SAMURAI: Shallow **A**nalysis of Copy nu**M**ber alterations **U**sing a **R**eproducible **A**nd **I**ntegrated bioinformatics pipeline

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Abstract

Shallow whole-genome sequencing (sWGS) offers a cost-effective approach to detect copy number alterations (CNAs). However, there remains a gap for a standardized workflow specifically designed for sWGS analysis. To address this need, in this work we present SAMURAI a bioinformatics pipeline specifically designed for analyzing CNAs from sWGS data in a standardized and reproducible manner.
SAMURAI is built using established community standards, ensuring portability, scalability, and reproducibility. The pipeline features a modular design with independent blocks for data pre-processing, copy number analysis, and customized reporting. Users can select workflows tailored for either solid or liquid biopsy analysis (e.g., circulating tumor DNA), with specific tools integrated for each sample type. The final report generated by SAMURAI provides detailed results to facilitate data interpretation and potential downstream analyses.To demonstrate its robustness, SAMURAI was validated using simulated and real-world datasets. The pipeline achieved high concordance with ground truth data and maintained consistent performance across various scenarios.
By promoting standardization and offering a versatile workflow, SAMURAI empowers researchers in diverse environments to reliably analyze CNAs from sWGS data. This, in turn, holds promise for advancements in precision medicine.

Keywords: bioinformatics-pipeline, nextflow-pipeline, shallow whole genome sequencing, copy number alterations

Introduction

DNA copy number alterations (CNAs) are defined as gains or losses of DNA segments (at least 50 bp long) [1]. They are distinct from copy number variations (CNVs) that are smaller in length and often inherited [2].

CNAs and somatically acquired CNAs (SCNAs) can contribute to different types of diseases, such as schizophrenia, Crohn's disease, developmental diseases and many others [3]. In addition, CNAs have very important roles in cancer, which are frequently characterized by genomic instability [4–6].

Recently, more insights on CNAs and SCNAs have been made possible through the use of next generation sequencing (NGS) technologies. In particular, shallow whole genome sequencing (sWGS), that is sequencing of the whole genome at low depth (from 1X to as low as 0.1X), provided to be a viable and cost-effective solution towards the investigation of CNAs in cancer and other pathologies [4,7–9]. Additionally, sWGS also proved effective in the identification of CNAs in biological fluids [5,10,11], such as routine noninvasive prenatal testing (NIPT) [12] or as a potential approach to monitor cancer patients or evaluate therapeutic options [5,13].

Over the course of the years, the bioinformatics community has developed several approaches for the analysis of CNAs with sWGS data, such as QDNAseq [7], WisecondorX [9], ichorCNA [10,14] and others [15,16] on both formalin-fixed paraffin-embedded (FFPE) tumor tissues or bodily fluids. These are stand-alone tools, which are often integrated into custom bioinformatics pipelines, which are tailored for specific use-cases. This is a significant challenge for standardization and reproducibility of the results produced with these pipelines.

To tackle this problem, standards such as the workflow description language (WDL) [17] or the common workflow language (CWL) [18] along with workflow managers such as Snakemake [19] and Nextflow [20] have been developed. In particular, the Nextflow-derived nf-core [21–23] offers a vast collection of bioinformatics pipelines, but at the time of writing no specific workflow suited for the analysis of sWGS data exists. To address this need, we have developed the first nf-core based pipeline to process sWGS data, SAMURAI (Shallow Analysis of copy nuMber alterations Using a Reproducible And Integrated bioinformatics pipeline). SAMURAI integrates different methods for preprocessing data, performing CNA analysis, along with optional post-processing steps, leveraging the nf-core standards and vast array of pre-made analysis modules. SAMURAI is freely downloadable at https://github.com/DIncalciLab/samurai and distributed under a free and open source (FOSS) license (MIT).

Materials and Methods

Implementation

SAMURAI has been implemented by using Nextflow workflow management system [20] and adhering to the existing nf-core guidelines for developers [21–23].

Analysis data sets

To develop and test the functionality of SAMURAI, we used three different datasets:

- A diluted data set from a simulated sample published by Smolander and coworkers [16] (hereafter called Data set S)
- A set of 218 sWGS samples from 205 Stage I ovarian cancer [4], EGA ID EGAS00001004961 (hereafter called Data set T)
- A set of 12 plasma samples withdrawn at time of diagnosis from 12 ovarian cancer patients part of a larger and previously published cohort [5], EGA ID EGAS00001004670 (hereafter called Data set P)

Simulated data downsampling

To simulate real-world coverage scenarios, data set S was downsampled with Picard DownSampleSam [24] to simulate different coverages (0.1X, 0.3X, 0.5X, and 0.7X).

For those analysis methods which relied on a panel of normals, we created 30 simulated control samples by downsampling normal sample SM-74-NEG from GATK test data (https://42basepairs.com/browse/s3/gatk-test-data/cnv/somatic) at identical coverages (*Supplementary Table S2)* using SAMtools [25], Sambamba [26] and Bedtools [27]. Script used for download data and downsample is available at https://github.com/DIncalciLab/SAMURAI_paper_scripts.

Benchmarking of copy number calls with simulated data

To compare results from SAMURAI to the ground truth provided by Smolander et al. [16] for their simulated sample, the genomic coordinates from the ground truth were lifted over from hg19 to the hg38 assembly using https://genebe.net/tools/liftover. The R package CNVMetrics [28,29] was used to compute the overlap (Szymkiewicz-Simpson coefficient) similarity score between inferred and ground truth copy numbers. We made the comparisons for results from ASCAT.sc, ichorCNA and WisecondorX.

Benchmarking of real-world data sets

Data set T was analyzed with SAMURAI starting from pre-aligned files (BAM; hg38 genome), using the solid biopsy pipeline. ASCAT.sc was run to obtain absolute copy number values, using a bin size of 30 Kbp. After copy number calling, overlap (Szymkiewicz-Simpson coefficient) similarity score was computed to evaluate the concordance between the inferred and reference copy number segments. Additionally, proportions of gains and losses were computed on 30 kbp bins on chromosome 8 for high grade serous (HGSOC) histotype with the function cnFreq() of the GenVizR package [30] and the Pearson correlation coefficient was computed between the two proportions.
Analysis of dataset P was carried out with SAMURAI using the liquid biopsy pipeline, ichorCNA as copy number caller and a 500 Kbp bin size. Prior to copy number calling, library target size selection was performed with the appropriate option in SAMURAI to increase sensitivity and specificity [31]. The initial normal contamination states of ichorCNA were set ranging from 0.9 to 0.999 instead of the default to increase sensitivity. GISTIC was used to identify recurrent CNA regions in specified sample groups, corresponding to the five major histotypes present in the data set (high grade serous, HGSOC; low grade serous, LGSOC; endometrioid, EC; clear cell, OCCC; mucinous, MOC).
A set of 11 healthy controls from Paracchini *et al*. was used as a panel of normals (PoN). Tumor fraction estimates from SAMURAI were compared to those from the original data set. To evaluate the concordance between the two analyses, we computed the Pearson correlation coefficient between SAMURAI and the fractions from the original work. Correlation plots for both analyses were obtained from the ggpubr R package [32].

Results

Workflow Architecture

SAMURAI is a reproducible pipeline for detecting copy number variations in low-pass or ultra low-pass whole genome sequencing data. The pipeline incorporates several tools from the bioinformatics community, containerized (either Docker [33] or Singularity / Apptainer [34]) to ensure the maximum reproducibility, and is divided into three main blocks : pre-processing, copy number detection, and post-processing (Figure 1).

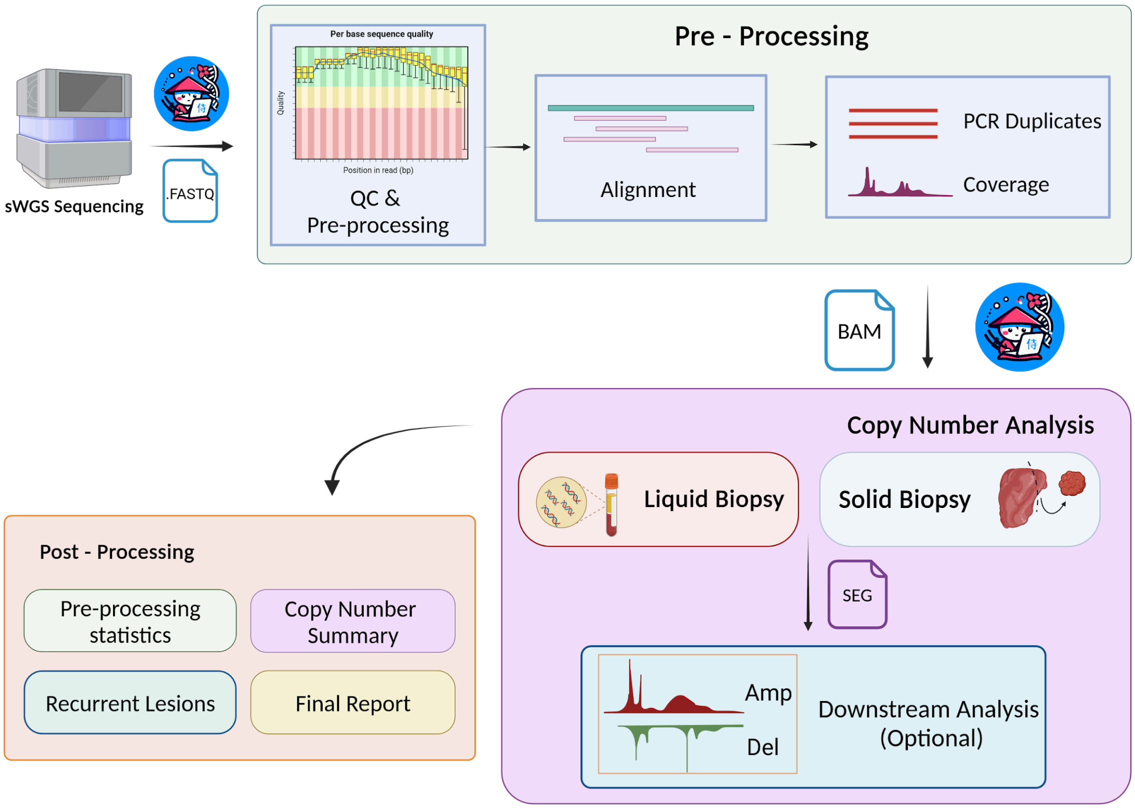


Figure 1. General workflow of SAMURAI.

Pre - processing

The pre-processing phase of SAMURAI includes a first step of quality control on the input data, followed by alignment to a reference genome. The entire pre-processing phase can be skipped when pre-aligned data is supplied.

The list of software included in SAMURAI's pre-processing phase is reported in *Table 1.*

Tool	Subworkflow	Ref.
FastQC	QC & Adapters Removal	[35]
fastp		[36,37]
BWA INDEX	Index Reference Genome	[38,39]
BWA-MEM	Alignment & Mark PCR duplicates	[38]
BWA-MEM2		[39]
DragMap		[40]

SNAP aligner		[41]
Samtools		[25]
Picard		[24]

Table 1. Detailed list of software included in SAMURAI pre-processing block.

Quality trimming and adapter sequence removal (optional)

Starting with raw sequence data, SAMURAI performs quality control checks with FastQC [35]. If required, adapter sequences removal and quality trimming can be performed with fastp [36]. Additionally, SAMURAI can process unique molecular identifiers (UMIs) if the library design includes them.

Alignment to reference genome

In case raw sequence data are supplied, SAMURAI will perform alignment against a reference genome with two different algorithms (BWA-MEM and BWA-MEM2). Reference genomes can be user-supplied, taken from Illumina’s iGenomes, or using the refgenie reference manager [42]. The pipeline will also create an aligner index in case it is missing. The alignment step is also coupled with removal of PCR duplicates.

Copy Number Analysis

The core of the SAMURAI pipeline is copy number calling. It offers two types of analysis workflow depending on the nature of the samples:one catering to the processing of tissues (“solid biopsy”) and another for the identification of aberrant CNAs in other biological fluids (“liquid biopsy”). This design allows users to specify the workflow based on their specific needs. The main tools used by both workflows are indicated in Table 2.

Solid Biopsy workflow		
Tool	**Description**	**Ref.**
QDNAseq	Generates copy number segments, correcting for sequence bias (GC content, mappability)	[7]
ASCAT.sc	Calls absolute copy numbers. It also estimates	[43]

	tumor purity and sample ploidy.	
CINSignatureQuantification	Quantifies chromosomal instability signatures based on absolute copy number values.	[8]
Liquid Biopsy workflow		
Tool	**Description**	**Ref.**
Samtools	Enhances ctDNA copy number calling performance by performing size selection on ctDNA.	[25,31]
ichorCNA	Calls absolute copy number values in ctDNA samples and estimates tumor fraction.	[10]
WisecondorX	Identifies regions with altered copy number and calculates a copy number profile abnormality (CPA) score for each sample.	[9,11]

Table 2. Summary of tools included in SAMURAI copy number analysis block.

The different steps are interconnected through the use of custom scripts provided with the pipeline to harmonize and integrate analysis outputs.

Solid Biopsy workflow

The solid biopsy workflow (*Figure 2*) processes data by binning, correcting for sequence biases such as GC content and mappability, and then segments of identical copy number. Depending on the needs of the user, two different tools can be used, either to generate log2 ratios of observed vs expected reads (QDNAseq) [7] or to call absolute copy numbers (ASCAT.sc) [43].

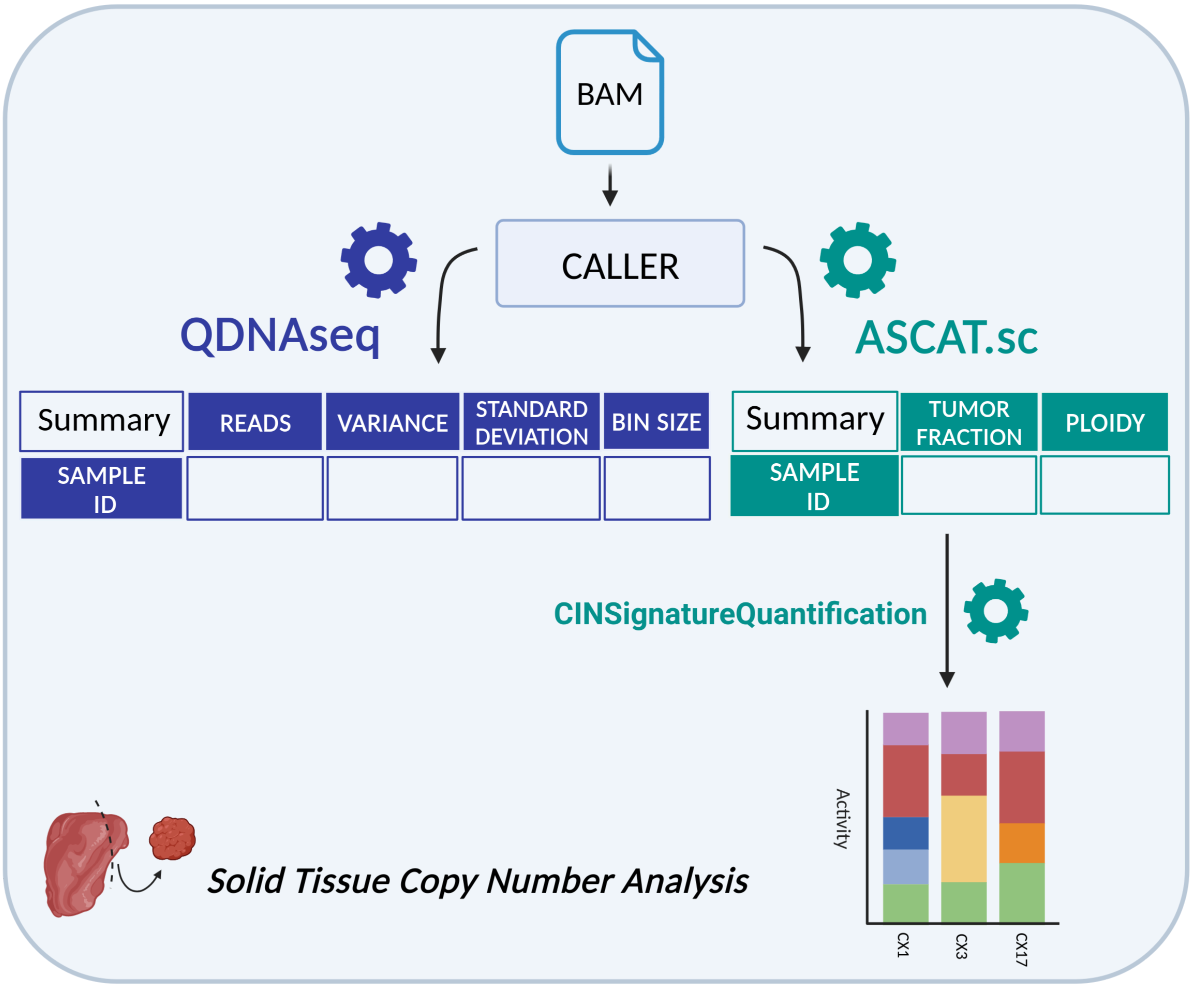


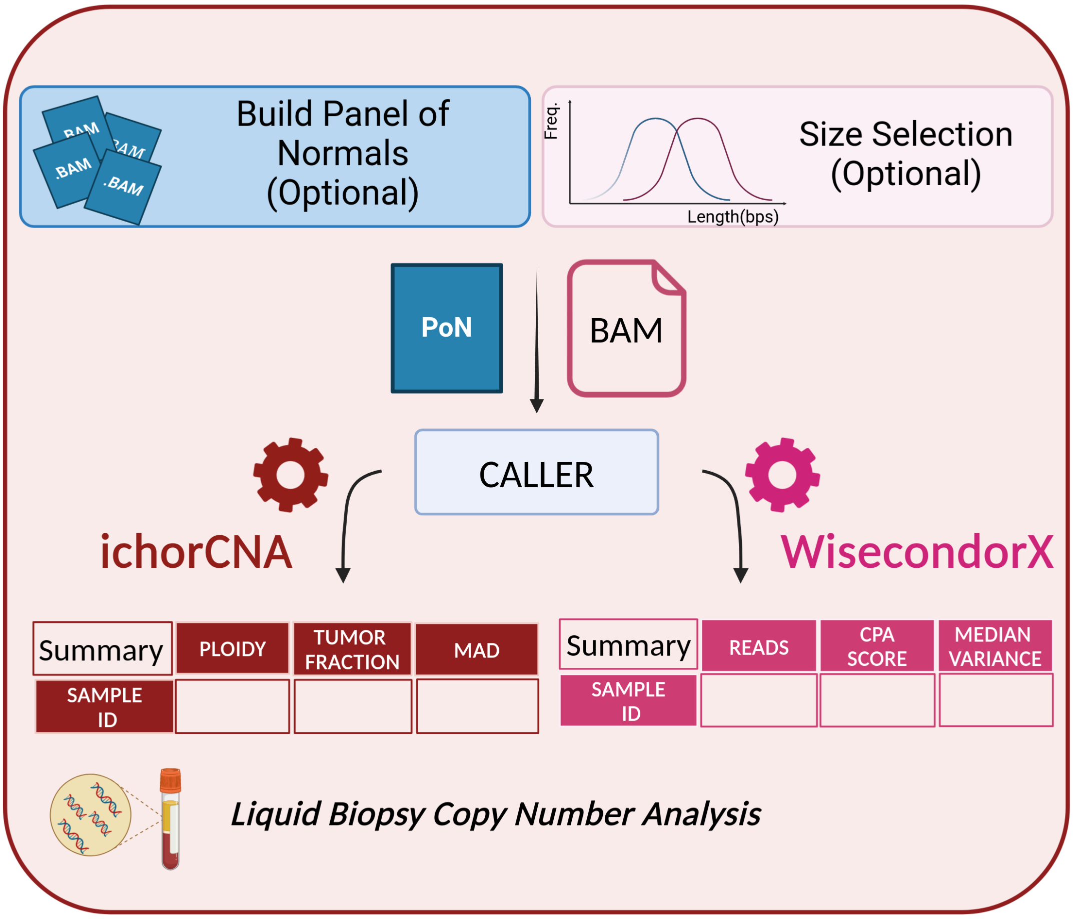
Figure 2. Schema of solid biopsy analysis workflow, including the types of data collected for the final report.

QDNAseq does not produce absolute CNA calls itself, but its results can be used as input for downstream analyses, both within SAMURAI and with external tools like shallowHRD [44], ACE [45] or RASCAL [15]. ASCAT.sc, an evolution of the ASCAT algorithm originally developed for microarrays, is used to estimate absolute copy number values from the supplied aligned data, and, in case of tumor samples, also estimate their purity and ploidy.

Both tools generate plots showing the state of genome-wide copy number profiles for each analyzed sample, which are then included in SAMURAI's final output files (an example report is available as Supplementary File 1).

Liquid Biopsy workflow

In addition to the analysis of solid samples, SAMURAI features a complementary workflow specifically designed for analyzing CNAs in cell-free DNA isolated from bodily fluids.
This workflow, summarized in *Figure 3*, uses specialized tools designed for this purpose: ichorCNA [14] and WisecondorX [9].


.BAM
.BAM
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Build Panel of Normals (Optional)
Freq.
Length(bps)
Size Selection (Optional)
PoN
BAM
CALLER
ichorCNA
WisecondorX
Liquid Biopsy Copy Number Analysis

Summary	PLOIDY	TUMOR FRACTION	MAD
SAMPLE ID			

Summary	READS	CPA SCORE	MEDIAN VARIANCE
SAMPLE ID			

Figure 3. Schema of liquid biopsy analysis workflow, with the output tables that are included in the final report.

Leveraging the knowledge that ctDNA fragments are typically shorter than healthy cfDNA [31], SAMURAI offers an optional size selection subworkflow. This subworkflow preferentially enriches for ctDNA fragments by selecting those within a specific size range, typically between 90 and 150 base pairs, potentially improving the accuracy of CNA detection in ctDNA analysis.
Similar to the solid biopsy analysis, depending on the needs of the user, two tools can be used to call absolute copy numbers (ichorCNA [10]) or to identify regions with altered copy numbers (WisecondorX [9]).

Both tools rely on a panel of normals (PoN) for normalization and to improve accuracy of CNA calls. SAMURAI provides users with the flexibility to either construct the PoN internally during the analysis, or incorporate a previously-built panel.
ichorCNA [10] estimates absolute copy number and, in case of tumor samples, estimates purity (expressed as tumor fraction, TF) and ploidy. WisecondorX [9] identifies regions of gains and losses and computes a copy number abnormality score (CPA) [11], an indication of the overall genomic instability of the sample.

In a similar fashion to the solid biopsy workflow, both tools included in the liquid biopsy analysis generate plots depicting the state of these copy number profiles for each analyzed sample. These plots are then included in SAMURAI's final output (an example of the liquid biopsy analysis is provided as Supplementary File 2).

Downstream Analysis of Copy Number Alterations

Chromosomal instability (CIN) signature extraction

To understand chromosomal instability (CIN) patterns, SAMURAI leverages a framework by Drews et al. [46] that analyzes absolute copy number profiles and identifies 17 distinct pan-cancer CIN signatures. By incorporating this framework, SAMURAI presents a matrix of normalized signature activities alongside a bar plot summarizing these activities, allowing users to easily interpret the CIN landscape within the report.

Identification of recurrent copy number alterations

SAMURAI also aids in identifying frequently recurring copy number changes (SCNAs) in cancer samples. It integrates GISTIC 2.0 [47] software to pinpoint these recurrent regions across multiple samples and localize any target genes within them. SAMURAI then transforms GISTIC's output into a user-friendly format, providing tables and plots that clearly represent these identified SCNAs and associated genes.

Post-Processing

To aggregate results from the different tools comprehensively, SAMURAI incorporates outputs from each phase into a final report generated with MultiQC [48]. This report includes information on quality control, providing an overview about sequencing run and pre-processing, aiding also in identifying potential problematic samples. SAMURAI also provides users with custom tables summarizing the copy number analysis section, which may include tumor fraction, ploidy values for each sample, or measures of copy number instability such as CPA from WisecondorX analysis. Additionally, SAMURAI also includes specific plots, such as recurrent alterations plots or signature activities plots, to assist in the interpretation of the results.

Alongside the final report, the pipeline stores outputs and versions of different software tools in the output folder chosen by the user.

Benchmarking SAMURAI

After developing SAMURAI, our aim was to evaluate the pipeline's performance both in terms of the entire workflow and from a biological perspective in order to verify reliably and reproducibly. To achieve this, we conducted tests using both simulated data (data set S; Materials and Methods) and two real data sets, a previously published sWGS analysis of biopsies withdrawn from patients with early-stage epithelial ovarian cancer (dataset T) and a data set with copy number data obtained from plasma samples withdrawn from patients with late-stage high grade serous ovarian cancer (dataset P).

Case Study 1 : Evaluation of SAMURAI on simulated data

We used a synthetic data set (data set S; see Materials and Methods) to test both solid biopsy and liquid biopsy sub-workflows within SAMURAI, setting different bin sizes to simulate real-world analysis scenarios (50 kbp and 500 kbp, respectively). All the tools used in the copy number analysis were run with default parameters.

We compared the inferred copy-number alterations from ASCAT.sc, ichorCNA, and WisecondorX with the ground truth CNAs for the original A1 sample using the Szymkiewicz-Simpson metric (overlap coefficient; Materials and Methods). All tools achieved a high degree of similarity, with an overlap coefficient greater than 0.9 for gains and 0.8 for losses (*Table 3*), indicating strong agreement between the inferred CNAs obtained using different tools in SAMURAI and the true CNAs.

Caller	**Gain**	**Loss**
ASCAT.sc	0.99	0.99
ichorCNA	0.91	0.98
WisecondorX	0.99	0.82

Table 3. Szymkiewicz-Simpson coefficients for gains and losses between original sample A1 and the ground truth sample.

To further evaluate real-world scenarios, we diluted the original samples at different coverages (*Supplementary Table S1*) and we evaluated the consistency of copy number calling across the random downsampling. Similar performance was observed for *in silico* diluted samples (*Supplementary Figure S1*). The overlap coefficient remained high for gains (> 0.8) and losses (> 0.7) in the diluted samples compared with the ground truth.

Case Study 2 : Solid Biopsy Analysis on Ovarian Cancer

In order to fully evaluate SAMURAI's capability to extract biologically meaningful results, we ran the pipeline over a previously published data set of 218 biopsies withdrawn from 204 patients with early-stage epithelial ovarian cancer (EOC; [4]). This data set contains samples from the five major histotypes of EOC (high grade serous, HGSOC; low grade serous, LGSOC; endometrioid, EC; clear cell, OCCC; mucinous, MOC) and is ideal for evaluating the pipeline as the various histotypes exhibit distinct copy number patterns.

After estimating absolute copy number values, we evaluated the concordance between the previously published result and SAMURAI output by computing the overlap coefficient in a similar fashion as the simulated data (Materials and Methods). The median values for all histotypes were all above 0.8, indicating a large agreement with the previously published results (Table 4). Similar results were observed in the majority of samples. SAMURAI correctly did not call alterations in samples without any gains or losses, such as sample 105 (EC histotype) and sample 156 (LGSOC histotype; *Supplementary Table S3*). Gains and losses included previously reported frequent alterations, such as copy number gains in HGSOC affecting the q arm of chromosome 8, as shown in Figure 4. Correlation between previously published data and the results from SAMURAI in this representative case was high (Pearson's correlation coefficient 0.99; Figure 4 and *Supplementary Figure S2*).

Histotype	Median Coeff. GAINS	Median Coeff. Losses
HGSOC	0.94	0.95
LGSOC	0.85	0.94
EC	0.92	0.95
MOC	0.93	0.92
OCCC	0.88	0.94

***Table 4**.* Median values of pairwise overlap coefficient for each sample, divided by histotype. The coefficient was computed for both gains and losses.

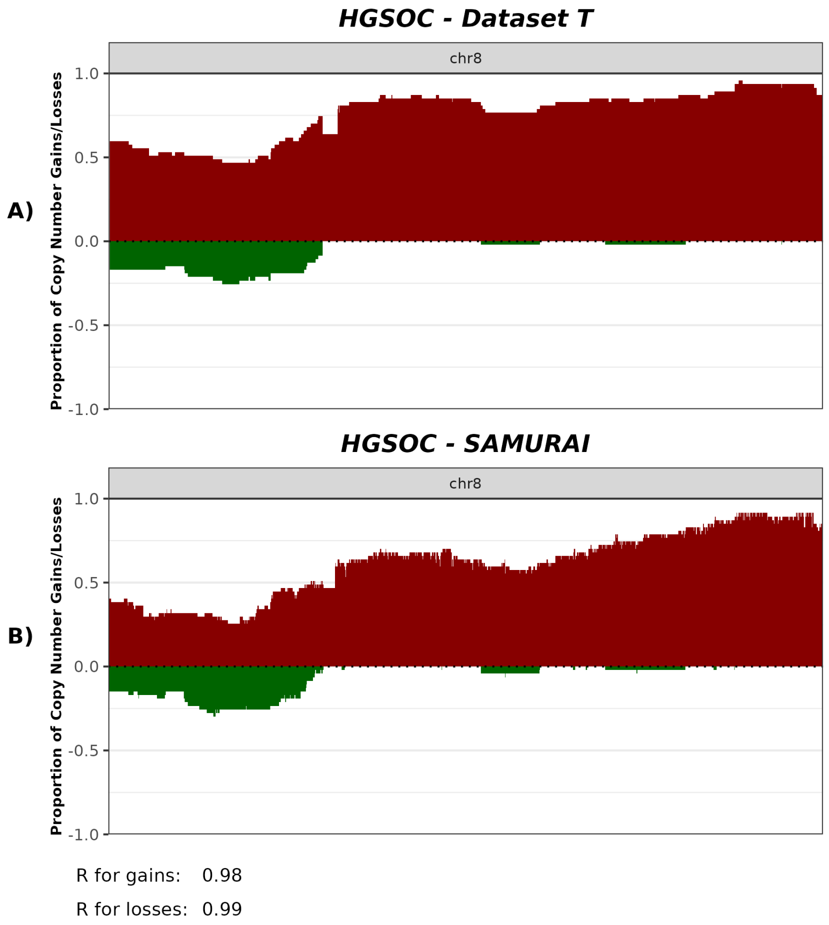

***Figure 4**.* Proportions of gains and losses on chromosome 8 of HGSOC samples. **A)** Proportions of gains and losses from the results of the original work. **B)** Proportion of gains and losses in SAMURAI. On the Y-axis are represented proportions of alteration; the X-axis represent the genomic coordinates on chromosome 8. R: Pearson’s correlation coefficient.

Case Study 3: Liquid Biopsy Analysis on Ovarian Cancer

In order to test SAMURAI's liquid biopsy workflow on real-world data, we retrieved sequencing data from 12 plasma samples from 12 distinct late-stage HGSOC patients (withdrawn at time of diagnosis), part of a previously published study (Dataset P), and then ran SAMURAI with ichorCNA to estimate CNAs and tumor fraction (see Materials and Methods). After estimating absolute copy number values, we ran GISTIC from SAMURAI, performing both focal and arm-level analyses, to identify recurrent regions of copy number alterations in each histotype (Materials and Methods).
The estimates of tumor fraction made by SAMURAI were largely comparable (Table 4) with the previous study. Pearson's correlation analysis with the previously published results yielded a high level of correlation (0.95; *Supplementary Figure S3*) . Analysis of recurrent alterations made by SAMURAI identified two significant regions with copy number gains (3q26.2 and 8q24.21) previously described with HGSOC.

Sample	**TF SAMURAI**	**TF Dataset P**
21531-PL1	12.91%	10.84%
21553-PL1	4.19%	5.75%
21557-PL1	8.45%	7.79%
21564-PL1	9.61%	6.63%
21566-PL1	13.58%	13.66%
21569-PL1	18.54%	18.6%
21572-PL1	9.22%	7.7%
21580-PL1	14.51%	14.76%
21611-PL1	13.32%	12.86%
21614-PL1	4.44%	5.81%
21624-PL1	10.86%	10.97%
21627-PL1	6.01%	6.13%

Table 5. ichorCNA tumor fraction (TF) estimates from SAMURAI compared to the original values from Dataset P.

Discussion

We have developed SAMURAI, a standardized and reproducible pipeline for the analysis of low pass whole-genome sequencing data. The field of shallow whole-genome sequencing has shown many useful practical applications, like non-invasive prenatal testing (NIPT) [12], cancer diagnostics applied to different sample matrices, such as liquid biopsies [49–51] or formalin-fixed, paraffin-embedded (FFPE) [52] samples with diagnostic and/or prognostic purposes. However, although established approaches exist for whole-genome and whole-exome sequencing [47], most of the analysis methods employed for sWGS rely on “ad hoc” approaches specific for one particular application, or even for a specific research group’s needs. Given the potential benefit of sWGS-based approaches in the clinic [14,53,54], it is imperative that analysis tools are built to be both reliable and reproducible. Thus, SAMURAI aims to fill this gap, by taking advantage of the pre-existing nf-core [21–23] resource to build a robust pipeline. SAMURAI prioritizes flexibility by incorporating optional subworkflows tailored to specific needs of the users. Moreover, some of these workflows can be particularly relevant for cancer analysis, such as size selection for ctDNA fragments enrichment, improving the accuracy of CNAs detection, or the identification of recurrent CNAs across a cohort of patients and identifying potential target genes among them.

By employing widely used bioinformatics tools for copy number analysis and container technologies for ensuring modular and immutable software in each step, SAMURAI adheres to established bioinformatics standards that maintain a reliable and reproducible analysis environment while offering customizable workflows.

We evaluated SAMURAI's robustness using simulated data (Dataset S). The analysis yielded very high copy number concordance (> 80%) compared to the ground truth, indicating strong agreement with actual alterations. We further tested SAMURAI's performance under various simulated dilution levels to reflect real-world scenarios, showing an overall consistent, robust and reliable performance.

While simulated data provides a controlled environment for testing, it is of course clear that simulations cannot fully represent real-world data. For this reason we also tested SAMURAI with two additional datasets: a large cohort of tumor tissue biopsies [4] and a selection of circulating free DNA (cfDNA) extracted from plasma of ovarian cancer patients [5].

With regards to dataset P, a collection of copy number data from early-stage epithelial ovarian cancer [4] we observed high concordance in the results with the previously published data. A small number of samples were unable to be analyzed properly and reported a purity of 1 and a ploidy of 2: these were either very low purity samples (only analyzable with additional, non-sWGS data), or samples with no detectable alterations [5].

Given the rise in use of liquid biopsy for tumor detection, monitoring, and prognostic purposes [55–57], it is essential for a well-constructed pipeline to be able to analyze ctDNA samples correctly and reproducibly. For this reason we used dataset P to benchmark the capabilities of SAMURAI in this setting, using ichorCNA. Our results closely matched the original data in terms of detected tumor fraction, with a correlation close to 95%. This was achieved also in samples which were particularly problematic due to low cfDNA concentration. Characteristic alterations of the pathology, for example copy number gains on chromosome 8q24.3 were also detected [4].

SAMURAI offers several advantages over custom-made pipelines. Firstly, it packages current state-of-the-art methods for sWGS analysis, widely used across the bioinformatics community; secondly, while allowing flexibility, it relieves the user of many data adjustment operations required for the interoperability between the different application, thus it is approachable even by entry-level bioinformaticians; thirdly, it heavily uses containerization (all the tools are offered through Docker or Singularity) to ensure that runs are as reproducible as possible; lastly, it builds upon a large *corpus* of existing, well-tested modules developed by the nf-core community [21].

Thus, SAMURAI represents a valuable first step towards standardized sWGS analysis. Future work will focus on incorporating additional copy number analysis methods and downstream analyses, further enhancing SAMURAI's capabilities.

Key Points

- SAMURAI offers a reproducible, scalable and standardized bioinformatics pipeline for the analysis of copy number alterations from shallow whole genome sequencing;
- SAMURAI’s copy number calling block offers two types of analysis workflow depending on the nature of the samples, one catering to the processing of tissues (“solid biopsy”) and another for the identification of aberrant CNAs in other biological fluids (“liquid biopsy”);

- SAMURAI provides a final report that allows an overall evaluation of the sequencing and alignment quality, as well as custom reports that facilitate the interpretation of copy number calling analysis.

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Data availability

SAMURAI can be downloaded from https://github.com/DincalciLab/samurai. The additional scripts used for the analysis are available at https://github.com/DIncalciLab/SAMURAI_paper_scripts. The real-world sequencing datasets used are deposited under controlled access at EGA (IDs EGAS00001004961 and EGAS00001004670)

Authors’ contributions

Conceptualization: S.P., L.B., and C.R.
Data curation: S.P., L.B., and C.R.
Formal analysis: S.P. and L.B.
Funding acquisition: D.B., D.P., S.M., and C.R.
Investigation: S.P., L.B., and C.R.
Methodology: S.P., L.B., and C.R.
Project administration: D.B., D.P., S.M., and C.R.
Resources: D.B., D.P., L.B., and C.R.
Software: S.P., L.B., and C.R.
Supervision: D.B., D.P., S.M., L.B., and C.R.
Validation: L.B. and C.R.
Visualization: S.P.
Writing - original draft: S.P., L.B., and C.R.
Writing - review & editing: All authors

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Chiara Romualdi is a full professor at the Department of Biology, University of Padova, Italy. She’s interested in the computational methods for genomic data analysis and integrations.

Conflict of interest

The authors declare no competing financial interests.

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