Bionano Solve v3.7.2 Release Notes

Document Number: RNOTE-30456

Document Revision: C

Table of Contents

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Revision History

Revision	Effective Date	Notes
A	11/03/2021	Initial release of document.
B	05/09/2022	Updated with additions for Solve 3.7.1 release
C	01/19/2023	Updated with additions for Solve 3.7.2 patch release

Introduction

This document describes the release of Bionano Solve 3.7. We provide an overview of the fixes and improvements of the Bionano Solve analysis tools and pipelines so that you may better understand the impact of moving to this version of our software. Should you have any questions, please contact support@bionanogenomics.com.

Bionano Tools and Bionano Solve are now combined and branded as Bionano Solve. Bionano Solve is installed on Saphyr Compute, Bionano Compute, and Bionano Access Servers before server shipment and installation. IrysSolve servers, which have been in use with Bionano Access, also have Bionano Solve installed during an upgrade.

Bionano Solve (folder “tools”) is located at the /home/bionano directory on the compute server. The folder contains a collection of tools and scripts. Each individual tool is versioned independently. These tools together perform bioinformatics analyses on the compute server.

Compatibility

Bionano Solve 3.7 is compatible with Bionano Access 1.7 only.

Use of IrysSolve servers

If you are using an IrysSolve server to perform computational analysis on data generated by the Saphyr instrument, contact Bionano Support to reconfigure the IrysSolve prior to running any samples labeled with the DLS chemistry.

References

Visit https://bionanogenomics.com/support-page/data-analysis-documentation/ for file format specifications and Theory of Operation documents.

Bionano EnFocus™ Fragile X Analysis Pipeline

- Initial release of targeted analysis of FMR1 repeat expansions that are related to Fragile X syndrome. Detailed performance specification and methods overview are described in the Bionano Solve Theory of Operation: Bionano EnFocus Fragile X Analysis Pipeline (PN 30457)

Bionano EnFocus™ FSHD Analysis Pipeline

- Fixed issue with identifying maps relevant to D4Z4 region that caused negative repeat counts to be reported
- Added ICS version to FSHD report
- Removed non-informative sections from report
- Added sample-level QC reporting based on molecule quality metrics and assessment of stable regions
- Updated report to clarify detection of CNVs overlapping SMCHD1
- Updated analysis to remove non-deterministic steps

AOH/LOH Detection

- Added detection of absence of heterozygosity (AOH)/loss of heterozygosity (LOH) events based on called zygosity of structural variants by the *de novo* assembly pipeline (not available as part of the Rare Variant Pipeline)
- Tested performance for detection of AOH/LOH > 15 Mbp in constitutional samples. Acceptable performance for > 25 Mbp was found and default filter was set accordingly.
- Implemented per variant estimate of probability that variant belongs to an AOH/LOH region
- Implemented initial model for confidence scoring of AOH/LOH regions based on size
- Added AOH/LOH stats to informatics report

Variant Allele Fraction estimation

- Implemented estimate of variant allele fraction for structural variants detected by de novo assembly and Rare Variant pipelines
- Implemented circular binary segmentation algorithm to detect segments of VAF similarity to aid visualization of aneuploidy and trisomy.

Copy number analysis pipeline

- Improved sensitivity of whole chromosomal aneuploidy detection

- Improved correction for systematic biases during coverage normalization
- Improved low VAF variant detection

De novo assembly pipeline

- Initial support for calling terminal deletions
- Preserve CNV and SV mask .bed files used in analysis in output .zip file
- Updated informatics reports to provide JSON version
- Add options to disable trimming of unlabeled molecule ends

Hybrid scaffolding

- Added option to override default N-base gap size

Molecule Quality Report (MQR)

- Standardized RefAligner parameterization to address differences in effective coverage estimates between MQR and assembly report
- Implemented MQR as JSON report to aid integration with external systems

Rare Variant Pipeline (RVP)

- Preserve CNV and SV mask .bed files used in analysis in output .zip file
- Updated informatics reports to provide JSON version to aid integration with external systems
- Added option to keep _full.xmap output for troubleshooting purposes

SV confidence

- Improved models for scoring translocation and inversion breakpoint confidence for human and non-human datasets using hyperparameter tuning and orthogonal SV data.
- Updated recommended confidence score filters based on new model

Variant Annotation Pipeline (VAP)

- Added annotation of CNV variant types
- Incorporated cross-reference of CNV events in duo and trio analyses.
- Added International System for Human Cytogenetic Nomenclature (ISCN) notation for all variant types (not aneuploidy, AOH, or triploidy)
- Updated cross-reference with control sample database to report frequencies by zygosity and ethnicity
- Recomputed DLE-1 control datasets for *de novo* assembly pipeline and RVP using Solve 3.7
- Streamline output by removing intermediate files from final .zip file

VCF conversion

- Added VAP annotation information to VCF for CNVs and SVs
- Standardized encoding of structural variant types and symbolic ALT alleles to meet VCF 4.2 spec
- Added LowConfidence and Mask FILTER values to synchronize with recommended confidence filtering levels in Access.
- Added INFO fields to preserve original Bionano structural variant type
- Added fractional copy number value for CNV gain and loss events
- Removed duplicate entries from SV calls on multiple maps
- Update SV size and orientation to synchronize with values reported in SMAP
- Added sample sex metadata fields
- Implement hemizygous genotype description on sex chromosomes
- Improve specification of breakpoint uncertainty
- Updated ALT allele of breakends to define location of mate per VCF spec

Miscellaneous

- Updated python2 software to python3
- Intra-chromosomal translocations renamed intra-chromosomal fusions
- Updated informatics reports to use JSON for improved chain-of-custody support and integration with external LIMS

Other known issues and limitations

- VAF calculation is performed independently from SV zygosity and AOH/LOH detection. We have observed cases where the LOH algorithm results and the VAF segments do not agree. This may occur because the analyses are performed independently using different rules for which variants to include in the calculation.
- Two enzyme hybrid scaffold analysis fails in some cases due to an underlying software defect. If an error is encountered, please contact Bionano Genomics Technical Support.

Solve 3.7.1 Updates

The following issues were addressed in the Solve 3.7.1 update:

Issue	Description
BIOIN-2252	Addressed increase in inversion and duplication calls by improving SV calls formerly categorized as 'complex'
BIOIN-2343	Fixed bug in handling unexpected match group configuration in complex inversions during confidence scoring
BIOIN-2359	Removed hybrid scaffold dependency on specific Perl versions
BIOIN-2390	Fixed bug where insertions at the same position but with different lengths were filtered from VCF
BIOIN-2391	Fixed bug in confidence scoring and sizing of inversions
BIOIN-2420	Fixed missing dependency in runCharacterize.py
BIOIN-2424	Fixed bug in MQR by updating memory allocation to manage .bnx files with more than two billion molecules
BIOIN-2425	Added variant allele frequency to INFO field in VCF export
BIOIN-2428	Mask file dependency needed for custom mask creation
BIOIN-2437	Fixed bug in RefAligner assertion of obsolete condition which caused failures in alignmolvref stage for 1.5 Tbp human RVP
BIOIN-2474	Fixed bug where translocations were incorrectly flagged as _repeat
BIOIN-2475	Fixed bug in de novo pipeline in handling cleanup command line options (-c) so that full .xmap file not kept when requested
BIOIN-2480	Fixed RefAligner assertion error in handling label interval sample size of zero
BIOIN-2531	Fixed bug in de novo assembly without reference where configuration warnings caused pipeline failure
BIOIN-2556	Fragile X report missing Solve version

Solve 3.7.2 Updates

The following issues were addressed in the Solve 3.7.2 update:

Issue	Description
BIOIN-2600	Addressed RVA bug in handling in handling multiple inversion lines that are not sequential in the SMAP
BIOIN-2767	Addressed RVA errors caused by RefAligner assertion failure in dealing with corner case where small inversion pair must be converted to regular inversion due to match group overlap and trimming
BIOIN-2950	Addressed RVA errors caused by RefAligner assertion failure due to unhandled case in indel confidence score with cross or fully overlapped matchgroups
BIOIN-2951	Updated de novo assembly informatics report to replace missing fields from non-haplotype assembly
BIOIN-2952	Addressed EnFocus™ FSHD errors due to RefAligner assertion failure resulting in missing alignment files
BIOIN-3005	Restored runCharacterize.py utility script in de novo assembly pipeline
BIOIN-3019	Addressed failure to align middle region of maps while flanking regions align due to bug in trimming duplication match group
BIOIN-3021	Fixed division by zero error in annotating CNV events made by a single label

Technical Assistance

For technical assistance, contact Bionano Genomics Technical Support.

You can retrieve documentation on Bionano products, SDS's, certificates of analysis, frequently asked questions, and other related documents from the Support website or by request through e-mail and telephone.

Type	Contact
Email	**support@bionanogenomics.com**
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