DRAGEN v3.7.7
Software Release Notes

June 07, 2021

Introduction

These release notes detail the key changes to software components for the Illumina® DRAGEN™ Bio-IT Platform patch release v3.7.7.

Changes are relative to DRAGEN™ v3.7.5. If you are upgrading from a version prior to DRAGEN™ v3.7.5, please review the release notes for a list of features and bug fixes introduced in subsequent versions.

DRAGEN™ Installers, User Guide and Release Notes are available here:
https://support.illumina.com/sequencing/sequencing_software/dragen-bio-it-platform.html

The 3.7.7 software package includes:
- DRAGEN™ SW Intel Centos 6 - dragen-3.7.7-4.el6.x86_64.run
- DRAGEN™ SW Intel Centos 7 - dragen-3.7.7-4.el7.x86_64.run

The following configurations are also available on request:
- Amazon Machine Image (AMI)
- RPM packages for Centos 7 and Ubuntu 14.04 for Amazon Web Services (AWS)

Support for IBM PPC has been deprecated and not available for DRAGEN™ v3.7 and later.

Contents

Issues Resolved

Component	Description	Type
SOS reporting	SOS reports are not collected on DRAGEN v3.7.5. Fix to the install path of the sos-report plugin.	Bug fix
System	Fix for intermittent crashes (segfaults) when BAM is input to VC without map/align. On DRAGEN v3.7.5, a HW UNZIP error is sometimes encountered on Phase2 servers and AWS (U200 boards), when an input BGZF block is zero length. The issue is fixed in the UNZIP block of the HMM FPGA image. The software segfault does not always happen, as it depends on the state of the RAM and is caused by a potential out of bounds read from memory. The issue does not cause any wrong output when a segfault is not encountered.	Bug fix
System	Fix to enable use of "dragen_reset -r". This command resets then re-loads a bitstream, which is able to recover rare FPGA lockup conditions for on-site servers. The fix avoids a deadlock during "dragen_reset -r".	Bug fix, Usability
System	Fix for FPGA board lockup due to race condition, when HW Zipper is configured while Partial Reconfig (PR) of the bitstream is in process. The issue has been seen rarely in the use case of VC+CNV, where the CNV opens an output .gz file for writing at the same exact time a PR to VC is in progress. The fix removes possibility for hardware race condition.	Bug fix, Stability
System	Fix for a rare race condition in hardware register accesses between threads, leading to HWAL assertion	Bug fix, Robustness
System, AWS AMI	Fix issue with docker hub rate limiting. During AMI startup, let the systemd service pull the latest amazon ecs agent from AWS ECR instead of dockerhub.	Usability
Map/Align	Fix for a run-run variation in the output of the mapper/aligner. In DRAGEN v3.7.5, occasionally a single read would get a different MAPQ score from run-run, potentially leading to a run-run variation in variants.	Bug fix

Component	Description	Type
Map/Align	Fix for rare issue where a read gets mapped to an invalid position instead of being unmapped. The issue is only present on AWS, for both DNA and RNA mappers. With DRAGEN v3.7.5 the issue is caught by software downstream of the mapper and leads to an assertion.	Bug fix
Graph Mapper	Fix to recompute NM tags when using multi-base codes from pop snps in reference genome. Applies when using Graph References	Bug fix
VC	Fix for crash when Joint Detection is enabled and "FRD max effective depth = 40"	Bug fix
VC	Fix for segfault encountered when haplotypes start with an indel	Bug fix
VC	Fix for crash in VCF Tabix generation when the reference chromosomes exceed 2^29 bases. Specifically, new Wheat references have chromosomes lengths exceeding 2^29 as required by Tabix, BAI, CRAI specification. Detect, and disable Tabix generation for such a reference. BAI/CRAI invalid indexes can be worked around by disabling them or ignoring them.	Stability improvement
VC	Add missing FT fields "DRAGENHardQUAL" and "LowGQ" in Joint Genotyping VCF header. Only encountered when Joint Genotyper runs on output of GvcfGenotyper	Bug fix
VC	Fix potential hang / WatchDog timeout when generating the systematic noise baseline file.	Bug fix, Stability
VC	Fix for rare run-run differences in DP, MQ and QD fields, caused by an uninitialized value in the read CIGAR field.	Bug fix
VC	Update handling of overlapping mates in homref regions for gVCF. Overlapping mates are handled by using only one read as evidence for the call, but in homref regions, they were double counted which resulted in differences in DP between homref and variant call.	Improvement
CNV	CNV stability fixes with Tumor / Normal somatic workflow. Fixes for various segfaults, watchdog timeouts.	Stability improvements, bug fixes

Component	Description	Type
CNV	Increase SLM segmentation sensitivity	Accuracy improvement
Structural Variants	Remove redundant incomplete insertion call in multi-junction SVs. By allowing large insertion calls in multi-junction SVs, a large insertion was called mistakenly, when there were other SVs called (e.g. DEL and TRA) that would better explain the SV locus.	Accuracy improvement
Structural Variants	Fix 6kb duplication FN using adjusted spanning significance filter.	Accuracy improvement
RNA	Fix for RNA library-type autodetect error, returning 'outward' for an 'IU' library	Bug fix
CYP2D6	Accuracy improvements for CYP2D6 caller: Use binomial model for calling differentiating sites; Prioritize small variant calls by likelihood.	Accuracy improvement
TMB	Allow optional enabling of the integrated Tumor Mutational Burden (TMB) biomarker for end-end runs including T/N	New feature
RNA metrics	Fix for rare run-run differences in RNA mapping metrics, caused by incorrect Cigar:SKIP handling	Bug fix, Robustness
Metrics	Fix issue where the sample cross contamination metric is not accurate for low coverage samples. The fix allows sample cross contamination to run on samples with lower coverage	Usability improvement
Metrics	Update sample cross contamination VAF reference files. The files are distributed with DRAGEN installer	Usability improvement
Metrics	Fix issue where DRAGEN VC metrics do not match RTG, due to RTG counting of the MNVs as SNV. The fix updates DRAGEN to match RTG	Bug fix
EH	Allow EH to process multiple libraries (RGLB) for one sample	Usability improvement
UMI	Fix for long analysis time during UMI read collapsing on some samples, due to verbose debug logging. Disable the verbose debug logging	Usability improvement

Component	Description	Type
UMI	Fix for incorrect UMI metrics when running with very large input file (very deep coverage)	Bug fix
UMI	Fix a WatchDog hang when very large input fastq files are used, due to UMI thread not checking in with Watchdog	Stability improvement
UMI	Fix for issue in UMI DEBUG mode where the DBAM record does not have an index to help identify the source of the read.	Usability (Debug)
UMI	Add more error checks and error handling for the umi-lookup-table input, to avoid segfault and/or wrong output.	Robustness
BCL	Fix issue where a small number of unknown barcodes causes TopUnknownBarcodes to be empty	Bug fix
BCL	Fix for incorrect base masking when using both new options TrimUMI,0 and CreateFastqForIndexReads,1.	Bug fix
BCL	Fix a rare segfault caused by corrupted stack access.	Bug fix
BCL	Fix wrong index in Top Unknown Barcodes metrics.	Bug fix
BCL + FASTQ List	Fix bug with fastq-list.csv processing. The format of the fastq-list.csv generated by BCL convert, when no-lane-splitting option is used, was not supported correctly in DRAGEN v3.7.5, leading to wrong sample ID being used.	Bug fix
Methylation	Fix for an incorrect alignment produced by methylation mapper in multi-pass mode, only when using fastq-list.csv input, due to MD tag being calculated using wrong reads	Bug fix
Methylation	Fix for wrong results in methylation reports. Occurs only when the use case is a methyl reports only run, and the input is sorted paired end.	Bug fix
ROH caller	Fix for handling of DP 0 variants in the ROH caller. Since v3.7.5 DRAGEN will generate DP 0 variants	Bug fix
Joint Caller	Speed up of joint calling for gVCF mode on AWS when site VCF is generated	Improvement

Component	Description	Type
Nirvana	Update Nirvana from Microsoft dotnet executable to Linux native binary, and improve the stability (exceptions, timeouts) of Nirvana execution in a DRAGEN run	Stability improvement
HT Builder	Fix for HT builder error when the command line to DRAGEN is longer than 1024 characters.	Bug fix, Robustness
HT builder	Fix for undefined behavior when a specific file already exists in the output folder. Specifically encountered if HT was generated with pop_snp inputs, and a new HT is built without pop_snp using same output folder	Bug fix
HT builder	Fix segfault while building Hash Table when an expected input file is missing.	Bug fix

Known Issues and/or Impacts

- The following fixes mentioned above, may change the output (BAM) and VCF compared to DRAGEN v3.7.5. These changes are desired bug fixes

Map/Align	Fix for a run-run variation in the output of the mapper/aligner. In DRAGEN v3.7.5, occasionally a single read would get a different MAPQ score from run-run, potentially leading to a run-run variation in variants.	Bug fix
VC	Fix for rare run-run differences in DP, MQ and QD fields, caused by an uninitialized value in the read CIGAR field.	Bug fix

- The following changes mentioned above, are intended accuracy improvements that may change the VCF output of a caller

VC	Update handling of overlapping mates in homref regions for gVCF. Overlapping mates are handled by using only one read as evidence for the call, but in homref regions, they were double counted which resulted in differences in DP between homref and variant call.	Improvement
CNV	Increase SLM segmentation sensitivity	Accuracy improvement

Structural Variants	Remove redundant incomplete insertion call in multi-junction SVs. By allowing large insertion calls in multi-junction SVs, a large insertion was called mistakenly, when there were other SVs called (e.g. DEL and TRA) that would better explain the SV locus.	Accuracy improvement
Structural Variants	Fix 6kb duplication FN using adjusted spanning significance filter.	Accuracy improvement
CYP2D6	Accuracy improvements for CYP2D6 caller: Use binomial model for calling differentiating sites; Prioritize small variant calls by likelihood.	Accuracy improvement

SW Installation Procedure

- Download the desired installer from the Illumina support website and unzip the package
- The archive integrity can be checked using: `./<DRAGEN 3.7.7 .run file> --check`
- Install the appropriate release based on your Linux OS with the command: `sudo sh <DRAGEN 3.7.7 .run file>`
- Please follow the installer instructions. Cold boot may be required after installation, depending on the currently installed version. A cold boot is a hard reset or power cycle. An updated FPGA shell image needs to load from flash, this is only achieved with cold boot.
- Installing prior releases after v3.4.5 was installed:
  - Installing a prior release, v3.3.7 or older, will require the following two steps. The prior .mcs file needs to be flashed manually:
    - **Install the prior release:** `sudo sh <DRAGEN 3.3.7 .run file>`
    - `program_flash /opt/edico/bitstream/07*/*.mcs`
    - Power cycle