Bionano Solve v3.7 Release Notes

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Document Revision: A

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Revision History

Revision	Notes
A	Initial release of document.

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 together 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.

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
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