A roadmap to low-coverage whole genome sequencing (LC-WGS) for population genomics

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A guide on the design of LC-WGS

- Low-coverage whole genome sequencing (LC-WGS) is a cost-effective sequencing strategy for population genomic studies
- It costs as low as $20 per sample for a species with a 1Gbp genome when sequenced at 1x coverage
- It is not yet clear how we can best balance between its inference accuracy and cost
- We use forward genetic simulation to assess the power of different types of population genomic inference under different LC-WGS designs
- We compare LC-WGS with other widely-used sequencing strategies, including RAD-seq and pool-seq

A review on the methods for data analysis

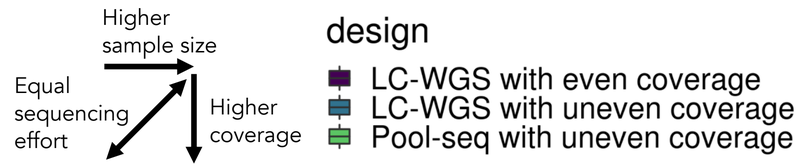
- A second part of this project aims to introduce, compare, and contrast existing methods that have been developed for LC-WGS data; please stay tuned
- We have deposited customizable scripts to implement and streamline many of these methods in our two GitHub repositories: one for data processing and the other for data analysis

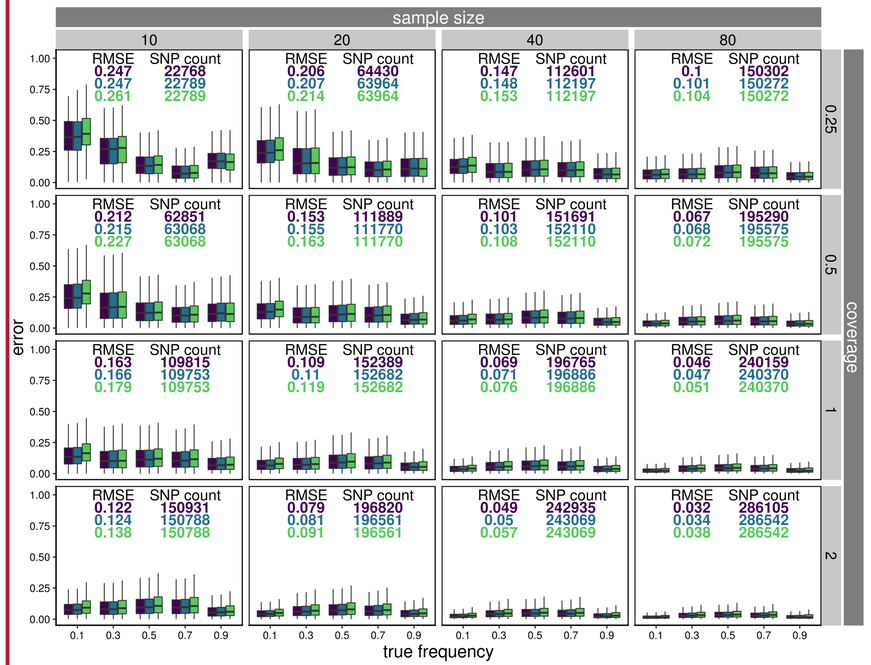
Simulation and analysis pipeline

Forward genetic simulation (SLiM[1])	High-throughput sequencing simulation (ART[2])	LC-WGS data analysis (ANGSD[3])
30Mbp chromosome, **θ**=0.0024, ~600,000 SNPs	150bp paired-end reads, 0.125-8x coverage, 5-160 samples per population	genotype likelihood, SNP calling, allele frequency, F_{ST}, PCA

Allele frequency estimation

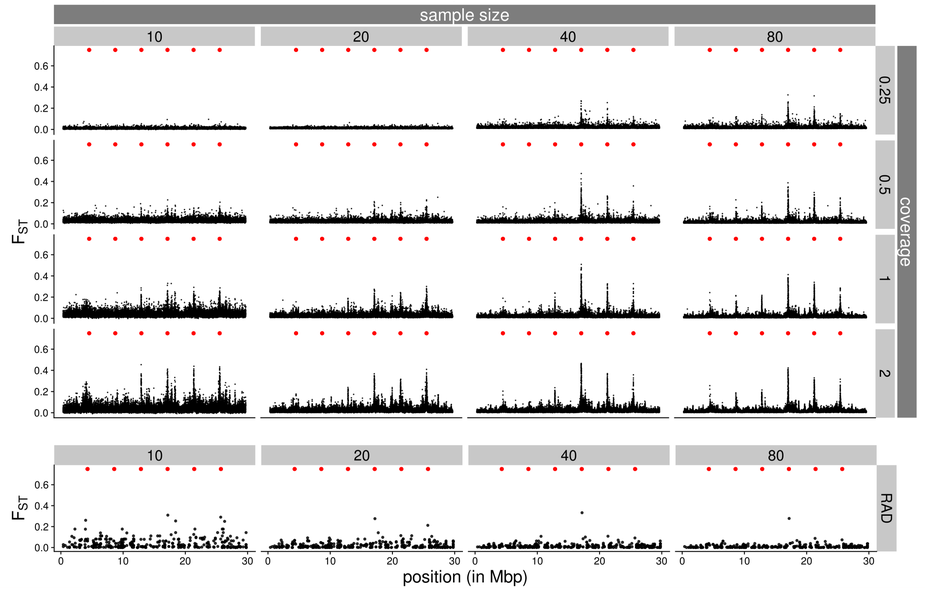
- It is preferable to increase sample size rather than sequencing coverage given the same sequencing effort in total
- LC-WGS can better account for uneven coverage among samples as compared to pool-seq





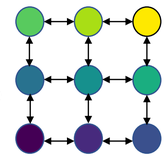
Genome-wide scan for divergent selection

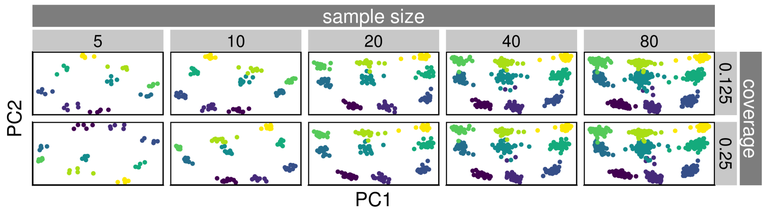
- Divergent selection in high-gene flow systems can create narrow genomic islands of differentiation[4] (F_{ST} peaks) surrounding the sites under selection (positions marked by **red dots**)
- With reasonable coverage and sample size, LC-WGS (**top panel**) can detect many of these signals, but RAD-seq (**bottom panel**) tends to miss them
- Distributing the same amount of sequencing effort across more samples tends to reduce false positive signals



Characterization of spatial population structure

- The true population structure, shown on the right, can be accurately inferred from PCA[3,5] despite extremely low coverage and sample size, since LC-WGS can take advantage of the aggregated genome-wide signal





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