Comparison of differents models infering selection from genomic time series data

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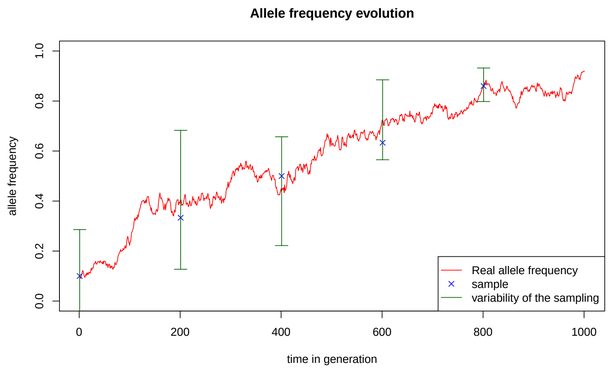
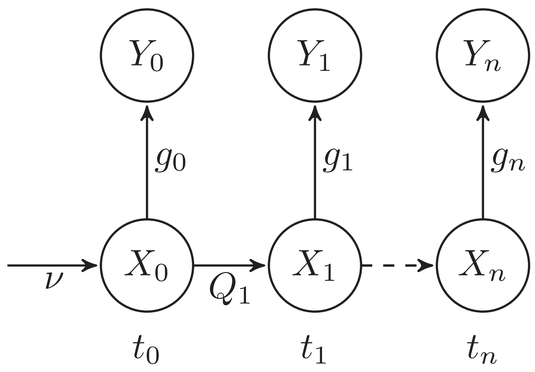
Introduction

Natural or artificial **selection** have a lot of impact on a population genetic pool. When a **beneficial mutation** occurs in a group of individuals, these carrying this new gene are more adapted than the others to their environment and so have a better chance to reproduce and spread this new mutation. Given genetic samples, there exists a lot of **method detecting the genome regions under selection**. These methods use **present data samples**. However, new genotyping techniques give genomic samples through time (From few decades to centuries). This new kind of data needs a new methodology to exploit this information. There already exists few recent methods using time series data to detect selection mainly concerning ancient DNA. The **objective** of my PhD is to design an algorithm detecting loci under selection given **genomic time series**. The purpose of this poster is to show differences between few theoretical models concerning selection detection and inference.

Theoretical framework [1]

- Selection impacts the part of populations carrying the selected allele (AF).
- Only some times are observed
- Each observation has a variability





- Hidden Markov Model takes into account these conditions
- AF is a hidden markov process
- Observations depends only of the current AF
- Efficient Forward / Backward algorithm to get likelihood of data

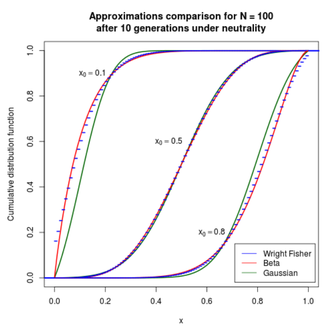
We developped (in python) a generic Likelihood calculator to compare selection detection / estimation under various scenarios and AF transition models.

A reference model : Wright Fisher [2]

- Single Nucleotide Polymorphism (SNP)
- X_t : derived allele frequency at time t
- Random mating : $X_{t+1}|X_t \sim \frac{1}{N}\mathcal{B}(N, f(X_t))$
Genotype	A_1A_1	A_1A_0	A_0A_0
Fitness	$1+s$	$1+sh$	1
- fitness function: $f(x) = \frac{(1+s)x^2+(1+sh)x(1-x)}{(1+s)x^2+2(1+sh)x(1-x)+(1-x)^2}$
- Not numerically tractable when N_e is large

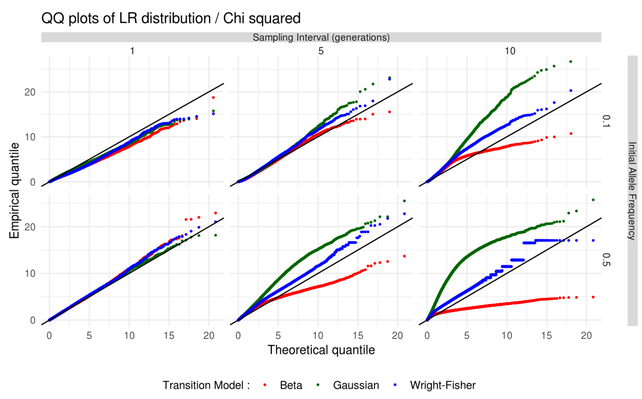
Alternative models : moment fitting

- Choose a parametrised distribution (beta, gaussian) [3, 4, 5]
- Approximate Wright Fisher process moments with a recursion derived from a Taylor expansion. [3, 4, 5]



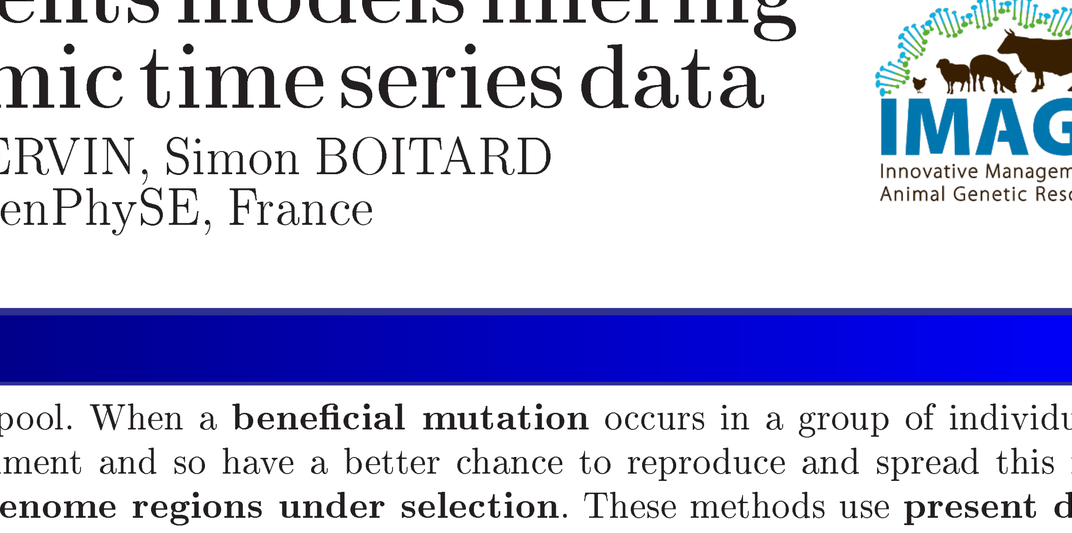
- Fit moments of this distribution with the moment approximation
- Compute likelihood of observations under the choosen model
- Use Likelihood Ratio statistic (LR) to detect selection via the Likelihood Ratio Test (LRT)

Calibration under neutrality

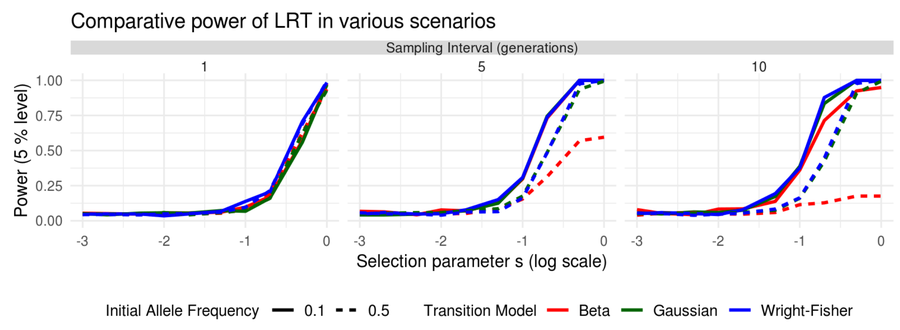


- $LR \sim \chi^2$ only when fixations events are not likely.
- Only empirical null distributions are used to get statistical power

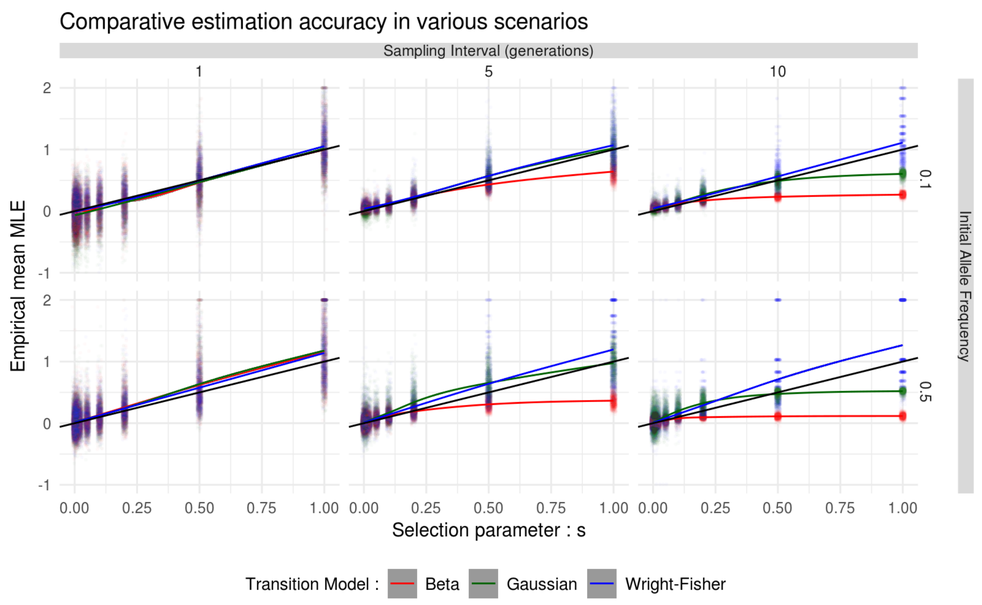
Detecting selection (on simulations)



- Time range has to be long enough to see variations
- Time range has to be short enough that allele is not fixed in population



- Statistical power increase as selection parameter is getting bigger
- Starting from $x_0 = 0.5$, selection is harder to detect if sampling time interval increase



- The Maximum likelihood estimator (MLE) is consistent with WF
- Approximations underestimate high selection parameter when sampling time interval increase.
- The estimator becomes less accurate (higher variance than low selection case) while selection increase

References

[1] Olivier Cappé, *Inference in Hidden Markov Models*, Springer
[2] Warren J. Ewens, *Mathematical Population Genetics*, Springer
[3] Lacerda & Seoighe, Genetics, Vol 198, 1237-1250, November 2014
[4] Terhorst *et al.*, PLOS genetics, 11(4): e1005069
[5] Tataru *et al.* Genetics, Vol 201, 1133-1141, November 2015