nf-LO: A Scalable, Containerized Workflow for Genome-to-Genome Lift Over

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Abstract

The increasing availability of new genome assemblies often comes with a paucity of associated genomic annotations, limiting the range of studies that can be performed. A common workaround is to lift over annotations from better annotated genomes. However, generating the files required to perform a lift over is computationally and labor intensive and only a limited number are currently publicly available.

Here we present nf-LO (nextflow-LiftOver), a containerized and scalable Nextflow pipeline that enables lift overs within and between any species for which assemblies are available. nf-LO will consequently facilitate data interpretation across a broad range of genomic studies.

Key words: liftover, assembly, Nextflow, workflow.

Significance

Studies such as the vertebrate genomes project (VGP) aim to produce high-quality genome assemblies for tens of thousands of species. However, these new genomes most often come with limited annotations, reducing their utility. One solution is to “lift over” annotations from better annotated genomes. This process is though complex, requiring multiple steps which differ depending on the distance between the species. In this article, we present nf-LO (nextflow-LiftOver), a streamlined, containerized Nextflow workflow that can enable rapid genome lift over between any pair of species and which can be easily implemented on any system. We believe that its ease of implementation, scalability, and flexibility will allow for widespread use and rapid adoption by the scientific community.
LO can directly pull genomes from public repositories, supports parallelized alignment using a range of alignment tools and can be finely tuned to achieve the desired sensitivity, speed of process, and repeatability of analyses.

nf-LO is a workflow to facilitate the generation of genome alignment chain files compatible with the LiftOver utility. It is written in Nextflow, a domain-specific language and workflow manager that allows easy implementation, redistribution, and scalability of complex workflows across every Unix-based operating system; ranging from a desktop machine to cloud computing and HPC clusters. The dependencies are shipped alongside the workflow as docker containers or as an anaconda environment, facilitating the diffusion and adoption of the workflow across different systems.

The software accepts any two input genomes in fasta format, or alternatively can download a resource by providing a web address, an iGenome identifier or an NCBI GenBank or RefSeq accession. The workflow is shown in figure 1, and in brief consists of three core steps, and one optional one: 1) chunking the two genomes, 2) pairwise alignment of the blocks, 3) generating the chain-net file that can be used to perform the lift over and, if a bed/gff/vcf/bam/maf file is provided, 4) performing the lift over from source to target. The chunking approach dramatically reduces the runtime of the analysis by parallelizing the alignments.

The alignment phase can be performed in different ways, depending on the type and sensitivity required by the user. For same-species alignments, we provide native support for both

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**Fig. 1.**—Scheme of the workflow of nf-LO with the chunking (step 1, in green), alignment (step 2, in blue), generation of the liftover files (step 3, in red), and optionally lifting of the variants to the target genome (step 4, in purple).
blat (Kent 2002), the aligner of choice for same species lift over files from the UCSC genome browser, and GSAAlign (Lin and Hsu 2020), a new, high speed same-species alignment software. For performing different-species lift overs, nf-LO also incorporates lastz (Harris 2007), used by the UCSC genome browser to generate between species LiftOver files, and minimap2 (Li 2018), one of the fastest genome-to-genome aligners. All these aligners are integrated within the workflow, keeping unchanged the UCSC backbone for downstream stages (UCSC 2018). We provide canned configurations for each aligner based on how distant the two genomes are (e.g., near or far), with the possibility to provide sets of custom parameters to achieve the desired balance between speed and sensitivity (supplementary table 1, Supplementary Material online). nf-LO achieves similar lift over coverage as LiftOver files from UCSC with appropriate tuning of the parameters (supplementary table 2, Supplementary Material online).

The third stage processes the alignments analogously to the UCSC processing pipeline, obtaining the chain-net files to perform the actual lift over. Finally, the fourth step supports both the standard bed format with the LiftOver software, or several additional formats using CrossMap (Zhao et al. 2014), including popular formats such as VCF, BAM, and GFF. Optionally, the workflow can collect metrics on the lifted annotation when provided, as well as take advantage of mafTools (Earl et al. 2014) to report metrics for the chain file generated by the workflow. These metrics are then provided in HTML format to facilitate the interpretation and collection across multiple runs.

In conclusion, we provide a transposition of the UCSC lift over pipeline within the Nextflow language, together with the necessary containers to run the analyses, allowing an easy, streamlined implementation in any Unix-based system. We believe that this workflow will be of use across genomics studies, facilitating research work and enabling data interpretation.

Supplementary Material
Supplementary data are available at Genome Biology and Evolution online.

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Author Contributions
A.T. and J.P. conceived the study. A.T. developed the software. A.T. and J.P. tested the code. A.T. and J.P. contributed to data interpretation and drafted the manuscript. All authors reviewed and approved the final manuscript.

Data Availability
The code described in the article is publicly available on GitHub at the repository https://github.com/evotools/nf-LO, last accessed August 18, 2021. The documentation for the software can be accessed in the wiki page of the website (https://nf-lo.readthedocs.io, last accessed August 18, 2021).

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