Maximum likelihood inference comparing sequence and allelic markers in a population of variable size: an Importance Sampling approach
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We choose a simulation strategy which consisted of varying the time since the contraction began (based on DIG's method. De Iorio & Griffiths (2004a,b) to a subdivided population framework for various mutation models between gene types. For sequence loci, the results of De Iorio & Griffiths (DIG) represent an improvement in terms of efficiency over those of Bahlo & Griffiths (2000) but this hasn’t been tested on more than a single panmictic population. DIG consider the DNA sequences to be evolving under an Infinitely-many Sites Mutation model (ISM). For allelic loci (microsatellites) evolving under a Step-wise Mutation model (SMM), we use the importance sampling proposal distributions of De Iorio et al. (2005). Here, we used results from Griffiths & Tavaré (1994c) in order to implement the case of a single exponentially contracting population (see box: The demographic model and contrasted the performance of estimation from sequence and allelic markers. This approach gave us an insight into the potential complementarity of the considered genetic markers for improving the precision of the demographic and mutational estimates.

Introduction & Objectives

We have developed software which simulate data in the well known Campa (for allelic data) and the Nexus (for sequence data) formats. These simulations were generated using IBDSim (http://raphaelleblois.free.fr/software) which follows an exact coalescent algorithm. This data was then analysed by the Migraine software (http://kimura.univ-montp1.fr/~rousset/Migraine.htm) for inferring the demographic and mutational parameters (using DIG's method). Note that the current version of Migraine can also handle more complex demographic models than the one presented here such as Isolation by Distance (IBD) based on DIG's method.

We choose a simulation strategy which consisted of varying the time since the contraction began (D = T/2N) keeping the other parameters constant. A total of 10 demographic scenarios were thus used, each of which was repeated 200 times. The initial size of the population was set to 200 000 individuals which progressively diminishes down to 200 individuals. Each sample consists of 100 individuals genotyped at 10 loci.

Software & Simulations

The demographic model: a single exponentially contracting population

The demographic model: a single exponentially contracting population

Results & Conclusions

The bottleneck scenario implemented here:
1° was successfully detected over a wide range of scenarios; 2° was inferred with reasonable precision for intermediate scenarios. The SMM estimates performed better than their ISM counterparts but this can be understood in terms of heterozygosity and the number of alleles/haplotypes present in the simulated data (see box: Differences between models).
3° the time taken in comparison to typical "MCMC" approaches was very short (~4 s for a single repetition); Slightly longer runs improve estimation performance (not shown here).
4° for all scenarios, the LRT's indicate a very good conformity of the likelihood surface generated by Migraine to the true likelihood.

Likelihood ratio tests (LRT)

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References:


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The extreme scenario (ISM, D = 0.025)

Very recent and extreme contractions result in flat profile likelihoods (right) or saddle point like situations (left). Here, the surfaces indicate that the markers have little information on the bottleneck and thus the current population size. This results in very wide confidence intervals for the parameters T and N. Finally large T values are confined with the true values of N_anc resulting also in wide confidence intervals.

Differences between markers

We accounted for the differences in the evolution of the genetic markers as follows: for microsatellites under a SMM, we assumed a mutation rate of 10⁻⁵ while for DNA sequences under an IBD we chose 3x10⁻⁶/sequence. The simulated data had the following number of haplotypes/alleles (N) and expected heterozygosity (H_exp) for the cases presented here:
ISM
D = 1.25: N_anc = 2.6, H_exp = 0.39
D = 0.025: N_anc = 4.4, H_exp = 0.65
D = 1.25: N_anc = 4.4, H_exp = 0.58
D = 0.025: N_anc = 13.4, H_exp = 0.87

Profile likelihood ratio

2*Nanc*µ = 0.204

N_ratio = 0.01

The profiles indicate that the markers have little information on the bottleneck and thus the current population size. This results in very wide confidence intervals for the parameters T and N. Finally large N values are confined with the true values of N_anc resulting also in wide confidence intervals.