DRAGEN v3.10.8
Software Release Notes

Introduction

These release notes detail the key changes to software components for the Illumina® DRAGEN™ Bio-IT Platform v3.10.8.

Changes are relative to DRAGEN™ v3.10.4. If you are upgrading from a version prior to DRAGEN™ v3.10.4, 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 3.10.8 software package includes installers for the on-site server:
- DRAGEN™ SW Intel Centos 7 - dragen-3.10.8-8.el7.x86_64.run
- DRAGEN™ SW Intel Oracle 8 - dragen-3.10.8-8.el8.x86_64.run

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

Deprecated platforms:
- Support for DRAGEN Server v1 FPGA cards has been deprecated since DRAGEN™ v3.10
- Support for Ubuntu has been deprecated since DRAGEN™ v3.9
- Support for Intel CentOS 6 has been deprecated since DRAGEN™ v3.8

Contents

Overview

Below is a summary of the changes included in this DRAGEN™ v3.10.8 patch release. This is a minor update.

Issues Resolved

Issues resolved on DRAGEN™ v3.10.8, compared to v3.10.4

Component/s	Defect ID	Description
Map/align	DRAGEN-16744	Fix for sub-optimal properly paired scores. Add `Aligner.pe-prop-pair-max-stddev` command line argument to allow adjustment.
Map/align	DRAGEN-15057	Fix for XB/XQ tags not working when mapper aligner is disabled
Deployment	DRAGEN-16742	Auto-publish 3.10.8 AMIs to Tokyo, Seoul, Singapore, Canada
Packaging	DRAGEN-16574	Remove unused U250 bitstreams from 3.10 packages to reduce package size
BCL	DRAGEN-16245	Fix for DRAGEN BCL assuming a fixed `MinimumTrimmedReadLength` value of 35 when using `MaskShortReads` in the sample sheet
BCL	DRAGEN-16403	Fix to DRAGEN BCL per-sample-settings feature: logging an incorrect error message when adapter settings used without `AdapterRead1/2`
BCL	DRAGEN-16404	Fix to DRAGEN BCL per-sample-settings feature: requiring `AdapterBehavior` setting for all samples, even when `AdapterRead1/2` is missing
BCL	DRAGEN-16405	Fix to DRAGEN BCL per-sample-settings feature: not aborting when global Adapter settings are used without `AdapterRead1/2`
BCL	DRAGEN-16406	Fix to DRAGEN BCL per-sample-settings feature: aborting when `AdapterRead2` specified for sequencing run with single genomic read
BCL	DRAGEN-16400	Fix to DRAGEN BCL per-sample settings feature: FASTQ checksums not identical between "per-sample settings" runs and "global settings" runs, for `BarcodeMismatchesIndex1/2` settings
BCL	DRAGEN-16402	Fix to DRAGEN BCL per-sample settings feature: Tests for `BarcodeMismatchesIndex1/2` must be same for combinatorial indices
BCL	DRAGEN-16544	Fix for DRAGEN BCL logging an incorrect error when excluded tiles are not in `--tiles` but are in `RunInfo.xml`
BCL	DRAGEN-16559	Fix for DRAGEN BCL not aborting when lane specified for both `--tiles` and `--bcl-only-lane`

Component/s	Defect ID	Description
BCL	DRAGEN-16561	Fix for DRAGEN BCL not aborting when lane is specified for both `--exclude-tiles` and `--bcl-only-lane`
BCL	DRAGEN-16564	Fix for DRAGEN BCL not excluding lane when `--exclude-tiles=s_1` is used
BCL	DRAGEN-16568	Fix for DRAGEN BCL bad error string formatting when `--exclude_tiles=s_2` is used when Lane 2 does not exist
Installer	DRAGEN-16276	Fix to prevent the dragen installer from breaking a dragen run that is in progress
bcl-convert	DRAGEN-16707	Fix a hang in the `bcl-convert` tool
PhenoHRD	DRAGEN-16706	Fix PhenoHRD hang when processing NTC samples
PhenoHRD	DRAGEN-16738	Harmonize the order of small region removal
PhenoHRD	DRAGEN-16754	Add a missing `totalMTC` metric to output, to use for acceptance on NTC samples
Azure cloud	DRAGEN-16911	Fix ubuntu docker operation by updating XRT RPMs to v2.8.832
HT Builder	DRAGEN-17118	Fix a floating-point exception in KmerChecker, when Building Hash Table with DRAGEN 3.10
TMB	DRAGEN-17116	Fix for an invalid VCF output with UMI pipeline. Expose a new parameter for input VCFs `tmb-intermediate-vcf`, to allow decomposed variants cleanup
TMB	DRAGEN-16855	Fix for an inaccurate MSAF due to low depth
SV Caller	DRAGEN-16801	Fix for missed fusion FKBP15-ALK
SNV VC	DRAGEN-17211	Fix for low sq call threshold setting introducing multi allelic calls, impacting downstream filters and classification

Known Issues

Known issues of the DRAGEN™ v3.10.8 release

Component/s	Defect ID	Issue Description	Remedy / Workaround
BCL	DRAGEN-16555	Minimum Adapter Overlap setting not working	Whether it's set to a valid or invalid value, an error message is displayed. No workaround
Infrastructure	DRAGEN-16498	AWS f1.4x l LICENSE_MSG| Challenge get token error: Get instance ID failed	Timeout while retrieving AWS instance ID has been observed. The rate of occurrence has been too low to measure. This leads to failure in the

Component/s	Defect ID	Issue Description	Remedy / Workaround
		(Unable to retrieve AWS identity signature)	licensing and dragen job exits, run fails. Re-run would pass
DNA Alignment	DRAGEN-16468	Bam generated from file conversion CRAM -> BAM with hg19_alt_masked_v2 reference has invalid header	Reproducible issue that has been shown to have existed since v3.7 or earlier. When converting from CRAM to BAM using dragen "file-conversion" method, the BAM has an invalid header due to a bug in the CRAM reader. No workaround. Re-header the file
DNA Alignment	DRAGEN-16467	Germline workflow is slower with graph hash table	Dragen run time is roughly 6.3% slower with graph aligner and graph reference is used, compared to non-graph. The increased run time is in both mapper and variant caller phases. No workaround
Dedup/UMI	DRAGEN-16412	Probabilistic UMI output is different from run to run	There is a run-run variation in the UMI probabilistic model. Non-prob model (non-random UMI) does not have run-to-run variation. The variation leads to ~2 reads being missing from output. This impact shall be a very small fraction.
DupMarking	DRAGEN-16399	Assertion `pos < m_num_bits' failed, in Dupmark:: DupmarkTable:: getDuplicates()	Crash in duplicate marking when there are more than 4G read pairs, which can happen when reads of multiple replicates are combined into one read group through manual BAM file editing. The system has a physical limit. Not a regression from prior releases
Cloud / Azure	DRAGEN-16335	popen exception on azure cloud suites	A very long running workflow such as TSO500 ctDNA crashes on Azure due to eventual failure in popen() calls. The issue is reproducible. No workaround
Somatic	DRAGEN-16319	Elevated SNP and INDEL FP on ICGC datasets	The impact of the issue is an elevated number of FPs for ICGC datasets in 3.10 compared to 3.9: a 5-6% increase in the SNP FPs and a 25%-30% increase in the INDEL FPs.

Component/s	Defect ID	Issue Description	Remedy / Workaround
DNA Alignment	DRAGEN-16308	read trimmer adapter trimming sigabort during RecomputeTags::computeTags	Reproducible when running different read trimmers back-back. Workaround to run dragen_reset
Amplicon Gene Fusion	DRAGEN-16254	Excessive RNA Amplicon runtime on large samples	RNA Amplicon run time is very long when the coverage is significantly higher than expected for typical Amplicon samples
SNV VC Somatic	DRAGEN-16149	Germline MNV - phased calls with same PS and GT and within distance threshold are not getting combined into MNVs	Some phased calls are not getting combined into MNVs to MNV output. Full support for germline MNV is planned for a subsequent release
Metrics scRNA	DRAGEN-15950	A run-run variation in scRNA output	Some datasets have run-to-run variations in the mapping metrics Q30 metrics field. The issue affects only the metrics output and not the caller output
BCL	DRAGEN-15944	DRAGEN BCL logs insufficient warning when corrupt files supplied	In the rare event of a corrupt aggregated bcl. bgzf input file, the customer will correctly receive an error message of the lane and the cycle that is corrupted, but not the specific file name.
Methyl-Seq	DRAGEN-15796	md5sum discordance b/w cloud and local runs	Impacts multi-pass mode and specific dataset. Single pass mode has been the recommended mode and does not have the issue. Multi-pass will be deprecated in future.
DNA Alignment EH	DRAGEN-15151	Large run to run variation of mapper run time for EH	Up to 20% run time variation seen for mapper phase
HW GRAPH RNA VC	DRAGEN-13717	RNA VC hits ERROR: Invalid node flags	Issue is a HW graph error and rare (happens once every 6-9 months in routine VC testing). The assertion check / trap will remain in place so that invalid results will not be produced for end user. If seen in field, recommendation is to re-run sample as it is expected to pass.
Compression	DRAGEN-10783	BAM input to DNA mapper: Deflate engine error: 0x9080 on stream 1	Extremely low repeatability. A re-run will pass

SW Installation Procedure

- Download the desired installer from the Illumina support website and unzip the package
- The archive integrity can be checked using: `./<DRAGEN 3.10.8 .run file> --check`
- Install the appropriate release based on your Linux OS with the command: `sudo sh <DRAGEN 3.10.8 .run file>`
- Please follow the installer instructions. Server power cycle may be required after installation, depending on the currently installed version. If an updated FPGA shell image needs to load from flash, this is only achieved with power cycle.
    - A power cycle is required when upgrading from v3.3.7 or older
    - A power cycle is required when downgrading to v3.3.7 or older
    - A power cycle is not required when upgrading from a release after v3.3.7
- Procedure to downgrade to v3.3.7 or older:
    - Requires the following three 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