d_{max} = 0.124$, $P < 0.05$. Fixed factors such as year and season of breeding, parity, and dam body mass at the time of breeding could cause this deviation. We analysed the effects of these factors in detail. Also we calculated the inbreeding coefficient for every dam and treated it further as an additional fixed effect. Statistical analysis showed that the effects of inbreeding, body mass of mother and parity were not significant at $\alpha = 0.05$ (Table 1).

The crosses continued throughout the year. To assess the effect of season we classified the birth dates of the litters into four seasons: summer (December–February), autumn (March–May), winter (June–August) and spring (September–November). We detected a significant effect of season ($P \approx 0.01$). Moreover, we observed a nearly linear increase in litter size from summer to spring. The linear regression of litter size on season was significant ($b = 0.285$, $P = 0.001$).

The data used in this analysis have been accumulated over 8 years. ANOVA analysis showed a significant effect of the year ($P \approx 0.02$). However, these effects may be ascribed to uneven seasonal distribution of the birth dates between the years. Indeed, we observed that in the years with low average litter size the litters were mainly obtained in summer or autumn. A high litter size was detected in the years when the majority of litters were born in winter or spring. For example in the Juiz de Fora pedigree the highest litter size was found in 1994, when 55 of 69 litters were obtained during winter or spring; the lowest litter size was in 1996, when all the litters were obtained during summer or autumn. The analysis of the combined influence of year and season demonstrated that only the season has a significant effect ($P < 0.05$).

Thus, these results indicate that only season should be included in further models as a fixed factor. Notably, when we corrected litter size for the season according to the linear regression model, the distribution of the transformed data approached normality ($K-S d_{max} = 0.06$, $P \approx 0.2$).

Table 1 shows a highly significant effect of the dam on litter size. This suggests that litter size is partially

| Variable          | Method of analysis | $b$  | df  | $F$-ratio | $P$  |
|-------------------|--------------------|------|-----|-----------|------|
| Inbreeding        | Regression         | -3.093 | 1,320 | 2.651     | 0.104|
| Mother’s body mass| Regression         | 0.022 | 1,171 | 1.979     | 0.193|
| Parity            | ANOVA              | 13.308 | 1,027 | 0.425     |      |
| Season            | ANOVA              | 3.318 | 3,864 | 0.010     |      |
| Season            | Regression         | 0.285 | 1,320 | 1.643     | 0.001|
| Year              | ANOVA              | 7.314 | 2.432 | 0.019     |      |
| Dam               | ANOVA              | 109.212 | 2.584 | < 0.001   |      |
| Pedigree          | ANOVA              | 1,320 | 0.225 | 0.636     |      |

*a* Linear regression coefficient.

*b* Further analysis has demonstrated that the effect of year is confounded with the effect of season, because the seasonal distributions of litters varied substantially from year to year.
The analysis of litter size in the Brazilian grass mouse

Table 2. Analysis of litter size in Akodon cursor under the mixed model

| Parameter | Sporadic (1) | No covariate (2) | Polygenic (3) | Mixed (4) | Arbitrary transmission (5) | Equal transmission (6) |
|-----------|--------------|------------------|--------------|-----------|---------------------------|-----------------------|
| $b_i$     | 0.285        | [0]              | 0.253        | 0.251     | 0.252                     | 0.258                 |
| $p_i$     | [0]          | [0]              | [0]          | 0.769     | 0.518                     | 0.790                 |
| $\mu$     | 3.535        | 4.111            | 3.498        | 4.037     | 4.146                     | 3.730                 |
| $A$       | --           | --               | 1.005        | 1.450     | 1.045                     |                       |
| $D$       | --           | --               | --           | 0.030     | 0.084                     | 0.473                 |
| $\tau_{00}$ | --          | --               | --           | [1]       | 0.880                     | 0.703                 |
| $\tau_{01}$ | --          | --               | --           | [0.5]     | 0.731                     | $\tau_{00}$           |
| $\tau_{11}$ | --          | --               | --           | [0]       | 0.175                     | $\tau_{00}$           |
| $\sigma^2_0$ | [0]         | 1.521            | 1.498        | 1.082     | 0.303                     | 0.445                 |
| $\sigma^2_0$ | 2.811       | 1.892            | 1.822        | 1.824     | 1.820                     | 1.822                 |
| $-\log L$ | 327.378      | 311.159          | 305.686      | 305.649   | 303.911                   | 304.775               |
| $\chi^2$ df column vs (4) | 43.578 (4) | 0.196 (3) | 3.476 (3) | (3) 1.728 (2) |
| $\chi^2$ df column vs (3) | 43.384 (4) | 10.946 (4) |           |           |}

a Parameters in square brackets are fixed at the values indicated.
b Parameter cannot be estimated under the hypothesis considered.
c $P < 0.001$.
d $P > 0.05$.

determined by some (possibly genetic) factors which vary from dam to dam.

(ii) Complex segregation analysis

Results from complex segregation analysis under the mixed model are presented in Table 2. Both the mixed and the polygenic model describe the data significantly better than the sporadic model ($\chi^2_{df=4}=43.578$, $P \leq 0.001$ and $\chi^2_{df=3}=43.382$, $P \leq 0.001$, respectively). This indicates a significant contribution of genetic factors to the variation in litter size.

To detect a major-gene effect we tested the Mendelian mixed model versus the arbitrary transmission model. These models did not differ significantly ($\chi^2_{df=2} = 3.476, P > 0.3$). According to Elston & Stewart (1971) this may be interpreted in favour of a major-gene contribution.

However, the same result may arise due to a small sample size, which does not allow one to distinguish between Mendelian and arbitrary transmission (Elston, 1981). Furthermore, some patterns of polygenic inheritance may imitate major-gene effects (Demenais et al., 1986). To exclude these causes of false positive results, we ran additional tests for a major gene using a comparison of the likelihoods of the arbitrary transmission and equal transmission models on the one hand, and those of mixed and polygene model on the other hand.

Both tests failed to confirm major-gene control: the polygene model did not differ from the mixed model ($\chi^2_{df=2} = 0.196, P > 0.8$) and the arbitrary transmission model did not differ from the equal transmission model ($\chi^2_{df=2} = 1.728, P > 0.4$).

A polygene model assumes an approximately equal contribution of the polygenes involved. However, we can imagine a situation where contributions of individual genes are unequal and there is a range of their effects. A major-gene model in this sense is an extreme case of the model of unequal contribution. Although we have rejected it, we decided to test a mild type of unequal contribution model. To do this we analysed our data using a finite polygenic model (Fernando et al., 1994; Stricker et al., 1995). We assumed that the genetic component of the variation in the litter size consisted of four diallelic Mendelian genes acting in a completely additive but unequal manner. Their effects were described as a linear function where two neighbouring elements of the ordered set of the effects differed for a constant value. Testing the hypothesis of equal effects against the more general one of linear ordering did not demonstrate a significant difference ($\chi^2_{df=1} = 0.04, P > 0.9$).

Statistical analysis demonstrated a significant effect of season on the litter size. The segregation analysis gave the same result. Exclusion of a seasonal covariate from the model led to a significant decrease in the likelihood ($\chi^2_{df=1} = 10.946$ and $P < 0.001$).

Thus, we can conclude that multiple genes of approximately equal effect control the variation of litter size in the pedigrees studied. Of course, we cannot exclude the possibility that there may be some difference in their effects. However, the material and
methods we have at hand do not enable us to detect this difference. The fixed effect of season also played an important role in the control. We estimated $h^2$ as the ratio $\sigma_G^2/(\sigma_G^2 + \sigma_e^2)$ obtained under the polygene model (Table 2, column 3). It was surprisingly high: additive genetic variation determined 0.44 of the total variation in litter size.

4. Discussion

(i) Statistical problems

We used a number of approximations: the likelihood of complex pedigrees with multiple loops was approximated by the cut-extension approach (Stricker et al., 1995, 1996; Wang et al., 1996), the polygenic component was approximated by the hypergeometric model (Cannings et al., 1978; Lange, 1997), the analysis of inequality of genetic effects in polygenic ensemble was undertaken under the finite polygenic model (Fernando et al., 1994; Stricker et al., 1995).

The cut-extension approximation of the likelihood for complex pedigrees with multiple loops was proven to be rather accurate (Stricker et al., 1996; Wang et al., 1996). Statistical problems may appear when multiple short inbred loops are being cut (Aulchenko & Axenovich, 1999a, b). However, this was not the case in our study: there were only two animals of the last generation that came from crosses between first-degree relatives (Fig. 1a). Therefore, for our data the cut-extension approximation is likely to work reasonably well.

The polygenic component was approximated by the hypergeometric model (Cannings et al., 1978; Lange, 1997). Lange (1997) has studied the accuracy of this approximation. His results indicate empirical as well as theoretical grounds for much optimism: the hypergeometric model correctly captures means, variances and covariances of a polygenic model for non-inbred pedigrees; also for inbred pedigrees the results of the approximation are very close to actual ones. The same is true for the finite polygenic model, which approximates a polygenic component by introducing a number (3–5) of genes of equal additive effect (Fernando et al., 1994; Stricker et al., 1995).

Furthermore, we can provide empirical evidence for the accuracy of the approximations. The polygenic model is tractable by exact methods even for pedigrees with multiple loops. We performed exact calculations using the FISHER software (Lange, 1988). The estimates of parameters were nearly the same irrespective of the method used. If we denote the exact likelihood as 1, then the likelihood under the hypergeometric polygenic model was 0.996 and the likelihood under the finite polygenic model was 0.997. This indicates a notable accuracy of our approximation. Thus, the results obtained in this study are statistically correct and reliable.

(ii) Tractability of results

Another methodological problem is how well the results represent the genetic architecture of the trait in the natural populations.

Variation in litter size as well as any other quantitative trait is under the control of genetic and random/fixed environmental factors. We analysed the inheritance of litter size in animals whose ancestors had been isolated from natural populations and then bred in controlled laboratory conditions. It is obvious that the random environmental factors were less variable in the laboratory than in the natural environment.

As for the fixed factors, we found that only one of them, namely the effect of the season, was significant. In the laboratory this effect was determined by the daylight only, while in the field the seasonal variations also involve effects of temperature, humidity, rainfall precipitation, abundance of food resources, etc. However, even in the field daylight plays a leading role in the control of reproduction. Thus the effect of season on the litter size of A. cursor detected in the laboratory might be extrapolated to natural populations of this species. Several studies in natural populations of different species of Akodon revealed a defined breeding season (Crespo, 1966; Gonzalez & Murea, 1983; Piantanida, 1987; Cerqueira & Lara, 1991). Piantanida (1985) demonstrated that the daylight, in addition to diet, influences the fertility in Akodon dolores females.

The random environmental effects (such as habitat heterogeneity, local and temporal changes of population density, etc.), which might seriously affect fertility in the field both directly and indirectly, were absent in the laboratory conditions.

The genetic component of the variation is determined by allele polymorphism. If the natural populations had been polymorphic, then the founders taken from these populations might carry various alleles. Since the number of founders in at least one stock was rather high (34), the polymorphism in the captive breed stocks is likely to represent the polymorphism of the parental natural populations. For this reason, we may suppose that the heritability of litter size in the natural populations of A. cursor is significant too. This does not mean that it has the same value as in the captive colonies.

We rejected both the major-gene and unequal contribution models of the inheritance of litter size and found that the polygene model with approximately equal contribution of the genes involved provided the best description of the genetic control of this trait. This model apparently holds for the natural populations of A. cursor, because we obtained the same estimates of genetic parameters from the analysis of two separate pedigrees which differed in the number
of founders (34 founders in the Sumidouro pedigree and only 4 in the Juiz de Fora pedigree) and localities of their origin. Even if there is a substantial QTL for litter size, it segregates at very low frequency in the natural populations of \textit{A. cursor}.

A classical polygene model was found to provide the best description of the variation in litter size in laboratory mouse, pig, rabbit and other prolific mammals studied regardless of the statistical method applied (Falconer, 1989), although major-gene effects of litter size have been detected in several special cases. These genes were found to be characteristic of particular breeds or lines of domestic sheep and pigs (Davis et al., 1982, 1991; Montgomery et al., 1994; Janss et al., 1997; Rothschild et al., 1996). An interesting case of a major-gene effect on litter size has been described in a hybrid stock derived from crosses between two geographical races of the house musk shrew \textit{Suncus murinus} (Aulchenko et al., 1998). Results of segregation analysis of this hybrid pedigree indicated that the parental populations differed in the allele frequencies of the major-gene and in the values of average polygenic effects. At the same time no major-gene effect was found in several captive close breed (non-hybrid) colonies of the same species, derived from different natural populations of \textit{S. murinus} (Aulchenko, unpublished observation). Apparently the major-gene effects on litter size determine inter-population differences, while in the local populations genetic variation for this trait is predominantly determined by the polygene component.

(iii) \textbf{Heritability of litter size in domestic and wild mammals}

Our data showed that the contribution of the additive genetic component to the phenotypic variation (heritability) for litter size in \textit{A. cursor} was rather high. A high level of heritability of litter size has also been detected in some other studies carried out in natural populations (Weigensberg & Roff, 1996). At first glance these data contradict the theoretical expectations based on Fisher’s theorem (Fisher, 1930) and the results obtained in laboratory and farm animals (Falconer, 1989).

However, these contradictions are more semantic than real. Litter size at birth is an important component of fitness, but is not fitness itself. Many mammals display a negative correlation between litter size and body mass of the littermates. Therefore maximal fitness is described by a set of different combinations of litter size and body mass, rather than by a unique combination of these values. Natural selection in a fluctuating environment thus leads to accumulation of genetic variance in separate components of the fitness, rather than to their exhaustion. That is exactly what we are observing in natural populations of mammals and birds. Farm and laboratory animals are reared in a stable, controlled environment with abundant and guaranteed food supply. In these conditions litter size at birth can be shifted by artificial selection to the right of its distribution in nature. This leads to a substantial decrease in genetic variation of this trait.

We analysed the stocks of \textit{A. cursor} shortly after their introduction into laboratory conditions and found a high value of genetic variance for litter size. It means that natural selection was not able to exhaust a reserve of genetic variation for this trait accumulated in natural populations. This variation is apparently hidden in natural populations due to diverse homeostatic mechanisms, involving various developmental, physiological and environmental correlations.

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