Genetics and population analysis

purgeR: inbreeding and purging in pedigreed populations

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Abstract

Summary: Inbreeding depression and genetic purging are important processes shaping the survivability and evolution of small populations. However, detecting purging is challenging in practice, in part because there are limited tools dedicated to it. I present a new R package to assist population analyses on detection and quantification of the inbreeding depression and genetic purging of biological fitness in pedigreed populations. It includes a collection of methods to estimate different measurements of inbreeding (Wright’s, partial and ancestral inbreeding coefficients) as well as purging parameters (purged inbreeding, and opportunity of purging coefficients). Additional functions are also included to estimate population parameters, allowing to contextualize inbreeding and purging these results in terms of the population demographic history. purgeR is a valuable tool to gain insight into processes related to inbreeding and purging, and to better understand fitness and inbreeding load evolution in small populations.

Availability and implementation: purgeR is an R package available at CRAN, and can be installed via install.packages(“purgeR”). Source code is maintained at a GitLab repository (https://gitlab.com/elcortegano/purgeR).

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Supplementary information: Supplementary data are available at Bioinformatics online.

1 Introduction

Inbreeding may result in the decline of biological fitness due to the increase in the frequency of homozygote genotypes for deleterious recessive alleles, causing the so-called ‘inbreeding depression’ (Charlesworth and Charlesworth, 1987). However, as deleterious alleles become more exposed under inbreeding, selection also becomes more effective removing, or ‘purging’, them (Charlesworth, 2018; Glemin, 2003). Consequently, the expectation of population fitness evolution under inbreeding changes with purging, possibly allowing for the survival of small populations (Hedrick and García-Dorado, 2016).

Pedigree information has attracted the attention of genetic purging models, as these allow for direct inferences on single individuals based on their genealogical history, and many conservation programs maintain studbooks with pedigree records. Boakes and Wang (2005) used ancestral inbreeding coefficients (\(F_a\), Ballou, 1997) to measure the consequences of purging on fitness, given the expectation that individuals born from more inbred ancestors are expected to be more fit than individuals with the same level of inbreeding but less inbred ancestors. Gulisija and Crow (2007) developed a method to evaluate the potential reduction in the individual inbreeding load (\(B\)) using the probability of transmission of highly deleterious recessive alleles under inbreeding. García-Dorado (2012) defined a purged inbreeding coefficient (\(g\)) that measures the expected frequency of recessive deleterious loci in homozygosity, as a function of a purging coefficient (\(d\)) that relates to the recessive component of deleterious effects.

While many software packages have been developed to compute inbreeding, resources for purging analysis are more limited. To my knowledge, \(F_a\) is only computed by a few software packages (Basmung et al., 2015; Doekes et al., 2012; García-Dorado et al., 2016), and only PURGd estimates \(g\) (García-Dorado et al., 2016). No informatic tool is available to compute Gulisija and Crow’s parameters for the opportunity of purging. purgeR computes all these parameters and others, including parameters related to population diversity and demography (e.g. effective population size, \(N_e\)), all functions being introduced in tutorials accessible via browseVignettes(“purgeR”).

2 Input data

For illustrative purposes here, a population with known fitness and \(B = 4.4\) was simulated with size \(N = 10^3\) for \(10^3\) generations and then bottlenecked to \(N = 25\) for \(50\) generations using SLiM 3.5 (Haller and Messer, 2019), under conditions favorable to the detection of purging, similarly as in García-Dorado et al. (2016). Details on the mutational model used and code to reproduce the simulation are given in Supplementary File S1. The simulated pedigree is included as Supplementary Table S1. Input pedigrees are required to be ‘data.frame’ objects in R, and to include individual, maternal and paternal identities.
consequence of having inbred ancestors, Oe

more usable, a heuristic approach was developed to correct
grees derived by Gulisija and Crow involve highly nested complex

j

Gulisija and Crow, 2007). However, equations for complex pedi-

path, these parameters need to be corrected by discounting from

j

j

function and others in the package are provided in Supplementary

i

of individuals

Oe

Referred to ancestor

j

population, together with expectations based on normalized Oe

functions, respectively). A dashed line indicates the value Oe

expected under the original model, and in these cases

0 (e.g. from consecutive generations) under-

n

B

¼

Fj(k)

> 0, where j is an intermedi-

electronic supplementary information

k

Figure 1A shows the observed decline of

B

in the bottlenecked

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pairwise and partial inbreeding coefficients using a gene dropping approach. J. Anim.

Breed. Genet., 132, 100–108.

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Hedrick,P.W. and García-Dorado,A. (2016) Understanding inbreeding depres-

sion, purging, and genetic rescue. Trends Ecol. Evol., 31, 1109–1144.

Observe the decline of B in the bottlenecked

population, together with expectations based on normalized Oe

estimated from the pedigree (i.e. Oe/Fj), and also based on purged

inbreeding. Figure 1B shows the substantial variation in Oe for indi-

viduals with the same level of inbreeding. It also shows the problem

of obtaining Oe> F estimates. However, as illustrated in Figure 1A,

assuming Oe= F in such cases allows to estimate B reasonably well.

Results for alternative mutational models, and an example on a real

population, are given in Supplementary File S3, and show that using

both corrected and uncorrected Oe estimates might be useful setting,

respectively, lower and upper bounds to B decline.

It must be noted that Gulisija and Crow’s (2007) model assumes

highly deleterious and recessive mutations, thus relating to the most

deleterious component of the inbreeding load, and ignoring the pos-

sible purging of variants with low effect sizes. Evidence from genom-

ic studies however suggest that purging is only relevant for highly

deleterious variants (Grossen et al., 2020). In small populations

affected by drift, purging is also expected to be efficient only for

strongly deleterious alleles (Glémín, 2003). Therefore, assumptions

of the model should hold in most practical cases. In addition, estima-
tion of inbreeding load decline using O and Oe provide a way to esti-

mate inbreeding load decline that is not dependent on accurate

measures of fitness and other factors, which can be troublesome or

be incomplete in many real scenarios.

3 Opportunity of purging

Here, the computation of opportunity of purging measures is pre-

sented, since this is the major novelty in purgeR compared to its pre-

decessor PURGd (from which many functions are reimplemented),

apart from other improvements related to portability, performance

and usability. Some assays on the performance of purgeR are given in

Supplementary File S2.

Total (O) and expressed (Oe) opportunity of purging can be

computed for every individual to provide an estimate of the expected

reduction in B. While O measures the potential reduction of B as a

consequence of having inbred ancestors, Oe relates to the reduction

in expressed B as a consequence of having inbred ancestors, and

being homozygous for alleles derived from them (Gulisija and Crow,

2007). They can be computed in simple pedigrees for an individual i as:

\[
O_{i} = \sum_{j} (1/2)^{n-1} F_{j}
\]

where the summation j is over all inbred ancestors, and the summa-

tion k is over all paths from i to ancestor j (each involving a number

of individuals n, i and j included). \( F_{ij} \) is the partial inbreeding of

i

referred to ancestor \( j \), indicating i’s probability to be inbred by des-

cent for alleles derived from \( j \). O and Oe are computed via the func-

tion purgeR::ip_op(), and notes on the validation for this

function and others in the package are provided in Supplementary

File S3.

For complex pedigrees involving several autozygotes in the same

path, these parameters need to be corrected by discounting from

close ancestors’ contributions the contribution made by far ancestors

(Gulisija and Crow, 2007). However, equations for complex pedi-

grees derived by Gulisija and Crow involve highly nested complex

loops and recursivity, and are not scalable. To make this method

more usable, a heuristic approach was developed to correct O and

Oe measurements. This approach skips far ancestors, that

contribute little to O and Oe, and also to its correction terms. Specifically, given

an individual i of interest, contributions to Oi and Oei from far

ancestors k are ignored as long as \( F_{ik} > 0 \), where j is an interme-
diate ancestor. As a drawback, this method can result in estimates of

O > 1 and Oe > F, particularly in cases involving many recent ances-
tors such that \( F_{ik} = 0 \) (e.g. from consecutive generations) under-

going selection or breeding very close relatives. These situations

are unexpected under the original model, and in these cases O < 1 and

Oe = F should be considered.

Figure 1A shows the observed decline of B in the bottlenecked

population, together with expectations based on normalized Oe

estimated from the pedigree (i.e. Oe/Fj), and also based on purged

Opp. 4

Concluding remarks

purgeR is a versatile toolkit to measure inbreeding and purging

parameters in pedigreed populations. The inclusion of opportunity

of purging parameters is a valuable contribution to the field, since it

allows for the inference of purging without requiring more informa-
tion than the pedigree structure.

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