Selection For An Improved Disease Resistance Using Factorial Mating Designs And Molecular Based Pedigrees In Fish: A Simulation Study

H. Chapuis[*], M. Vandeputte[†‡], M. Dupont-Nivet[‡], P. Haffray[§] and E. Quillet[‡]

Introduction

Diseases are a major threat for fish farming all over the world. Selective breeding for natural genetic resistance is considered as a promising tool to reduce the economical impact of disease outbreaks and the environmental issue associated with the use of veterinary drugs. When available, heritability estimates are usually medium to high for a wide range of diseases (Quillet et al., 2007), supporting the idea that a potential for progress through selection does exist. Yet, few commercial breeding programmes have been implemented up to now, one reason being the cost of the facilities dedicated to infectious challenges for many families. Using a posteriori marker-based parentage rebuilding now makes it possible to get the pedigree information when families are reared in a common garden environment since fertilization. The feasibility and power of such a system has been well established for growth and quality traits (Dupont-Nivet et al., 2008; Vandeputte et al., 2008). The limitation comes from the cost of genotyping, which must be designed in order to optimize the associated genetic gain. This paper aims at simulating a selection procedure for disease resistance considered as a binary trait (0 if the fish dies, 1 if it survives) in a population of mixed families where the parentage of both selection candidates and challenged animals is established *a posteriori*. The Bayesian methods based on the maximization of the posterior distribution of unknowns (MAP) as proposed by Gianola and Foulley (1983) and Harville and Mee (1984) are used to estimate breeding values. The expected genetic progress is simulated according to the genetic determinism of the trait, the number of genotyped individuals and their distribution among candidates and related challenged animals, considering that for sanitary reasons, challenged animals cannot be used anymore as future breeders.

Material and methods

Simulation features. The additive genetic values of founders were sampled as normal deviates with a known variance σ_a^2. A non genetic maternal effect common to all offspring of the same dam was sampled as $c_d \mapsto N\left(\mathbf{0}, \sigma_{\mathbf{c}}^{\mathbf{2}}\right)$. At each generation, N_0 challenged animals and N_1 selection candidates were simulated. For each of them, a sire and a dam were randomly

[*]SYSAAF, INRA-URA, 37380 Nouzilly, France
[†]IFREMER, 34250 Palavas les Flots, France
[‡]INRA GABI, 78350 Jouy en Josas, France
[§]SYSAAF, INRA-SCRIBE, 35135 Rennes, France

sampled from a uniform distribution, among the ones compatible with the mating plan. The sex of the selection candidates was sampled form a Bernouilli distribution ($p = 0.5$). The genetic value u_k of offspring k from sire s and dam d was computed as $u_k = 0.5 \times (u_s + u_d) + \Phi_k$, where Φ_k is the Mendelian sampling, accounting for the inbreeding coefficient of sires and dams. For each challenged animal, a residual noise ϵ_k was sampled and added, in order to obtain the underlying performance η_k, which was made binary according to its value, assuming a threshold model, following Wright (1934).

Model of analysis. Each generation, the model of analysis, following Gianola and Foulley (1983), accounted for the binary nature of the data. Let η_{ijkl} be the underlying variate for the animal k, offspring of sire s and dam d, and born in generation l. We have then $\eta_{ijkl} = \mu_l + s_i + d_j + \varepsilon_{ijkl}$, where s_i and d_j are the breeding values to estimate, and μ_l the mean effect of the generation considered on the survival rate. For each selection candidate k, a parental index is derived as $EBV_k = s_i + d_j$. Males and females candidates were then ranked, based on this EBV.

Factors of variation. The key variation factors divide into genetic and demographic parameters. The former describes the genetic determinism of the assumed polygenic disease resistance. Heritability coefficients of 0.1, 0.2 and 0.5 were addressed, assuming a strictly additive genetic determinism. A situation with environmental effects such that $h^2 = 0.2$ and $c^2 = 0.1$ was also studied. The latter factor relates to the number of genotyped individuals. Each generation, 10 independent factorial designs of 10 males and 10 females were used to produce the challenged animals and the selection candidates. Thus, 100 sires and 100 dams were selected at each generation, producing 1000 distinct families of offspring. In a first approach, we adressed the influence of $N_T = N_0 + N_1$, *i.e.* the total number of genotyped animals. In a second approach, we addressed the effect of the accuracy of the selection index. This was done by examining the influence of N_0 for a given value of $N1 = 1000$. In these conditions, the selection pressure was of 20%.

Assessment of genetic gain. Preliminary results have shown that the estimation of the genetic parameters in such a design was possible, as long as the issue of the challenged lied between 30% and 70% of survival rate. That is the reason why the threshold was fixed as 0, assuming a survival rate of 50%. The selection carried out resulted in an increase of the underlying variate η, which was easily translated in a decrease of the mortality rate. Up to 10 generations were simulated according to the rules above described. 200 replicates were launched in order to derive the trends.

Results and discussion

As can be seen on figure 1, the higher the heritability, the quicker the decrease in the mortality rate. Assuming $N_0 = N_1 = 2000$ and $h^2 = 0.5$, the mortality rate can be reduced below 10% in 5 generations, while 10 generations are necessary to reach this gain if $h^2 = 0.2$. In the unfavourable situation where $h^2 = 0.1$, the mortality rate cannot be reduced below 20% in the same interval. In the case of a c^2 of 0.1, amounting to half the heritability, a gain can still be achieved, yet less effective. As expected, selection succes is greatly influenced by the total number of genotyped animals, but with such a design it is impossible to disentangle the effects of the selection intensity (influenced by N_1) and of the index accuracy (which depends

on N_0).

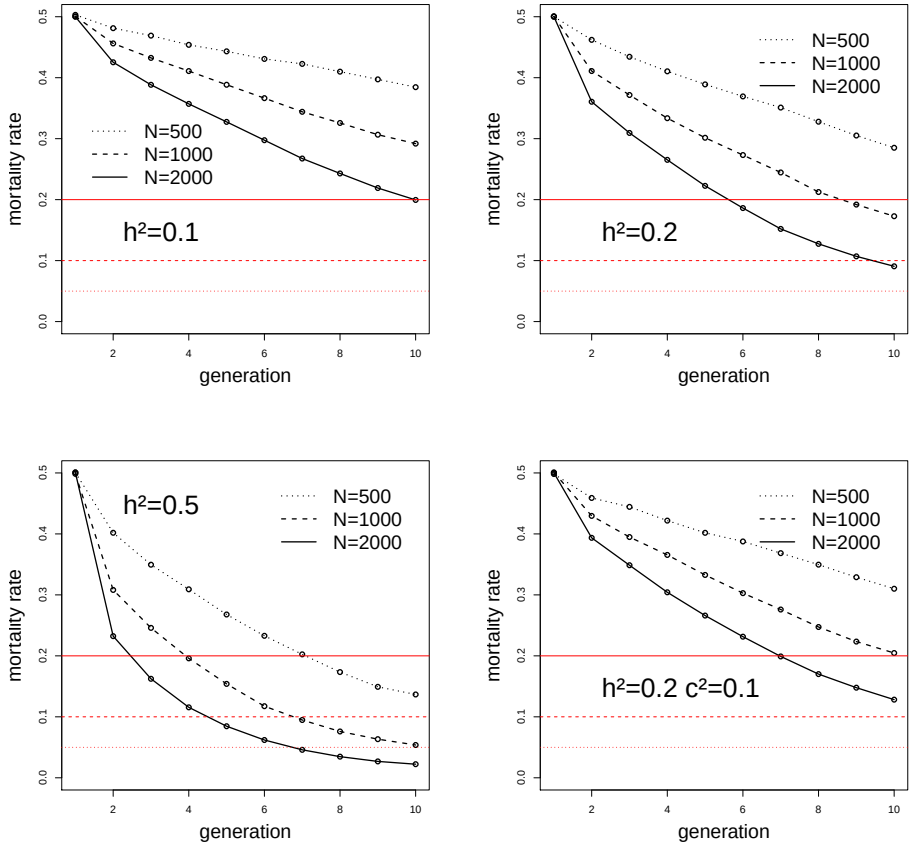

Figure 1: Efficiency of the selection as a function of the genetic determinism of the disease resistance and of the number of genotyped animals. $N = N_0 = N_1$ **is the number of challenged individuals and selection candidates submitted to genotype.**

As can be seen on figure 2, however, increasing the number of challenged genotyped animals for a given selection intensity improves the efficiency of the selection. With $N_0 = 2000$, the mortality rate can be reduced below 20% within 7 generations. This level can be reached in only 6 generations if $N_0 = 3000$, while 10 generations are not sufficient if $N_0 = 500$. In this context, $N_0 = 2000$ seems an acceptable compromise between selection efficiency and genotyping costs. A selection pressure of 20% was deemed reasonnable. In practice, efficiency of selection will depend on the marginal selection intensity that can be dedicated to the viability traits. Other values of the selection intensity were adressed, with simular results.

Conclusion

The study confirms the potential for a significant genetic gain when selecting for disease resistance considered as a threshold trait. Gain is expected in a range of situations for both heritabilities and selection pressure. The benefit of increasing the number of genotyped individuals will depend on the selection intensity applied on this particular trait as well as on the number of challenged animals. Improvement of the prediction tool when introducing selection of other (possibly correlated) traits such as growth, quality or another disease would help at making a decision.

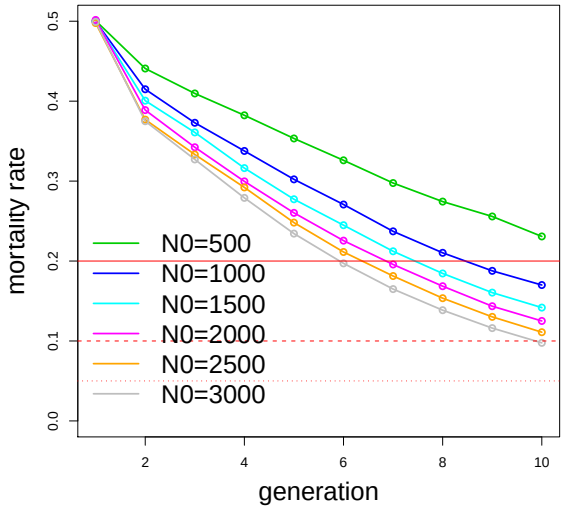

Figure 2: Effect of N_0, the number of genotyped challenged animals on the reduction of the mortality rate, for a given selection pressure of 20%.

References

Dupont-Nivet, M., Vandeputte, M., Vergnet, A., Merdy, O., Haffray, P., Chavanne, H., and Chatain, B. (2008). *Aquaculture*, 275:81–87.

Gianola, D. and Foulley, J. (1983). *Génét. Sél. Evol.*, 15(2):201–224.

Harville, D. and Mee, R. (1984). *Biometrics*, 40:393–408.

Quillet, E., Boudry, P., and Lapègue, S. (2007). *INRA Prod. Anim*, 20:239–252.

Vandeputte, M., Kocour, M., Mauger, S., Rodina, M., Launay, A., Gela, D., Dupont-Nivet, M., Hulak, M., and Linhart, O. (2008). *Aquaculture*, 277:7–13.

Wright, S. (1934). *Genetics*, 19:506–536.