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# Methodological approaches to estimate effective population size

**Modul no.3: Animal Breeding**

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# Effective population size

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# The effective population size Ne

## The most important parameter in conservation genetics

**The effective population size (Ne)** of a **real population** X is the size of a **hypothetical ideal population** (Wright-Fisher) that will result in the **- same amount of genetic drift -** as in the **real (actual) population considered**.

By definition $N_{eLD}$, $N_{eV}$, $N_{eI}$ and $N_{eE}$ are not the always equal (same) !

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# Effective population size (Ne)

An ideal Wright-Fisher population (Fisher 1930; Wright 1931) is;

- discrete generations,
- diploid individuals,
- sexual reproduction,
- the population size is constant across generations,
- no migration,
- mating is random,
- no mutations,
- the sex ratio is 1:1,
- no selection,
- the average number of recruits produced by each individual is Poisson distributed with a mean and variance of two

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# In an ideal Wright-Fisher population on a timescale;

Infinite population size;

- No change in allele and genotype frequencies
- No change in inbreeding level
- No "random extinction" of alleles
- Alleles of non-linked genes are in gametic phase/linkage equilibrium

Finite population size –> genetic drift;

- Change in allele frequencies
- Change in inbreeding level
- Lost of genetic variation (fixation / loss of alleles)
- Change in gametic phase/linkage disequilibrium

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# The effective population size Ne

## The most important parameter in conservation genetics

**The effective population size (Ne)** of a **real population** X is the size of a **hypothetical ideal population** (Wright-Fisher) that will result in the **- same amount of genetic drift -** as in the **real (actual) population considered**.

**Effective variance population size ($N_{eV}$):**

- same change in allele frequencies -

**Effective inbreeding population size ($N_{eI}$):**

- same change in inbreeding level -

**Effective eigenvalue population size ($N_{eE}$):**

- same long term rate at which genetic variants are lost -

**Effective linkage disequilibrium population size ($N_{eLD}$):**

- same change in gametic phase/linkage disequilibrium -

By definition $N_{eLD}$, $N_{eV}$, $N_{eI}$ and $N_{eE}$ are not the always equal (same) !

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# Effective linkage disequilibrium population size (NeLD)

The linkage disequilibrium effective population size $N_{eLD}$ of a real population X with an observed LD for a given interval length is the size of hypothetic ideal population that in an equilibrium state would display the same pattern of LD for the same interval length as observed in real finite population (H. Simianer, 2012; LCG)

Note that by definition $N_{eLD}$ is not the same as those defined for $N_{eV}$, $N_{eI}$ and $N_{eE}$ !

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# NeLD

In an ideal population of infinite size that has reached an equilibrium state, all loci are in linkage equilibrium.

⇕

In an ideal population of finite size that has reached an equilibrium state, loci are in linkage disequilibrium while the amount of LD is a function of the genetic distance of the considered loci and the size of population.

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# Widely used in calculation of the effective population size

| Author | Software | Ne type | Information |
|---|---|---|---|
| *Gutiérrez et al., 2008 GSE, 2009 JABG* | *Endog* | $N_{el}$ | *Pedigree* |
| *Barbato et al., 2015 FG* | *SNeP* | $N_{eLD}$ | *Genomic* |
| *Do et al., 2014 MER* | *NeEstimator V2* | $N_{eGD}$ | *Genomic* |
| *Santiago et al., 2020 MBE* | *GONE* | $N_{eGLD}$ | *Genomic* |
| *Santiago et al., 2020 MBE* | *CurrentNe* | $N_{eGD}$ | *Genomic* |
| *Browning et al., 2018 PLOS G.* | *IBDNe* | $N_{eIBD}$ | *Genomic* |
| *Fournier eta al., 2023 NC* | *HapNe* | $N_{eIBD}$ | *Genomic* |

SNeP estimated $N_e$LD in the current generation estimated by linear regression based on historical estimates as applied in Kukučkova et al., 2017

# Empirical population with informative pedigree

## The Old Kladruber horse (OKH)

### Informative pedigree

# Individuals in pedigree: 9288 (1729 – 2018)

Tracing up to 55 generations

The **Kladruber** (Czech *Starokladrubský kůň*) is the oldest Czech horse breed and one of the world's oldest horse breeds, bred for more than 400 years.

## Calculation based data set

### Genotyped animals (n = 215; 1994 - 2014)

Q1: **38996** autosomal SNPs

Q2: **60645** autosomal SNPs

# Individuals in pedigree: 3120 (1729 – 2014)

Tracing up to 49 generations

ECG: 15.9 (13.5 – 17.4)

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# Results of the current effective population size: OKH

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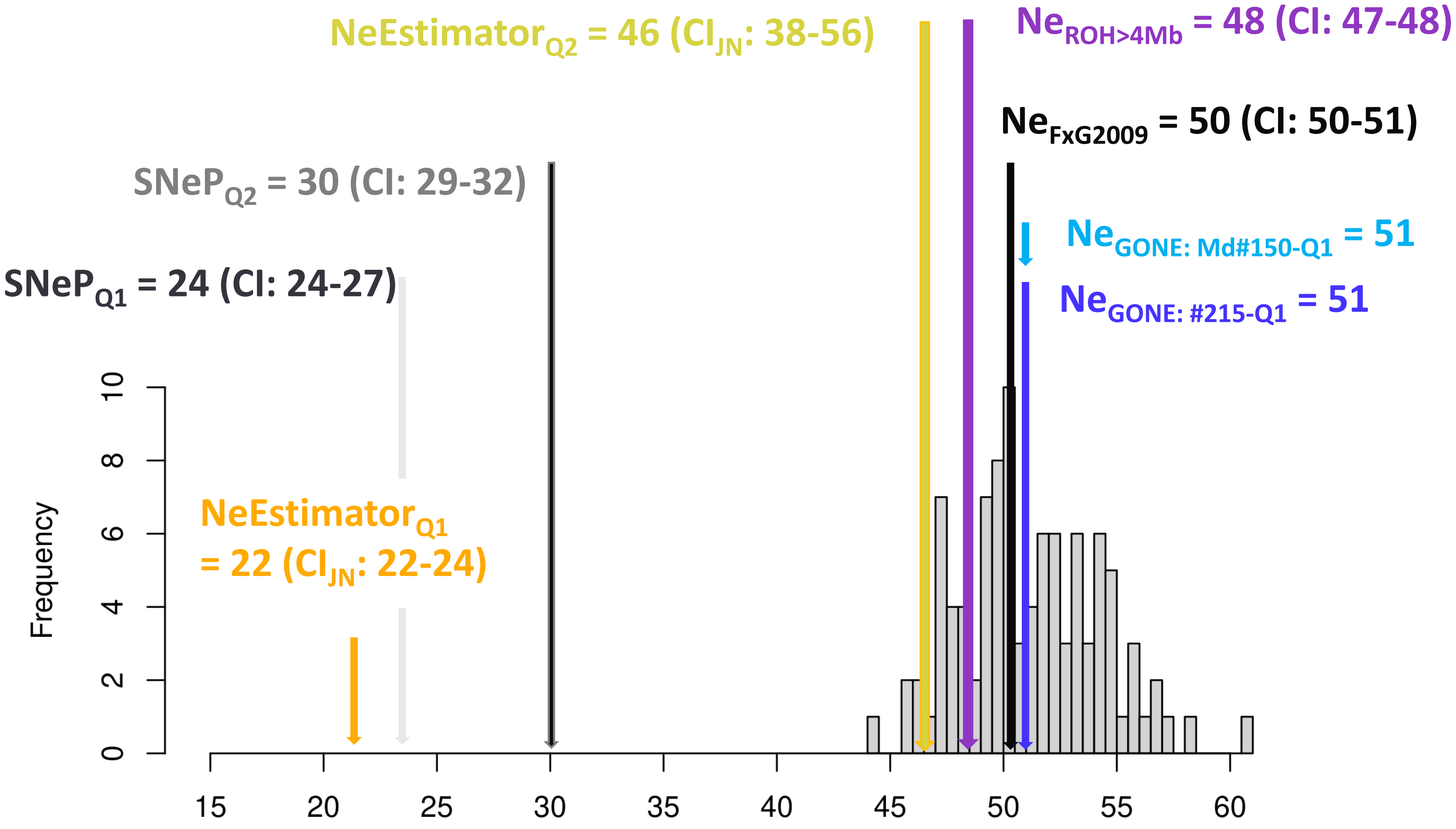

NeEstimator$_{Q2}$ = 46 (CI$_{JN}$: 38-56)

Ne$_{ROH>4Mb}$ = 48 (CI: 47-48)

Ne$_{FxG2009}$ = 50 (CI: 50-51)

SNeP$_{Q2}$ = 30 (CI: 29-32)

Ne$_{GONE: Md\#150-Q1}$ = 51

SNeP$_{Q1}$ = 24 (CI: 24-27)

Ne$_{GONE: \#215-Q1}$ = 51

NeEstimator$_{Q1}$ = 22 (CI$_{JN}$: 22-24)

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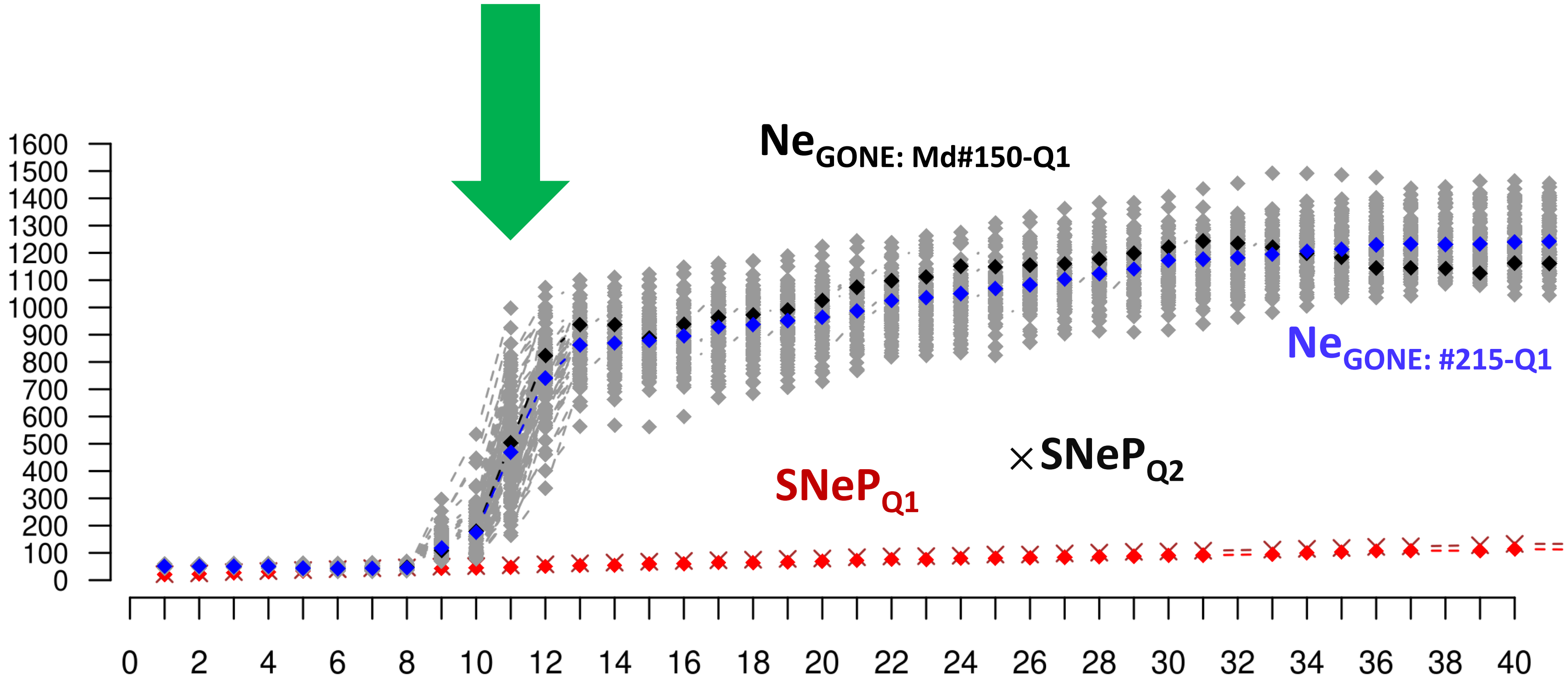
# Results of the historical effective population size: OKH

≈ 100 years back / fall of Austro-Hungarian Monarchy / drop in the number of horses



# Conclusions

## Highly recommended

**Software GONE**

### Recent Demographic History Inferred by High-Resolution Analysis of Linkage Disequilibrium

Enrique Santiago,[*,1] Irene Novo,[2] Antonio F. Pardiñas,[3] María Saura,[4] Jinliang Wang,[5] and Armando Caballero[2]

*Mol. Biol. Evol.* 37(12):3642–3653 doi:10.1093/molbev/msaa169

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# Estimation of effective populations size with software GONE

## - First run

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# Download

- https://github.com/esrud/GONE

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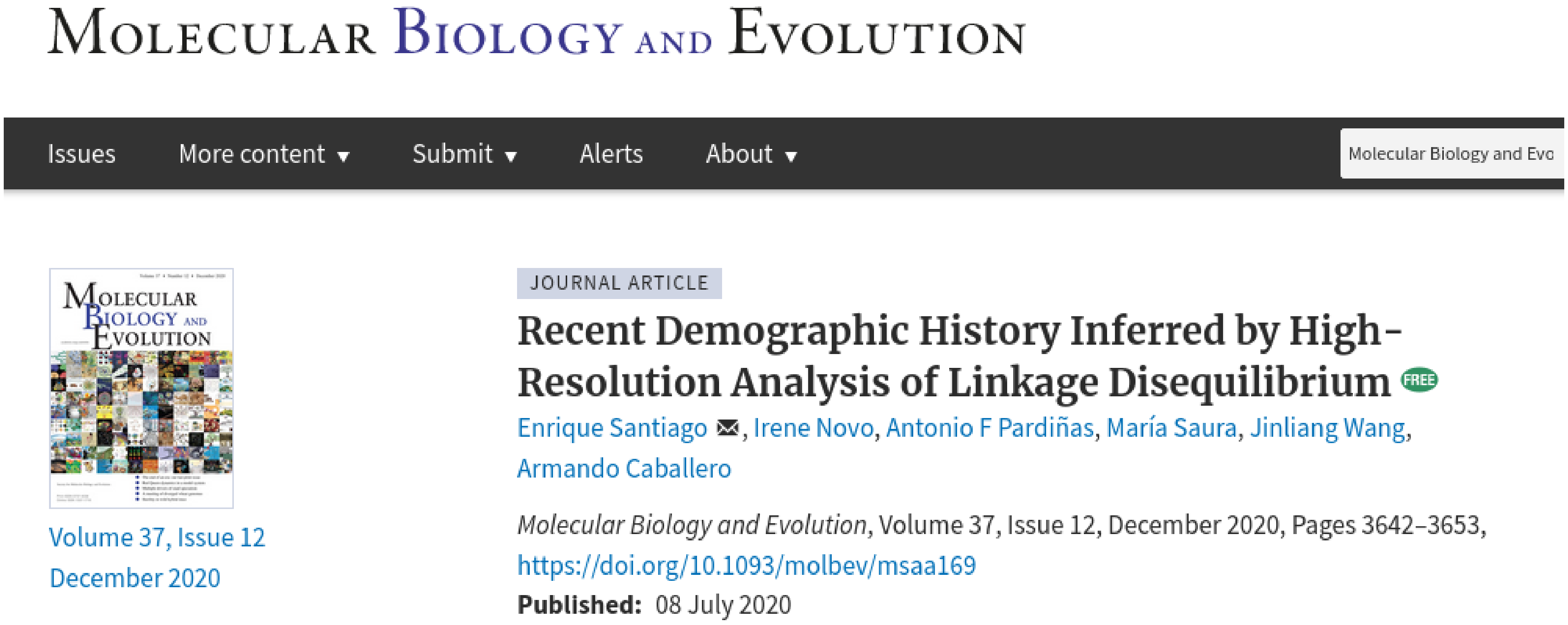
# Methodological approach



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JOURNAL ARTICLE

**Recent Demographic History Inferred by High-Resolution Analysis of Linkage Disequilibrium** FREE

Enrique Santiago ✉, Irene Novo, Antonio F Pardiñas, María Saura, Jinliang Wang, Armando Caballero

*Molecular Biology and Evolution*, Volume 37, Issue 12, December 2020, Pages 3642–3653, https://doi.org/10.1093/molbev/msaa169

**Published:** 08 July 2020

https://doi.org/10.1093/molbev/msaa169

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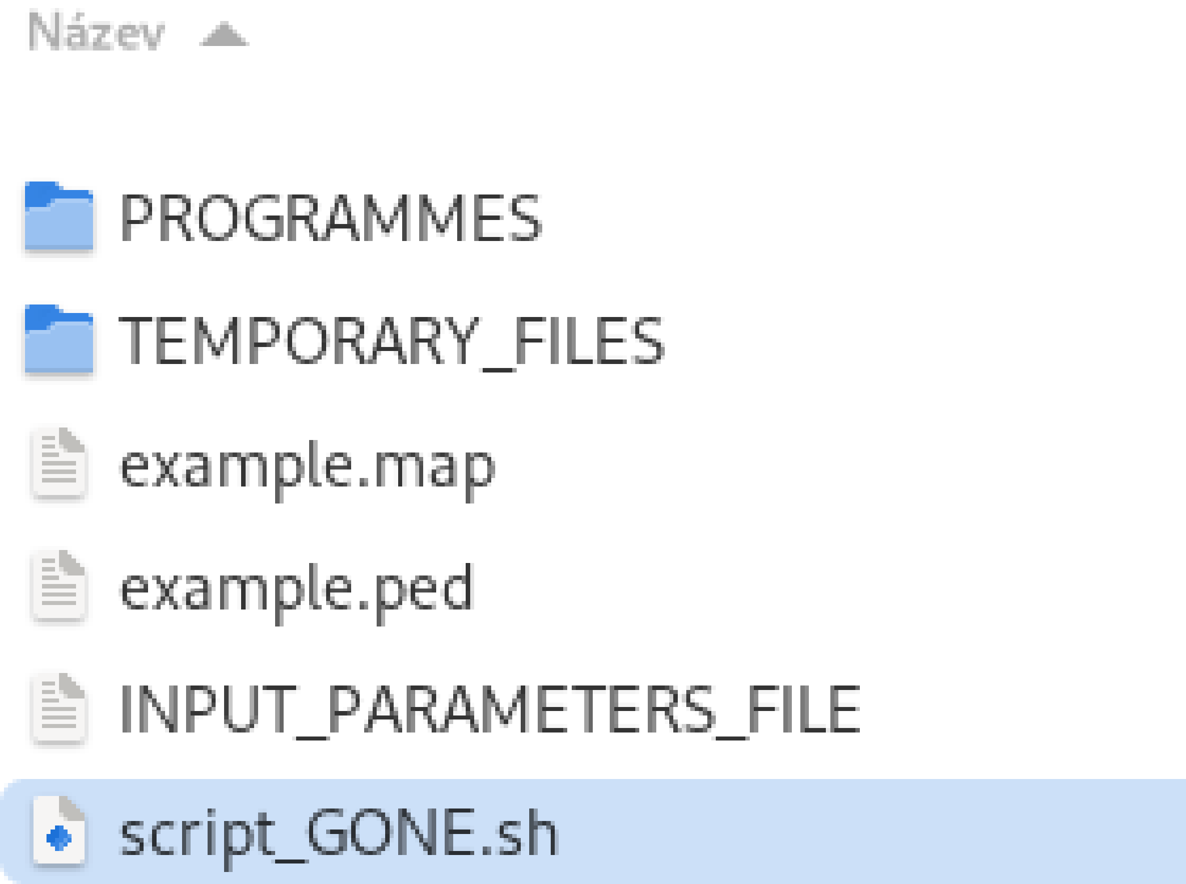
# After download



Název

PROGRAMMES
TEMPORARY_FILES
example.map
example.ped
INPUT_PARAMETERS_FILE
script_GONE.sh

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# Input files

- Plink format
  - .map
    - Maximum number of SNPs per chromosome: 100,000
    - Maximum number of SNPs per genome: 1 million
  - .ped
    - 1 IND1 0 0 1 -9 T A A T ...
    - 1 IND2 0 0 1 -9 T T A T …

      or
    - 1 IND1 0 0 1 -9 2 1 1 2 ...
    - 1 IND2 0 0 1 -9 2 2 1 2 …

      Minimum number of individuals: 2
    - Maximum number of individuals: 1,800

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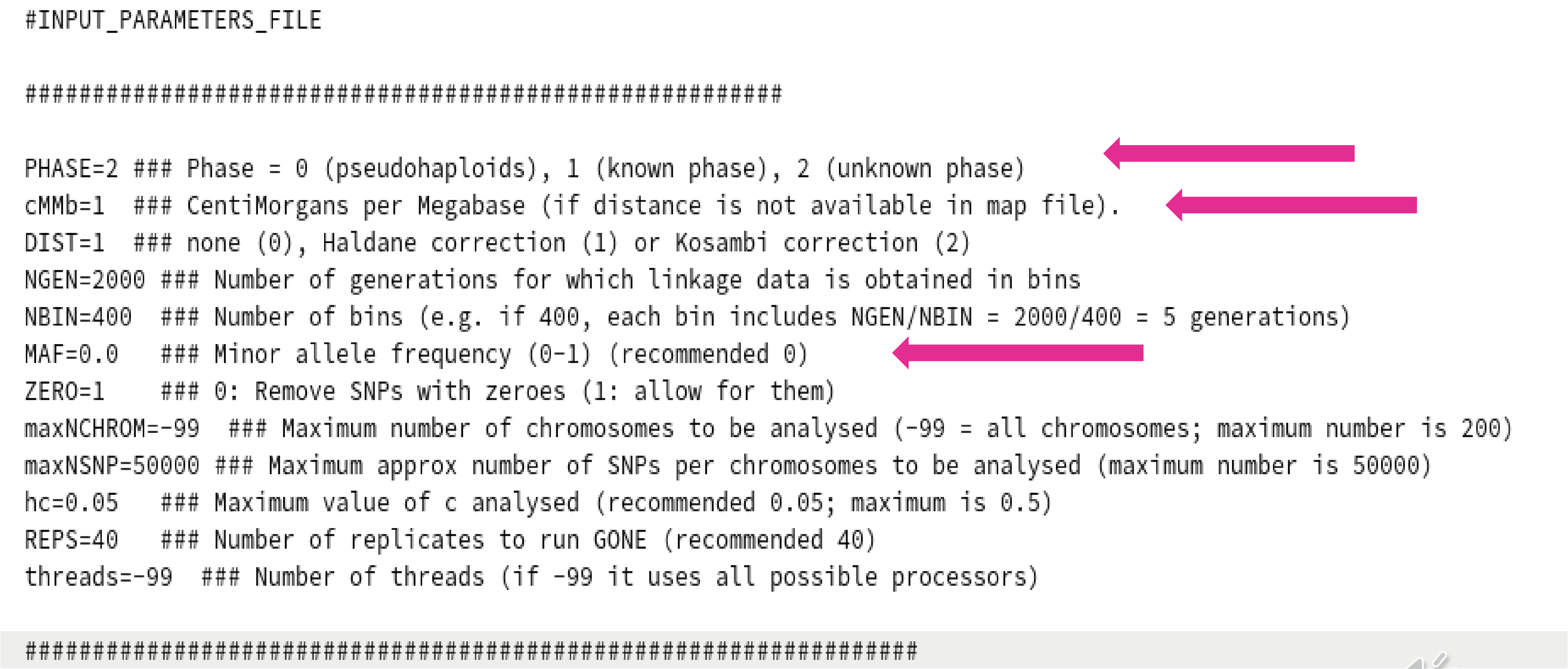
# INPUT_PARAMETERS_FILE



```
#INPUT_PARAMETERS_FILE

###########################################################

PHASE=2 ### Phase = 0 (pseudohaploids), 1 (known phase), 2 (unknown phase)
cMMb=1  ### CentiMorgans per Megabase (if distance is not available in map file).
DIST=1  ### none (0), Haldane correction (1) or Kosambi correction (2)
NGEN=2000 ### Number of generations for which linkage data is obtained in bins
NBIN=400  ### Number of bins (e.g. if 400, each bin includes NGEN/NBIN = 2000/400 = 5 generations)
MAF=0.0   ### Minor allele frequency (0-1) (recommended 0)
ZERO=1    ### 0: Remove SNPs with zeroes (1: allow for them)
maxNCHROM=-99  ### Maximum number of chromosomes to be analysed (-99 = all chromosomes; maximum number is 200)
maxNSNP=50000 ### Maximum approx number of SNPs per chromosomes to be analysed (maximum number is 50000)
hc=0.05   ### Maximum value of c analysed (recommended 0.05; maximum is 0.5)
REPS=40   ### Number of replicates to run GONE (recommended 40)
threads=-99  ### Number of threads (if -99 it uses all possible processors)

##################################################################
```

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# To run the software

```
bash script_GONE.sh <FILE>
```

```
bash script_GONE.sh example
```

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# Tips 1

- maxNSNP=50000 ### Approximated number of SNPs per chromosome to be analysed (maximum is 100,000; default 50,000). If the number of SNPs in the chromosome is **lower than this number, all SNPs of the chromosome will be analysed**.

- **If the value is larger, however, a random sample of 50,000 SNPs will be used. This is useful to avoid too lengthy estimations. In addition, different runs may include different random subsets of SNPs allowing for empirical errors of temporal Ne to be obtained. If you do so, do not sent all runs at the same time, as the initial random seed is taken from the computer clock time.**

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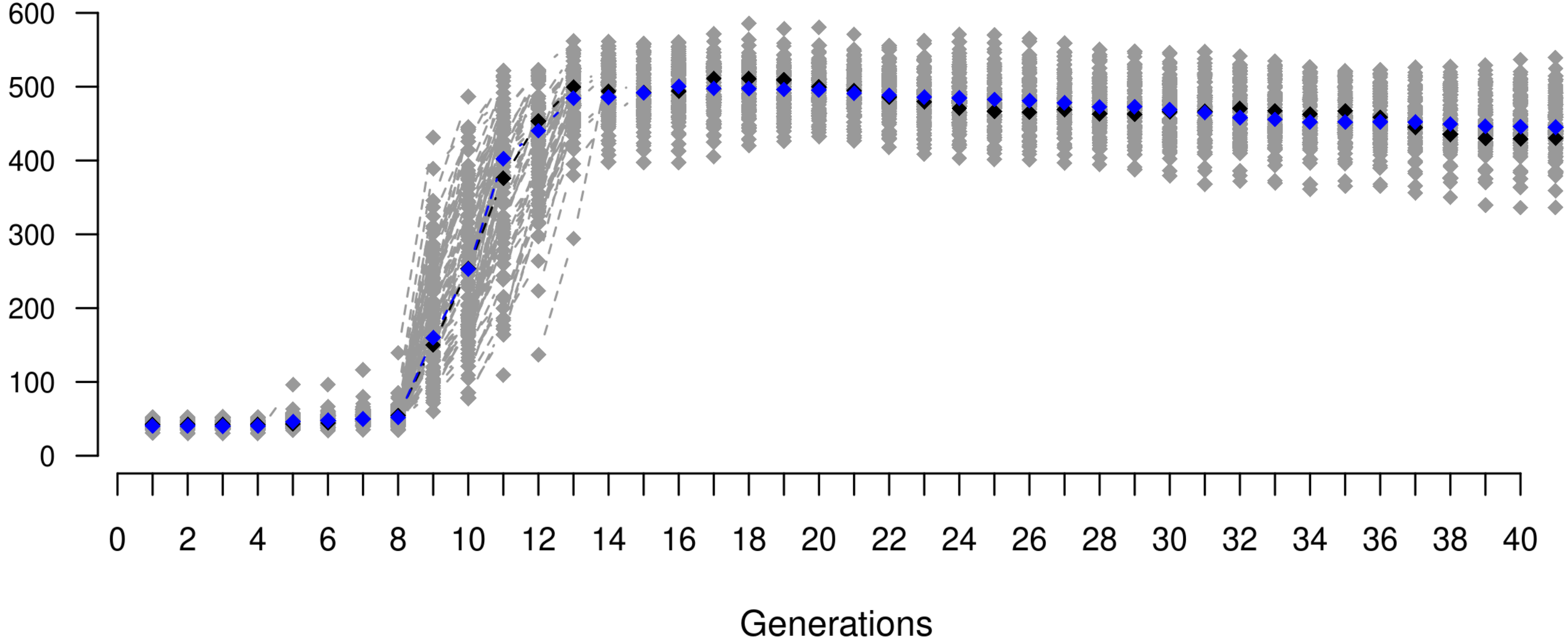
# Confidence intervla



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# Tips 2

- NGEN=2000 ### Number of generations
  - Realistic estimation on midle density SNPs are 100 generations
    - Questions???? 100 generation by livestock?

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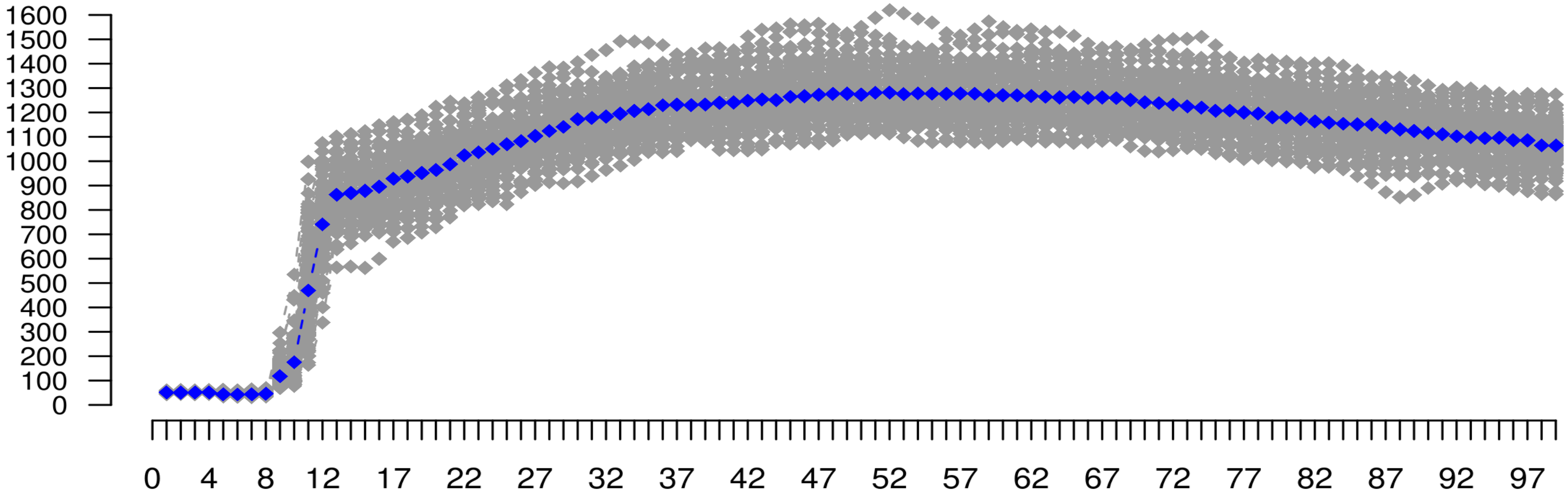
# 100 generations – Old Kladruber horse



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# Case studie
# Estimation of effecitve population size

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# Aims of the study

Estimation of effective population size for local sheep breeds in the Danube region

1. **Estimation current effective population size**

2. **Estimation historical effective population size**

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# Analysed breeds

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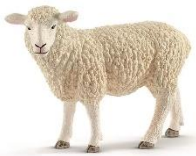
**Czechia**
Improved Valachian
Original Valachian
umava sheep

**Slovakia**
East Friesian
Improved Valachian
Lacaune
Original Valachian
Texel
Tsihaja
Slovak Dairy
Crossbreed



**Czechia**
White shorthair
Brown shorthair
Landrace
Alpine

**Slovakia**

White shorthair

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# Methods: Identification of selection signals

NeEstimator v.2 (Do et al., 2014)

- The leading software in the last decades
- STR/SSR data and SNP data
- In **small sample size** – **infinity** when pop. Size is large

- GONE (Santiago et al., 2020) - historical and current $N_e$

  - average over the most recent generations in the past
- CurrntNe (Santiago et al., 2020) - current $N_e$

k = 0, monogamy was ignored, that is, the number of full siblings, k, of a random individual was set to 0

k = 2, corresponding to full lifetime monogamy,

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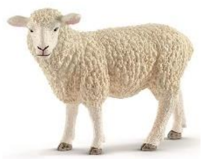
# Results - sheep

|  | **Breed** | **N.** | **NeEstimator** | **GONE** | **CurrentNe k=2** |
|---|---|---|---|---|---|
| CZ | Improved Valachian | 39 | 352 (217-873) | 303 (211-435) | 542 (317-927) |
|  | Sumava sheep | 48 | 52 (37-78) | 73 (58-92) | 98 (78-123) |
|  | Valachian | 72 | 40 (30-55) | 65 (55-77) | 80 (76-104) |
| SK | East Friesian | 44 | ***30 (21-48)*** | 67 ( 53-84) | 52 (43-64) |
|  | Improved Valachian | 71 | **106 (73-177)** | 265 (210-331) | **169 (138-208)** |
|  | Lacaune | 104 | 81 (63-109) | 121 (105-140) | 111 (98-126) |
|  | Valachian | 94 | **34 (29-40)** | 75 (64-85) | 75 (67-84) |
|  | Tsihaja | 70 | 97 (58-233) | 552 (421-725) | 39 (33-45) |



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# Results - goat

|  | **Plemeno** | **N.** | **NeEstimator** | **GONE** | **CurrentNe k=2** |
|---|---|---|---|---|---|
| CZ | White shorthair | 36 | 105 (68-205) | 254 (179-356) | 181 (125-263) |
|  | Brown shorthair | 34 | 46 (31-82) | 127 (93-173) | 90 (67-122) |
|  | Landrase | 20 | 21 (13-29) | 116 (74-179) | 37 (26-52) |
|  | Alpine | 28 | 44 (28-87) | 127 (89-180) | 91 (63-130) |
| SK | White shorthair | 24 | **37 (23-78)** | 118 (79-173) | 74 (51-108) |

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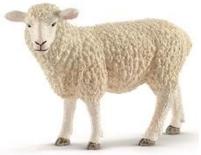
# Results - sheep

| | **Breeds** | **N.** | **NeEstimator** | **GONE** | **CurrentNe k=2** |
|---|---|---|---|---|---|
| SK | Crossbreed | 19 | 13 (4-77) | 57 (41-80) | 28 (20.-38) |
| | Slovak Dairy | 36 | 46 (30-62) | 94 (70-123) | 78 (60-103) |
| | Texel | 5 | Inf. | 138 (45-427) | 182 (27-1231) |



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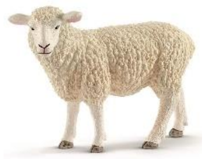
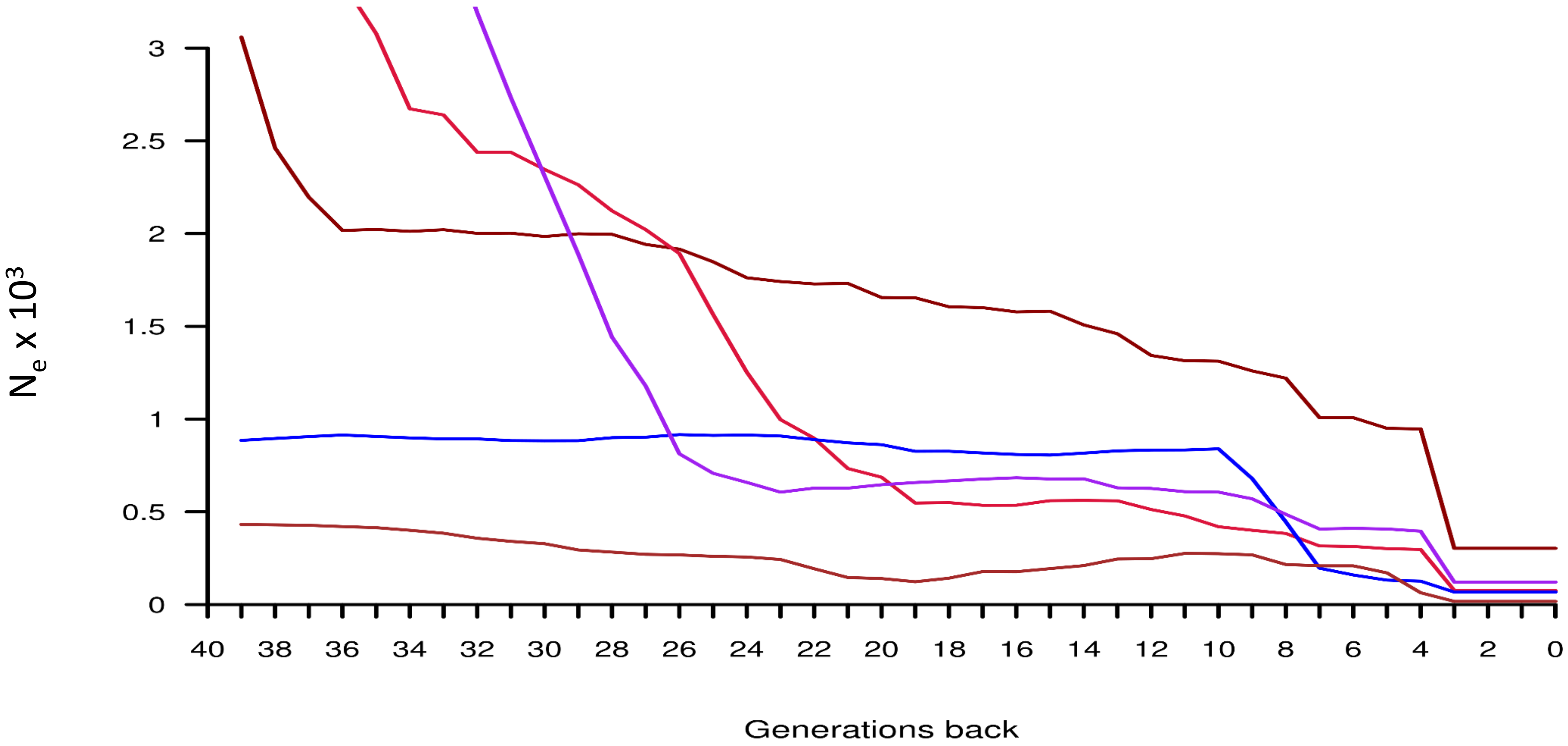
# Results - sheep





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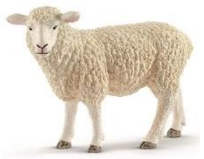
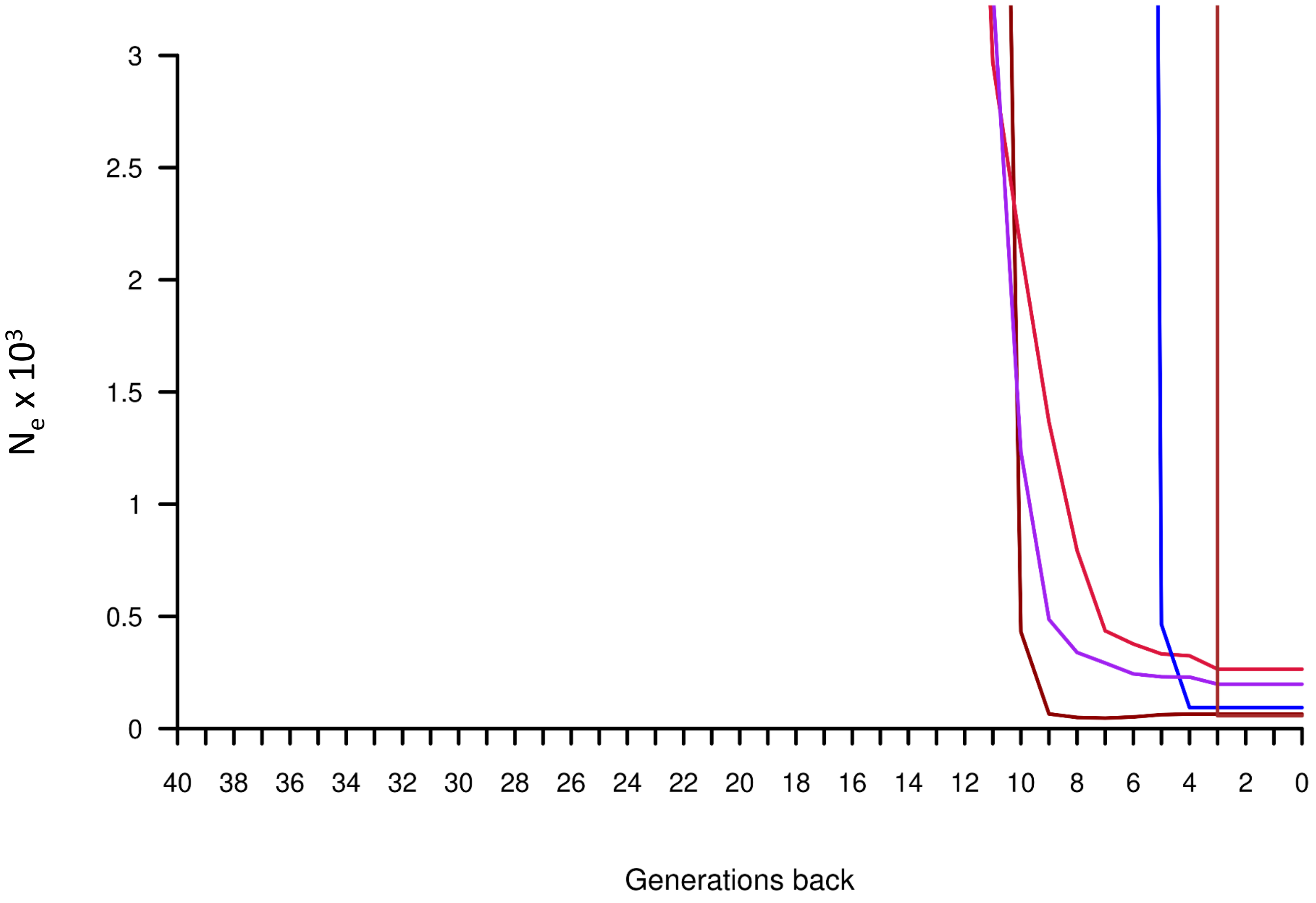
# Results - sheep





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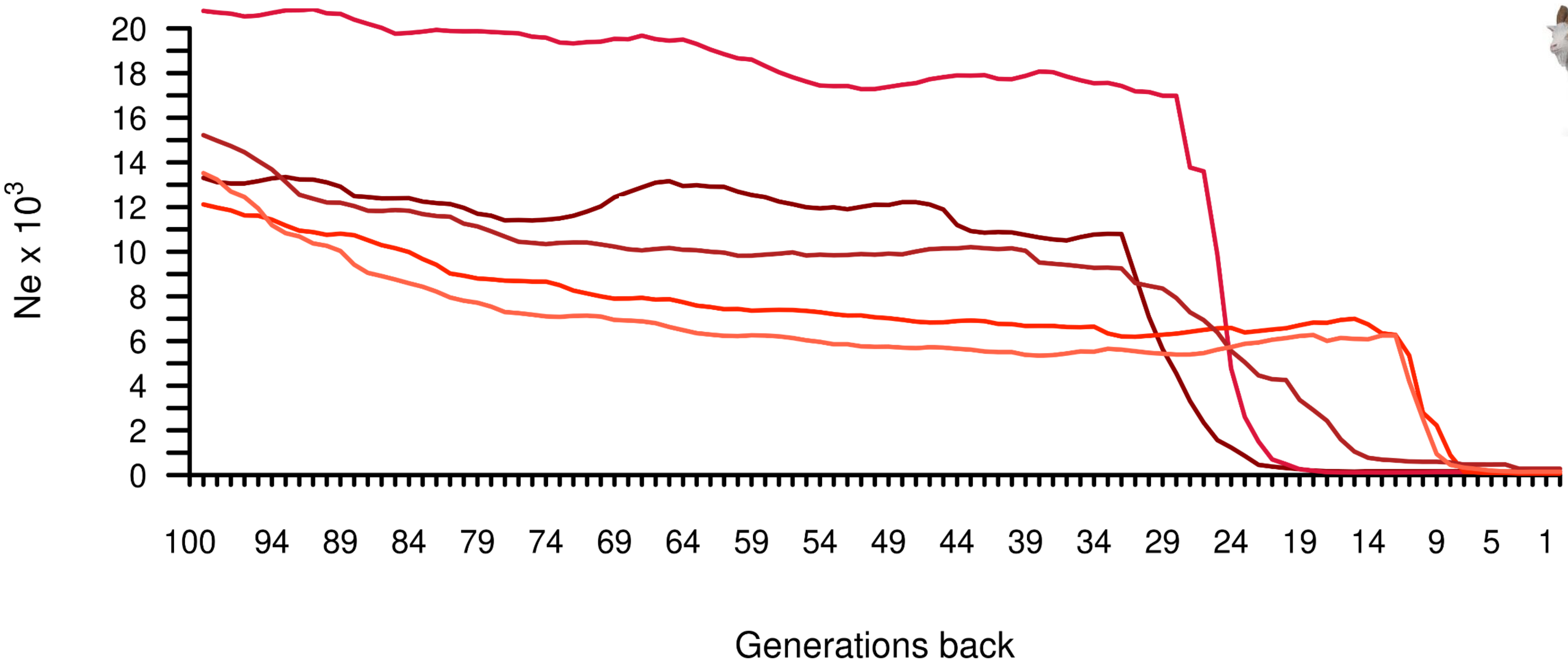
# Results - goat



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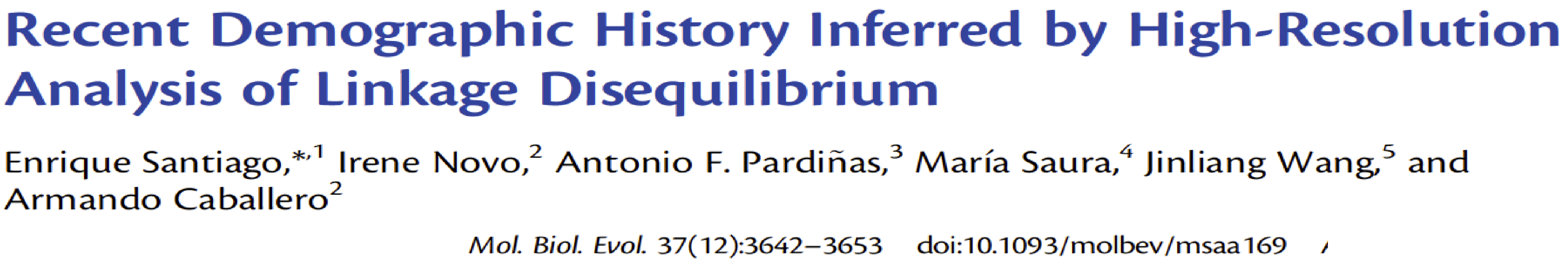
# Conclusion – Case study

**Software GONE**



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# Reference

https://www.nhkladruby.cz/fotogalerie

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# Thank you for your attention!

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