Heterogeneity in effective population size and its implications in conservation genetics and animal breeding

Belén Jiménez-Mena^{1,2,3} · Frédéric Hospital^{1,2} · Thomas Bataillon³

Received: 31 May 2015 / Accepted: 7 December 2015 / Published online: 14 December 2015
© The Author(s) 2015. This article is published with open access at Springerlink.com

Abstract Effective population size (N_e) is defined as the size of an idealized population undergoing the same rate of genetic drift as the population under study. It is a central concept in population genetics and used extensively in the design and monitoring of conservation and breeding programs. It is most often assumed that genetic drift effects are homogeneous across the genome and thus, so is N_e . However, theory predicts that various processes can modify rates of genetic drift experienced by a locus in the genome. In particular, selection affecting linked neutral sites and rates of recombination can modulate the intensity of genetic drift throughout the genome. The increasing availability of sequence data has made it possible to test whether a single N_e can account for the evolution of the genome. In this article, we discuss reasons why a heterogeneous N_e can be expected theoretically and review what evidence is available from empirical studies. We finish by discussing potential implications for conservation and breeding practices. The evidence suggests that heterogeneity in N_e can be just as important as heterogeneity in mutation rates in determining levels of genetic diversity throughout the genome.

Keywords Heterogeneous effective population size · Local inbreeding · Genome evolution · Conservation genetics · Livestock genomics

Introduction: the concept of N_e and its importance

Effective population size (N_e) is a central concept in evolutionary genetics and conservation biology (Charlesworth 2009). Briefly, N_e is defined as the size of an idealized population undergoing the same rate of genetic drift as the population under study (Wright 1931). In practice, N_e is used in the design of conservation/selection breeding programs and for the interpretation of molecular evolutionary data (Charlesworth 2009).

The effective population size does not usually match the census size (N) of the population. Discrepancies can sometimes be extreme, as for example in the case of the Holstein cattle breed. Despite being a worldwide dairy cow breed with a census size of millions of individuals, the N_e of the whole population is considered to be no larger than 100 (Flint and Mott 2001). This means that the Holstein breed accumulates inbreeding at the same rate as an ideal population of only 100 individuals.

Based on population genomics data, recent studies in model animals and humans suggest that different segments of the genome might undergo different rates of genetic drift, potentially challenging the idea that a single N_e can account for the evolution of the genome (Gossmann et al. 2011; Jiménez-Mena et al., in review). Heterogeneity in N_e across the genome has been specifically estimated and reported in eleven species (Fig. 1). As N_e is important in guiding conservation programs, it is important to evaluate whether heterogeneous N_e is the exception or the rule. Despite a few studied examples of heterogeneity in N_e , is

✉ Belén Jiménez-Mena
belen@birc.au.dk

¹ UMR1313 Génétique animale et biologie intégrative, AgroParisTech, 16 rue Claude Bernard, 75231 Paris 05, France

² UMR1313 Génétique animale et biologie intégrative, INRA, 78350 Jouy-en-Josas, France

³ Bioinformatics Research Centre, Aarhus University, C.F. Møllers Allé 8, 8000 Aarhus C, Denmark

Fig. 1 Empirical distributions of the variation in local N_e found in the species over which heterogeneity in N_e have been studied (Gossmann et al. 2011; Jiménez-Mena et al. in review). These distributions of local N_e were all fitted from empirical data by assuming that variation in local N_e follows a log-normal distribution. Distributions have been scaled so that they all have a mean of 1 to make comparisons of N_e heterogeneity on a comparable scale

N_e in reality constant overall, or has heterogeneity in N_e been overlooked so far and commonly occurring? If N_e is heterogeneous across the genome and pervasive across species, conservation guidelines that typically assume a single N_e in a population may be overly optimistic. Let us illustrate this point with an example. Consider that the N_e of a population is estimated to be 250. The rate at which the population is building up consanguinity (as measured by the rate of increase in inbreeding coefficient, or ΔF), corresponds to $\Delta F = 1/(2N_e) = 0.2\%$. However, if portions of the genome are drifting at very different rates, the actual N_e describing the building up of consanguinity in these regions might be quite different from 250. Under that assumption, let us consider a portion of the genome with say $N_e = 50$, thus, the ΔF of that specific region would be 1 %. In this case, the population would locally be accumulating homozygosity at a much faster rate than expected given the average N_e . If the population harbors a sizable mutation load, e.g. strongly deleterious and fairly recessive mutations, this extra local drift might actually incur much higher inbreeding depression than what would be predicted if all regions consistently accumulated a constant and very modest amount of consanguinity throughout the genome.

Here, we first review the empirical evidence available so far that has revealed the existence of heterogeneity in N_e throughout the genome, explaining the methods that allow us to detect such heterogeneity in N_e and addressing the possible theoretical causes. We close by discussing the

potential implications of such heterogeneity for conservation and breeding practices.

Evidence available for the heterogeneity in N_e throughout the genome

Under selective neutrality and constant population size, a single N_e is expected to capture the rate of genetic drift of all autosomes throughout the genome. In this case we refer to this N_e as a “global N_e ”, where the whole genome is affected by a homogeneous rate of genetic drift. But allele frequencies at a given focal site in the genome can also be influenced by selection operating at adjacent sites. N_e , the number of individuals effectively contributing to future generations, is affected by the fact that, due to selection, some individuals contribute disproportionately to future generations because they are carrying more beneficial and/or less deleterious mutations around the site of interest. There is a wealth of population genetics theory that has accumulated since the mid-60s (see recent exhaustive review by Charlesworth 2012; Cutter and Payseur 2013) showing that selection can locally reduce the N_e experienced by a genomic site reducing both the level of genetic variability and the efficacy of selection at that site. We hereafter talk about this “local N_e ” to describe the potential heterogeneity in N_e in the genome.

Levels of genetic diversity are typically summarized using measures such as mean marker heterozygosity, levels of pairwise nucleotide diversity, or number of distinct alleles in a sample. It turns out that under a model where mutation is selectively neutral, these measures are all determined jointly by N_e and mutation rate μ , through the composite parameter $\theta = 4 N_e \mu$. Thus, observed variation in levels of genetic diversity can be in principle caused by variation in N_e and/or μ . Since the seminal study of Begun and Aquadro (1992), there has been evidence that levels of genetic diversity can be heterogeneous and correlated with recombination rates. In principle a unique N_e can account for the correlation between mutation and recombination rate if regions of higher recombination are also more mutable. However, several studies in *Drosophila* spp. and humans show that a mere correlation between these two factors cannot account for the observed heterogeneity of diversity (Lohmueller et al. 2011; Comeron 2014). These studies provide evidence for selection at linked sites and thus challenge the theoretical expectation that N_e should/could plausibly vary.

Different methods can be used to detect heterogeneity in N_e

Studies that have reported variation in N_e across the genome used different kinds of methods to estimate N_e as well

as different amounts of data. Despite the numerous methods available to estimate N_e , i.e. demographic, pedigree, or molecular methods (Caballero 1994; Luikart et al. 2010), not all have the potential to detect heterogeneity in N_e . Methods that rely on demographic and pedigree information assume per se a single N_e across the whole genome. Demographic factors, such as fluctuations in population size over time or variance in progeny size, are assumed to affect the “global N_e ” of a population. DNA variation, however, is affected by several processes that modify levels of genetic diversity locally along the genome (Sella et al. 2009) and methods that use this information can potentially be useful to detect different rates of genetic drift along the genome and measure a “local N_e ” (Wang 2005; Luikart et al. 2010).

Molecular methods can be divided according to the number of samples taken from a population used to estimate N_e . Methods that use only one contemporary sample from a population will estimate a long-term N_e (also referred to as ancient or historical; Luikart et al. 2010). This long-term N_e will reflect the accumulated effects of genetic drift over past generations and how demographic and selective evolutionary processes have changed diversity levels in the population throughout time. This yields a very integrative average of the population size history over a rather long time period but is not necessarily informative about the recent or current rate of genetic drift in the population (Wang 2005). Most evolutionary studies published so far that explicitly consider heterogeneity in N_e along the genome use patterns of polymorphism, estimated at a single point in time, together with patterns of between-species divergence as a way to assess heterogeneity in mutation rates. By their nature these studies can only indirectly document heterogeneity in N_e over long historical periods. Gossman et al. (2011) estimated the long-term N_e of 10 eukaryotic species from data of joint patterns of population polymorphism and divergence at neutral sites within protein-coding regions. The number of loci used for each species differed, ranging from 49 to 918 loci. The number of sites per locus also varied among species. The authors first detected variation in levels of genetic diversity using two different statistical tests (Chi² test and HKA test). These two tests differ in their assumptions about recombination within and between the loci studied for each species, i.e. Chi²-test assumes that there is free recombination within loci, whereas HKA test assumes that there is no recombination. Assuming that N_e varied locally and this variation followed a log-normal or gamma distribution (Fig. 1), the authors estimated the distribution of the variation in local N_e for each species. Although significant, the variation in N_e found was modest, ranging from 7.2-fold (*Capsella rubella*) to < four-fold (*Mus musculus castaneus*, *Capsella grandiflora*, *Boechera strycta*, and *Saccharomyces paradoxus*). The study of Gossman et al. (2011) represents

the first study that directly assessed the existence of heterogeneity in N_e across the genome and quantified it. However, this study does not specifically report the locations in the genome where N_e is heterogeneous.

A second type of molecular method uses information from a single population sampled at two different time points. With two temporal samples, it is possible to measure the increase in inbreeding coefficient, or a change in allele frequencies between the two time points and estimate a “realized N_e ” over a defined time period (Wang 2005). The temporal information allows us to measure this realized N_e using the temporal standardized variance in allele frequencies (Waples 1989; Jorde and Ryman 2007). Temporal datasets thus allow estimating directly the realized N_e and studying its heterogeneity. Orozco-terWengel et al. (2012) analysed the change of allele frequency over 37 generations in a set of three replicated experimental lines of *Drosophila melanogaster*. They used temporal samples and directly measured the realized N_e along the genome. They observed different rates of genetic drift, as estimated by loss of heterozygosity, among the chromosomes; these rates ranged from very low levels of genetic drift found in the sexual X chromosome to very high levels presented by chromosome 3. Tobler et al. (2014) combined experimental evolution and next-generation sequencing (NGS) to detect candidate SNPs associated with thermal adaptation in *D. melanogaster*. They estimated a chromosome-specific N_e for each chromosome, using a total of 1.45 million SNPs. N_e was compatible with a genome-wide realized N_e of about 300 individuals over 15 generations, but several chromosome arms (2L, 3R) exhibited a (significantly) reduced realized N_e of approximately 150 in some treatments.

The animal breeding sector generates large amounts of genomic data, typically genotyping thousands of individuals at different time points in breeding populations of livestock species. This type of data can in principle be used to infer the realized N_e in different segments of the genome over 1–10 or possibly 20 generations. However, work studying the heterogeneity in N_e in livestock populations is very scarce. Some indirect results bearing on heterogeneity in genetic drift can be found in MacEachern et al. (2009). They looked at more than 7500 SNPs located along the genome for two common cattle breeds (Angus and Holstein). They found that many high-frequency SNP alleles showed some evidence of non-neutrality throughout the genome. Most of these high-frequency alleles seemed to be grouped in a few regions along the genome, particularly in Holstein. The authors interpret these patterns as instances of hitchhiking events occurring along the genome but do not test per se whether N_e is heterogeneous in regions not strongly affected by hitchhiking. The majority of studies within the animal breeding sector are interested in the implementation of genome-wide scans for selection

footprints since domestication by comparing breeds (see Qanbari and Simianer 2014 for a review). Jiménez-Mena et al. (in review) explicitly used SNP data obtained from three cohorts of individuals of the Danish Holstein cattle breed to examine the rate of genetic drift or N_e throughout the genome. This analysis is also strongly suggesting a heterogeneous N_e . Using a 54 K chip data from the Danish Holstein population, they estimated the standardized variance in allele frequency changes from temporal samples in different bins comprising 100 SNPs along the genome and estimated a realized N_e in each bin. They found evidence for significant variation in N_e along the different chromosomal regions with 472 chromosomal segments spanning 100 SNPs (scale of 3–10 Mb) exhibiting a realized N_e that varies considerably (N_e : 40–250). This range of variation is genuine and exceeds the mere sampling variance around estimates (Fig. 1).

Causes for the heterogeneity in N_e

Neutral regions linked to selected regions may undergo selection through genetic hitchhiking, whereby adaptive mutations sweep through a population (see the ‘genetic draft’ theory developed by Gillespie 2000), and/or background selection, whereby deleterious mutations are removed by selection. Positive and background selection affect diversity across the genome (Sella et al. 2009), but distinguishing their relative importance is challenging (Elyashiv et al. 2014). Some analytical results—holding when selection is strong—show that local N_e at a site experiencing background selection is scaled by the fraction of individuals free from deleterious mutations (Charlesworth et al. 1993; Charlesworth 2012). We thus have a neutral site that is apparently neutrally evolving, albeit with a N_e lower than the one in absence of background selection. In the case of hitchhiking the effects of selection on a linked neutral site can be drastic and cannot even be described properly by a mere reduction of N_e .

How widespread along the genome are these linked selection effects? The magnitude of N_e reduction by linked selection ultimately depends on the frequency and intensity of selective sweeps and the magnitude of background selection. Recombination is key as, all other things being equal, a site in a region with a low recombination rate (per physical length) is more prone to linked selection at neighboring sites. The recombination rate is not constant but varies across the chromosome (Simianer et al. 1997; Nachman 2002) and N_e is expected to be lower in regions of low recombination rates and higher in regions of high recombination rates.

When testing whether heterogeneity in N_e correlates with regions undergoing genetic hitchhiking and background selection, empirical studies use different genetic

proxies for selection at linked sites to study this relationship, e.g. density of selected sites, rates of recombination. Although these proxies are expected to be correlated to levels of variation in N_e , empirical studies have not been able to show this relationship in a consistent way. From the four species tested, Gossmann et al. (2011) only found a significant correlation of the heterogeneity in N_e with the recombination rate in *D. melanogaster* (positive), and with density of genic sites in *Homo sapiens* (positive) and *Arabidopsis thaliana* (negative). The authors argue that these inconsistent correlations between N_e and recombination rates and density of selected sites might be explained by their measure of the mutation rate, which was indirectly obtained from the synonymous diversity. Jiménez-Mena et al. (in review), surprisingly, did not find any correlation of the variation of N_e reported with density of genic sites, local recombination rate, or presence of past selective sweeps or QTL. This is probably due to the large window size used for the estimation of N_e across the genome and possibly the very short time interval used to measure drift.

The different studies that have reported variation in N_e across the genome differed in (1) the method used to estimate N_e , (2) the kind of N_e estimated and (3) the amount of molecular data used. Nevertheless, they seem to reveal a substantial heterogeneity in N_e within the genome of the species for which heterogeneity in N_e was significant. The amount of variation in N_e differed between the eleven species studied (Gossmann et al. 2011; Fig. 1) but this variation did not show a clear pattern between groups of species, e.g. plant or animal species analyzed so far did not have different levels of heterogeneity. Only *Drosophila* spp. was studied using both long-term and realized N_e . Variation in N_e was reported at large scale such as entire chromosome arm (Orozco-terWengel et al. 2012; Tobler et al. 2014), as well as between gene fragments (Gossmann et al. 2011). The other nine species studied in Gossmann et al. (2011) also reported statistically significant variation in N_e between gene fragments. In the case of *Bos taurus*, variation in N_e was found in relatively large genomic windows of average size of 5 Mb within and between chromosomes (Jiménez-Mena et al. in review).

Outlook: consequences for conservation and sustainable breeding practices

N_e is used to evaluate the threat status of a population and to design breeding programs for both wild/captive populations and livestock (local breeds). As a ‘rule of thumb’, it has been suggested that a minimum N_e of 50 is required to avoid the effects of inbreeding depression in the short-term (Soulé 1980), and larger than 500 if the interest is to

maintain the evolutionary potential of the population over a long term (Franklin 1980). There is general disagreement on the appropriate values for these two lower limits and there has been an intense discussion ever since the influential work of Franklin (1980) and Soulé (1980) were published. The short-term threshold of N_e ($N_e = 50$) was derived from the “one percent inbreeding per generation” rule, obtained from practical experience of livestock breeders (Soulé 1980). The long-term threshold of N_e ($N_e = 500$) was conceived based on the importance of mutational accumulation over time. Lande (1995) and Lynch and Lande (1998) later suggested increasing this value to 5000 based on the assumption that the majority of mutations occurring are deleterious, whilst approximately only 10 % are not deleterious and thus potentially evolutionary favourable. Franklin and Frankham (1998) argued against this recommendation by Lynch and Lande to increase Franklin’s original threshold to 5000. Their reasoning was that (1) a portion of these deleterious mutations can also have evolutionary potential in a different environment, (2) the mutation rate and heritability estimates that were used to derive the N_e limit of 5000 were not very realistic, i.e. too low mutation rate and too high heritability estimate. Very recently, Frankham et al. (2014a) recommended increasing these two thresholds to $N_e = 100$ and $N_e > 1000$, respectively, and it continues to be the subject of a controversial discussion (Franklin et al. 2014; Frankham et al. 2014b; Rosenfeld 2014). With all these recommendations, N_e is implicitly discussed assuming homogeneity of N_e throughout the genome. What are the potential consequences of a heterogeneous N_e in that context?

International agencies such as IUCN (International Union for the Conservation of Nature) and FAO (Food and Agriculture Organization of the United Nations) use N_e as a parameter, amongst others, to evaluate the threat status of a population (IUCN 2011; FAO 2013). Strategies for managing small populations typically focus on maximizing N_e to limit the loss of genetic variation (Ballou and Lacy 1995; Fernández et al. 2011). If variation in N_e turns out to be substantial, it would be important to study the consequences of unforeseen local homozygosity on inbreeding depression in managed populations.

In livestock selection programs, the objective is to increase genetic value for a set of economically valuable traits but also to impose restrictions on the rate of increase in inbreeding coefficient, ΔF , as inbreeding depression might offset the genetic gains achieved (Toro et al. 2009). These programs rely on phenotypic and pedigree information (Hayes and Goddard 2010), but increasingly also on genome-wide marker information to select the breeding individuals (Meuwissen et al. 2001). So-called *genomic selection*, has transformed the breeding industry (Hayes

et al. 2009). There are different selection schemes to manage the contribution of individuals in selection breeding programs. The selection scheme based on optimum contributions (OCS, Meuwissen 1997) is of particular interest in our context. Briefly, the idea is that increasing genetic gain and restricting the level of inbreeding of the population can be achieved by controlling the co-ancestry of the selected parents. The estimation of the breeding values can be obtained from pedigree or genomic information, and the breeding scheme to manage inbreeding can also be based on pedigree or genomic relationships. Current methods seek to restrict ΔF as estimated from pedigree (these methods are assuming ΔF is homogenous) or using co-ancestry estimated by molecular markers. An open question is whether local control of the rate of drift (and ΔF) is desirable and can be achieved.

Interestingly, simulation results from Sonesson et al. (2012) show that using genomic information both to obtain the estimated breeding values (EBV) and to restrict inbreeding in the breeding scheme result in a more homogeneous build up of inbreeding around selected regions harboring loci of interest. So when genomic information is used both for the EBV and the breeding scheme, the OCS method indirectly takes into account the selection forces acting on the evaluated markers and neighboring regions, and thus, actually might control the local N_e . Importantly the authors also found that merely using pedigree-based information for restricting inbreeding among selected parents does not guard against the fact that ΔF can be far above the desired rate locally at specific regions of the genome. More recently, a slightly alternative OCS strategy that builds upon Sonesson et al.’s results proposes to combine weighting rare alleles with the OCS method that uses genomic information. This strategy also reduces excessive build up of local inbreeding along the genome while obtaining higher genetic gain (Liu et al. 2014).

Although evidence of a heterogeneous N_e has been found in several species, we currently lack a clear picture of the extent of heterogeneity in N_e . As empirical information on genome-wide diversity in livestock accumulates, there is the opportunity to exploit that wealth of information for other purposes. Currently, this wealth of SNP data is predominantly used to search for strong selective sweeps between breeds and in artificial selection programs to predict breeding values. But, these datasets could also be used (1) to assess empirically the magnitude of the heterogeneity in N_e realized over generations and (2) to monitor more precisely the rate at which inbreeding builds up locally in the genome of livestock breeds. Both conservation and breeding programs might be improved by the knowledge gained about the interaction between drift and linked selection in well-studied livestock populations.

Acknowledgments The authors would like to thank James H. Williams and Susan F. Bailey for English revisions, and Freddy Bugge Christiansen for constructive comments. B.J.M. benefited from a joint grant from the European Commission and the Institut National de la Recherche Agronomique (INRA) Animal Genetics, within the framework of the Erasmus-Mundus joint doctorate “EGS-ABG”.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

References

- Ballou JD, Lacy RC (1995) Identifying genetically important individuals for management of genetic variation in pedigreed populations. In: Ballou JD, Gilpin M, Foose TJ (eds) Population management for survival and recovery. Columbia University Press, New York, pp 76–111
- Begun DJ, Aquadro CF (1992) Levels of naturally occurring DNA polymorphism correlate with recombination rates in *D. melanogaster*. *Nature* 356:519–520. doi:10.1038/356519a0
- Caballero A (1994) Developments in the prediction of effective population size. *Heredity* 73(6):657–679
- Charlesworth B (2009) Effective population size and patterns of molecular evolution and variation. *Nat Rev Genet* 10(3):195–205
- Charlesworth B (2012) The effects of deleterious mutations on evolution at linked sites. *Genetics* 190(1):5–22
- Charlesworth B, Morgan MT, Charlesworth D (1993) The effect of deleterious mutations on neutral molecular variation. *Genetics* 134(4):1289–1303
- Comeron JM (2014) Background selection as baseline for nucleotide variation across the *Drosophila* genome. *PLoS Genet* 10:e1004434. doi:10.1371/journal.pgen.1004434
- Cutter AD, Payseur BA (2013) Genomic signatures of selection at linked sites: unifying the disparity among species. *Nat Rev Genet* 14(4):262–274
- Elyashiv E, Sattath S, Hu TT, Strustovsky A, McVicker G, Andolfatto P, Coop G, Sella G (2014) A genomic map of the effects of linked selection in *Drosophila*. arXiv preprint [arXiv:1408.5461](https://arxiv.org/abs/1408.5461)
- FAO (2013) In vivo conservation of animal genetic resources. FAO Animal Production and Health Guidelines. No. 14. Rome. <http://www.fao.org/docrep/018/i3327e/i3327e00.htm>. Accessed 17 Nov 2014
- Fernández J, Meuwissen THE, Toro MA, Maki-Tanila A (2011) Management of genetic diversity in small farm animal populations. *Animal* 5:1684–1698
- Flint J, Mott R (2001) Finding the molecular basis of quantitative traits: successes and pitfalls. *Nat Rev Genet* 2(6):437–445
- Frankham R, Bradshaw CJ, Brook BW (2014a) Genetics in conservation management: revised recommendations for the 50/500 rules, Red List criteria and population viability analyses. *Biol Conserv* 170:56–63
- Frankham R, Bradshaw CJ, Brook BW (2014b) 50/500 rules need upward revision to 100/1000—response to Franklin et al. *Biol Conserv* 176:286
- Franklin IR (1980) Evolutionary change in small populations. In: Soulé ME, Wilcox BA (eds) Conservation biology: an evolutionary-ecological perspective. Sinauer, Sunderland, pp 135–149
- Franklin IR, Frankham R (1998) How large must populations be to retain evolutionary potential? *Anim Conserv* 1(01):69–70
- Franklin IR, Allendorf FW, Jamieson IG et al (2014) The 50/500 rule is still valid—reply to Frankham et al. *Biol Conserv* 176:284–285
- Gillespie JH (2000) Genetic drift in an infinite population: the pseudohitchhiking model. *Genetics* 155(2):909–919
- Gossman TI, Woolfit M, Eyre-Walker A (2011) Quantifying the variation in the effective population size within a genome. *Genetics* 189(4):1389–1402
- Hayes B, Goddard M (2010) Genome-wide association and genomic selection in animal breeding. *Genome* 53(11):876–883
- Hayes BJ, Bowman PJ, Chamberlain AJ, Goddard ME (2009) Invited review: genomic selection in dairy cattle—progress and challenges. *J Dairy Sci* 92(2):433–443
- IUCN. Technical report (2011) Guidelines for using the IUCN Red List categories and criteria. Version 9.0. prepared by the standards and petitions subcommittee. <http://www.iucnredlist.org/documents/redlistguidelines.pdf>. Accessed 15 Nov 2014
- Jorde PE, Ryman N (2007) Unbiased estimator for genetic drift and effective population size. *Genetics* 177:927–935. doi:10.1534/genetics.107.075481
- Lande R (1995) Mutation and conservation. *Conserv Biol* 9(4):782–791
- Liu H, Sørensen AC, Berg P (2014) Optimum contribution selection combined with weighting rare favourable alleles increases long-term genetic gain. In: Proceedings of the 10th world congress on genetics applied to livestock production (WCGALP)
- Lohmueller KE, Albrechtsen A, Li Y, Kim SY, Korneliusen T, Vinckenbosch N, Tian G et al (2011) Natural selection affects multiple aspects of genetic variation at putatively neutral sites across the human genome. *PLoS Genet* 7(10):e1002326
- Luikart G, Ryman N, Tallmon DA, Schwartz MK, Allendorf FW (2010) Estimation of census and effective population sizes: the increasing usefulness of DNA-based approaches. *Conserv Genet* 11(2):355–373
- Lynch M, Lande R (1998) The critical effective size for a genetically secure population. *Anim Conserv* 1(01):70–72
- MacEachern S, Hayes B, McEwan J, Goddard M (2009) An examination of positive selection and changing effective population size in Angus and Holstein cattle populations (*Bos taurus*) using a high density SNP genotyping platform and the contribution of ancient polymorphism to genomic diversity in Domestic cattle. *BMC Genom* 10(1):181
- Meuwissen TH (1997) Maximizing the response of selection with a predefined rate of inbreeding. *J Anim Sci* 75(4):934–940
- Meuwissen THE, Hayes BJ, Goddard ME (2001) Prediction of total genetic value using genome-wide dense marker maps. *Genetics* 157(4):1819–1829
- Nachman MW (2002) Variation in recombination rate across the genome: evidence and implications. *Curr Opin Genet Dev* 12(6):657–663
- Orozco-terWengel P, Kapun M, Nolte V, Kofler R, Flatt T, Schloetterer C (2012) Adaptation of *Drosophila* to a novel laboratory environment reveals temporally heterogeneous trajectories of selected alleles. *Mol Ecol* 21(20):4931–4941
- Qanbari S, Simianer H (2014) Mapping signatures of positive selection in the genome of livestock. *Livest Sci* 166:133–143
- Rosenfeld JS (2014) 50/500 or 100/1000? Reconciling short-and long-term recovery targets and MVPs. *Biol Conserv* 176:287–288
- Sella G, Petrov DA, Przeworski M, Andolfatto P (2009) Pervasive natural selection in the *Drosophila* genome? *PLoS Genet* 5(6):e1000495

- Simianer H, Szyda J, Ramon G, Lien S (1997) Evidence for individual and between-family variability of the recombination rate in cattle. *Mamm Genome* 8(11):830–835
- Sonesson AK, Woolliams JA, Meuwissen TH (2012) Genomic selection requires genomic control of inbreeding. *Genet Sel Evol* 44:27
- Soulé ME (1980) Threshold for survival: maintaining fitness and evolutionary potential. In: Soulé ME, Wilcox BA (eds) *Conservation biology: an evolutionary-ecological perspective*. Sinauer, Sunderland, pp 151–169
- Tobler R, Franssen SU, Kofler R, Orozco-terWengel P, Nolte V, Hermisson J, Schlötterer C (2014) Massive habitat-specific genomic response in *D. melanogaster* populations during experimental evolution in hot and cold environments. *Mol Biol Evol* 31(2):364–375
- Toro MA, Fernández J, Caballero A (2009) Molecular characterization of breeds and its use in conservation. *Livest Sci* 120(3):174–195
- Wang J (2005) Estimation of effective population sizes from data on genetic markers. *Philos Trans R Soc B* 360(1459):1395–1409
- Waples R (1989) A generalized approach for estimating effective population size from temporal changes in allele frequency. *Genetics* 121(2):379–391
- Wright S (1931) Evolution in mendelian populations. *Genetics* 16(2):97–159