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cnvPartition v3.2.0 CNV Analysis Plug-in
for GenomeStudio® Software

1. General Information

The cnvPartition CNV Analysis Plug-in is a software library that works with Illumina's GenomeStudio data analysis software. This document provides information about downloading, installing, and using the cnvPartition CNV Analysis Plug-in.

2. Downloading and Installing the cnvPartition CNV Analysis Plug-in

1. Download the cnvPartition CNV Analysis Plug-in from one of three places:
   - The GenomeStudio Portal
   - The software downloads section of iCom
   - The illumina•connect web page
2. Run the setup program for the plug-in.
3. Follow the instructions in the installation prompts.

   The setup program places the *.dll and configuration file into this GenomeStudio directory on your computer:

   C:\Program Files (x86)\Illumina\GenomeStudio\CNVAlgorithm\cnvPartition

3. Using the cnvPartition Plug-in with GenomeStudio Software

1. Open a genotyping project using GenomeStudio software.
2. [Optional] Adjust the cnvPartition parameters as needed (see Section 5 of this document).
3. Select **Analysis** | **CNV Analysis**.

   The CNV Analysis dialog appears.
4. Select **Create New CNV Analysis** | **cnvPartition 3.2.0**.
5. In the CNV Analysis Name area, enter a name for this CNV analysis.
6. [Optional] Adjust the cnvPartition parameters as needed (see Section 5 of this document).
7. Click **Calculate New CNV Analysis**.
8. When the analysis is complete, click **OK**. After running the analysis using GenomeStudio software, you can view the results in many ways:
   - In the **Full Data Table**, in the CNV Value and CNV Confidence columns
     Use the column chooser ▌▌▌ to display the CNV Value and CNV Confidence columns.
   - In the CNV Region Display tool, by selecting **Analysis** | **Show CNV Region Display**.
   - In the Illumina Genome Viewer (IGV), by selecting **View** | **CNV Analysis as Bookmarks**.
   - In the Bookmark Viewer, by going to the IGV and selecting **View** | **Bookmark Viewer**.

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4. Configuring the cnvPartition Plug-in

Starting with v1.2.0 of the cnvPartition Plug-in, the parameters can be changed via an editable configuration file. When you install the cnvPartition Plug-in, a configuration file is installed on your computer in this location:

C:\Program Files (x86)\Illumina\GenomeStudio\CNVAlgorithm\cnvPartition

When you modify and save the default configuration file, your changes are preserved for future sessions.

Note: You can also adjust cnvPartition parameters from within GenomeStudio software.

Perform the following steps to adjust cnvPartition Plug-in parameters from within GenomeStudio:

1. In a GenomeStudio genotyping project, go to **Analysis** | **CNV Analysis**.

   The CNV Analysis dialog appears.

2. Select **cnvPartition 3.2.0** from the drop-down menu.

3. In the **Options** area of the CNV Analysis dialog, modify the parameters as needed.

The following table lists cnvPartition parameters, descriptions, and related information for GenomeStudio software.

Parameter Name	Description	Default Value	Required	Visible in GUI?	Applies to LOH Regions	CNV Regions
AdjustYLRR	Set this flag to true to adjust Log R Ratios downward for Y SNPs.	True	True	False	False	True
AveragePloidy AdjustLRR	Set this flag to true to turn on Average Ploidy Adjustment of the Log R Ratio.	False	True	False	False	True
AveragePloidy AdjustLRR Threshold	The threshold for activating the Average Ploidy Adjustment.	2.5	True	False	False	True
ChiSquare Threshold	Minimum Chi Square value needed to detect a region of extended homozygosity. See the DNA Copy Number Analysis Algorithms Technical Note for more details.	23.5	True	False	True	False
Confidence Threshold	CNV regions with a confidence threshold below this value are excluded from analysis results.	35	True	True	False	True
CopyNeutral LOHOnly	If set to true, detects regions of extended homozygosity only if they are copy neutral.	True	True	False	True	False
DetectExtended Homozygosity	Detect regions of extended homozygosity (regions exhibiting LOH but no change in copy number.)	True	True	True	True	False

					Applies to	
Parameter Name	**Description**	**Default Value**	**Required**	**Visible in GUI?**	**LOH Regions**	**CNV Regions**
	Note: The algorithm for detecting regions of homozygosity is similar to that used in the LOH Detector Autobookmarking Plug-in, and is described in detail in the [DNA Copy Number Analysis Algorithms Technical Note](#). This algorithm is run only on regions with a copy number of 2 as detected by cnvPartition. Additionally, the calculated ChiSquare for the homozygous region is used to populate the CNV Confidence value reported in the Full Data table, and is not subject to filtering by the `ConfidenceThreshold` parameter. Homozygous regions can be filtered independently of CNV regions using the `MinHomozygousRegionSize`, `ChiSquareThreshold` and/or `MinHomozygoteCount` parameters. CNV regions can be filtered independently of homozygous regions using the `ConfidenceThreshold` and/or `MinProbeCount` parameters. To run only CNV detection, toggle `DetectExtendedHomozygosity` to False. To run LOH detection on Copy Number = 2 regions only, set `CopyNeutralLOHOnly` to 2. To detect only extended homozygous regions, set `ConfidenceThreshold` to a very high value, such as 10,000,000. Because even phenotypically normal samples contain many regions of homozygosity, you may want to set this threshold higher, to minimize the number of detected regions.					
`Exclude IntensityOnly`	Set this flag to true if you want to exclude intensity-only probes from your analysis.	False	True	True	True	True
`ExcludeProbes WithAuxValue`	Enables you to filter a probe by setting its Aux value in the SNP table to -1. All probes with an Aux value of -1 will be excluded.	-1	True	False	True	True
`GapSize Threshold`	Regions within probe gaps larger than this value are not considered to be within CNV regions. This helps prevent CNVs from being called across large probe gaps, such as centromeres.	1,000,000	True	False	False	True
`GcFile`	Enables you to specify the full path to the optional GC content file.	[blank]	False	False	False	True
	Note: The GC content file is a tab-delimited file containing two columns for each probe, with no header. The content is organized as follows: Probe name<tab>GC content Where the GC content is a numeric value in the range of 0 to 1. The GC content file is not used by default.					
`GcWaveAdjust GCBins`	The number of GC value bins used in the polynomial-based GC wave adjustment method.	50	True	False	False	True
`GcWaveAdjust LRR`	Set this flag to true if you want to adjust Log R Ratios for GC waves.	True	True	True	False	True

Parameter Name	Description	Default Value	Required	Visible in GUI?	Applies to LOH Regions	Applies to CNV Regions
GcWave Adjustment Window	The sliding window size, in bases, used by the linear-based GC wave adjustment method.	115000	True	False	False	True
GcWaveAdjust Type	Specifies whether to use a polynomial- or linear-based method for the GC wave adjustment. Valid options are Polynomial or Linear.	Polynomial	True	False	False	True
GenTrain Threshold	Probes with a GenTrain score below this value will not be included in the analysis.	0.00	True	True	True	True
Include Mitochondria	Set this flag to True if you want to include mitochondrial chromosomes in this analysis.	False	True	False	True	True
IncludeSex Chromosomes	Set this flag to True if you want to include X, Y, and XY (pseudoautosomal) chromosomes in this analysis.	True	True	True	True	True
LogDiagnostic Info	Log diagnostic info to a file in the application's temp file directory. The log directory location varies depending on your operating system: **Windows XP –** C:\Documents and Settings\<username> \Local Settings\Application Data\Illumina\cnvPartition **Windows 7 –** C:\Users\<username>\AppData\Local\Illumina\cnvPartition	False	True	False	True	True
MinHomozygote Count	Minimum number of homozygotes needed to detect a region of extended homozygosity. See the DNA Copy Number Analysis Algorithms Technical Note for more details.	50	True	True	True	False
MinHomozygous RegionSize	Homozygous regions smaller than this are not detected.	1 Mb	True	True	True	False
MinProbeCount	Regions with probe counts smaller than this are removed from analysis results.	3	True	False	False	True
Smoothing Moving AveragePeriod	The smoothing moving average period.	2	True	False	False	True

Parameter Name	Description	Default Value	Required	Visible in GUI?	Applies to LOH Regions	Applies to CNV Regions
SmoothLRR	Set this flag to True if you want to smooth the Log R Ratio.	False	True	False	False	True
UseGcFile	Set this flag to True if you want to use an external GC content file for GC wave correction.	False	True	False	False	True
UseSimple HeterosomyFix	This parameter is still in development and should not be used at this time. Keep this value set at False to leave it off.	False	True	False	False	True

5. Technical Support

Direct questions about installing and using the cnvPartition CNV Analysis Plug-in to Illumina Technical Support at techsupport@illumina.com, 1.800.809.4566 (toll-free), or +1.858.202.4566 (outside North America).

6. Version History

Build	Date
v3.2.0 for GenomeStudio Software	**12/2/2011**

- Added compatibility with Illumina HumanOmni5M arrays.

- Simplified statistical methods to improve speed and memory utilization. This might lead to small changes in CNV boundaries and/or detection of lower confidence CNV regions.

Build	Date
v3.1.6 for GenomeStudio Software	**3/22/2011**

- Added ability to skip intensity-only probes.

- Added ability to skip probes with Aux value = -1 in the SNP table.

- Now call CN=2 on the X chromosome for males.

- Added LRR adjustment for Y chromosome probles.

- Now ignore LOH on the Y chromosome.

- GC wave correction can now be toggled on/off from within the CNV Analysis dialog box.

- Lowered the minimum homozygous region size to 1 Mb.

- Added parameter GcWaveAdjustType, set to Polynomial by default.

Build	Date
v2.4.4 for GenomeStudio and KaryoStudio Software	**11/11/2009**

- Improved consistency between 32-bit and 64-bit PCs—Fixed an occasional rounding issue with 32-bit PCs.

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- Improved consistency between GenomeStudio software and KaryoStudio software—The upcoming release of KaryoStudio also includes this fix.

- Improved detection of LOH regions—There are now fewer false positives. Also, the min LOH region size was changed to 10 Mb (from 1 Mb) for consistency with KaryoStudio software default settings.

- Added Log R Ratio smoothing—This feature is disabled by default (you can enable it via the config file).

The following experimental features have been added. These features are also disabled by default:

- You can now run LOH detection for the entire genome

  —Previously, you could run LOH detection only on regions for which CN=2

  —In the config file, `CopyNeutralLOHOnly` is set to True by default

- Optional adjustment to Log R Ratio for the Y chromosome

  —Y SNPs are clustered using only males, so the Log R Ratio appears as CN=2

  —To lower all Log R Ratios on Y, turn adjustment on

  —If Y chromosome SNP clusters are already adjusted, additional adjustment could result in inconsistent results

  —In the config file, use `AdjustYLRR`

- Support for highly amplified genomes has been added

  —This is a common situation with cancer samples

  —Log R Ratios are adjusted upward based on calculation of average genomic ploidy

  —In the config file, use `AveragePloidyAdjustLRR` and `AveragePloidyAdjustLRRThreshold`

- Optional GC Wave Adjustment has been added

  —This is based on linear regression of LRR vs. GC content in probes

  —In the config file, use `GcWaveAdjustLRR` and `GcWaveAdjustmentWindow`

Build	Date
v2.3.4 for GenomeStudio and KaryoStudio Software	**03/09/2009**

- Increased accuracy for calling smaller-sized CNVs.

- Improved logic for detecting CNVs on the sex chromosomes. Based on gender information from the sample sheet, single copies of X chromosomes are ignored for males.

Build	Date
v2.2.1 for GenomeStudio and KaryoStudio Software	**01/22/2009**

- cnvPartition v2.2.1 is compatible with Illumina's GenomeStudio and KaryoStudio software.

  Note: There are two different versions of cnvPartition v2.2 for KaryoStudio—one for 32-bit systems and one for 64-bit systems. Be sure to install the version of cnvPartition that is compatible with your computer.

- The cnvPartition algorithm now ignores Y-chromosome probes for females.

- The cnvPartition algorithm now ignores probes with NaN or a missing value for the Log R Ratio.

- Changed the minimum value for `MinHomozygousRegionSize` from 10Mb to 5Mb

Build	Date
v1.2.0 for BeadStudio	**10/10/2008**

- Added configuration file

- All chromosomes starting with letter "M" are now recognized as mitochondrial.

- B Allele Frequency is now ignored for Intensity Only probes.

- Added configuration option to detect extended regions of homozygosity such as copy-neutral LOH (default = True)

- Added configuration option for the minimum size of a detected region of homozygosity

- Added configuration option to ignore CNV regions with less than a minimum number of probes defined by the user (default=3)

Build	Date
v1.0.2 for BeadStudio	**03/11/2008**

- Added Confidence Threshold parameter—any CNV region with a confidence lower than this value will be removed from the CNV output. The recommended default is 35.

- Added Probe Gap Size Threshold parameter—a CNV region overlapping with a probe gap larger than this value will not be created. Helps prevent CNV regions from being found across centromeres and other large probe gaps. The recommended default is 1,000,000 base pairs.

- The internal expected Log R Ratio mean and standard deviation values for each copy number value have been changed to better reflect actual Log R Ratio values seen in normal HapMap samples. This results in higher overall accuracy and precision.

Build	Date
v1.0.1 for BeadStudio	**01/29/2008**

- Improved detection of smaller CNVs

- Both Log R Ratio and B Allele Frequency are used as inputs.

- Mitochondrial SNPs can be included in an analysis (optionally).

- The CNV Confidence score is now calculated.

Build	Date
v0.9.3 for BeadStudio	**09/04/2007**

- Improved classification of CN = 0 regions (homozygous deletions)

- Lowered the Min SNPs Per Bin parameter default to ten (from 30) to improve detection of CN = 0 regions (homozygous deletions)

Build	Date
v0.9.2 for BeadStudio	**07/23/2007**

- Initial release

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The cnvPartition CNV Analysis Plug-in incorporates portions of code from the Cephes Math Library.

Cephes Math Library Release 2.8: June, 2000 Copyright 1984, 1987, 1995, 2000 by Stephen L. Moshier

Contributors: * Sergey Bochkanov (ALGLIB project). Translation from C to pseudocode.

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