Acceleration of important sampling methods for the calculation of likelihood in population genetics
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Abstract

- **Model**: The population evolves under a Wright-Fisher model. Hence, the sample evolves according to the Kingman coalescent.
- **Problem**: The likelihood is the sum over all possible histories (not observed), which is not feasible in practice.
- **Solution**: A class of Monte-Carlo methods, based on Sequential Important Sampling (SIS), allows the likelihood calculation despite the hidden process. The efficiency of these methods was been proven by [1], [2], [3] and [5].

In the IS scheme, the importance sampling distributions propose histories which contribute most to the sum. But these distributions are not efficient for equilibrium population models and the computation time strongly increases for the same accuracy of the likelihood estimation, so that we can not have a correct estimation.

- **Improvement**: For changing population size model, we decide to use Sequential Important Sampling with Resampling (SISR). The idea is to resample, during the backward building of the histories, so that we learn with which the histories proposed by the IS distribution which really contribute most of the sum and so save computation time.

Genetic polymorphism modelling

### Evolution Model

- A sample of $n$ gene copies at a single locus from the population of effective size $N(t)$.
- For any given locus, each individual has exactly one ancestor in the previous generation.
- The ancestral relationships between the individuals of the sample going back in time to the MRCA are described by a gene tree, distributed according to the $n$-coalescent.

### Demographic model

We consider a demographic model, never treated before, where the population effective size varies in the time, note $N(t)$. In particular we work with an Exponentially Contracting Population. If we look backward in time, we have:

$$N(t) = \begin{cases} N_0 \left( \frac{t}{N_{anc}} \right)^D & \text{if } 0 \leq t \leq D \\ N_{anc} & \text{if } t \geq D. \end{cases}$$

### Likelihood of the data

The histories are not observed. The likelihood of the data is obtained by summing over all the possibilities:

$$\text{Prob}(n_{obs}, \theta) = \int_{\mathcal{H}} p_{\theta}(n_{obs}) \prod_{i=1}^{n_{obs}} f(s_{i}) | n_{obs}, s_{1}, \ldots, s_{n_{obs}} \rangle \rangle d\mathcal{H}$$

$$= \int g(n_{obs}, \theta) d\mathcal{H}.$$  

Where:

- $n_{obs}$: observed data,
- $(n_0, \ldots, n_{n_{anc}})$ count vector of lenght $(m+2)$, such as $n_{anc} = n_{obs}$ and $|n_{anc+1}| = |n_{anc}| + 1$,
- $s_0, s_1, s_2, \ldots$: dates of jump (in forward time),
- $g(n_{obs}, \theta, \mathcal{H}) = \mathcal{H}(\mathcal{H} \parallel \mathcal{H})$,
- $\mathcal{H}$: set of compatible histories with the observed data.

### Correction of Importance Sampling distribution by resampling (SISR)

Changing effective population size introduce a strong inhomogeneity in the WF model and the IS distributions become inefficient.

We decide to resample in our collection of simulated histories:

- to prune the bad histories,
- to generate multiple copies of good histories, to generate futur better histories.

Numerical results when comparing SIS and SISR

Our parameter of interest is the vector $(\theta, D, \theta_{anc})$. We try to estimate this parameter by maximum likelihood inference. The likelihood of the data is estimated by the SIS or SISR algorithm.

Comparison of relative Effective Sample Size when the true parameter is $\theta = 0.4$, $D = 0.25$ and $\theta_{anc} = 400$.

<table>
<thead>
<tr>
<th>SIS</th>
<th>SISR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rel. bias $\theta$</td>
<td>0.56</td>
</tr>
<tr>
<td>Rel. bias $D$</td>
<td>-0.0201</td>
</tr>
<tr>
<td>RMSE $\theta$</td>
<td>0.0479</td>
</tr>
<tr>
<td>RMSE $D$</td>
<td>0.711</td>
</tr>
<tr>
<td>With $\theta = 0.4$, $D = 1.25$ and $\theta_{anc} = 400$</td>
<td></td>
</tr>
</tbody>
</table>

Comparison of relative bias and Root Mean Square Error (RMSE), analysis with 100 (left) or 2000 (center and right) genealogies, by SIS and SISR of data sets simulated under the ECP model.

<table>
<thead>
<tr>
<th>SIS</th>
<th>SISR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rel. bias $\theta$</td>
<td>4.92</td>
</tr>
<tr>
<td>Rel. bias $D$</td>
<td>-0.0606</td>
</tr>
<tr>
<td>RMSE $\theta$</td>
<td>0.0438</td>
</tr>
<tr>
<td>RMSE $D$</td>
<td>0.717</td>
</tr>
<tr>
<td>With $\theta = 0.4$, $D = 0.25$ and $\theta_{anc} = 400$</td>
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### References


### Acknowledgments