

# cnvPartition v2.4.4 CNV Analysis Plug-in for GenomeStudio® and KaryoStudio Software

## 1. General Information

The cnvPartition CNV Analysis Plug-in is a software library that works with Illumina's GenomeStudio data analysis software and KaryoStudio cytogenetics 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

If you are installing the cnvPartition plug-in to use with GenomeStudio software, the setup program places the \*.dll and configuration file into this GenomeStudio directory on your computer:

[C:\Program Files\Illumina\GenomeStudio\CNVAlgorithm\cnvPartition](#)

If you are installing the cnvPartition plug-in to use with KaryoStudio software, the setup program places the \*.dll and configuration file into this KaryoStudio directory on your computer:

[C:\Program Files\Illumina\Illumina KaryoStudio\CNVAlgorithm\cnvPartition](#)

2. Run the setup program for the plug-in.
3. Follow the instructions in the installation prompts.

## 3. Using the cnvPartition CNV Analysis Plug-in with KaryoStudio Software


1. Create a cytogenetics project using KaryoStudio software.

**Note:** The gender column in the KaryoStudio sample sheet must be populated for CNV calling to work properly for the X and Y chromosomes.

The version number of the cnvPartition plug-in is displayed in the software application title bar.

2. After running the analysis, you can view the results in various ways:
  - The Found Regions Table displays the CNV data for all samples.
  - The genome viewer displays the CNV region selected in the Found Regions track.
  - Separate Cytogenetics Reports are created for each sample.

## 4. 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 v2.4.4**.
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**.

## 5. 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\Illumina\GenomeStudio\CNVAlgorithm\cnvPartition> for GenomeStudio software, or

<C:\Program Files\Illumina\Illumina KaryoStudio\CNVAlgorithm\cnvPartition> for KaryoStudio

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, but not from within KaryoStudio software.

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

1. In a GenomeStudio genotyping project, go to **Analysis | CNV Analysis**.  
The CNV Analysis dialog appears.
2. Select **cnvPartition v2.4.4** from the dropdown 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	Mandatory	Visible in GUI?
AdjustYLRR	Set this flag to true to adjust Log R Ratios downward for homozygous Y SNPs	False	True	False
AveragePloidyAdjustLRR	Set this flag to true to turn on Average Ploidy Adjustment of the Log R Ratio	False	True	False
AveragePloidyAdjustLRRThreshold	The threshold for activating the Average Ploidy Adjustment	2.5	True	False
ChiSquareThreshold	Minimum Chi Square value needed to detect a region of extended homozygosity See the <a href="#">DNA Copy Number Analysis Technical Note</a> for more details	23.5	True	False
ConfidenceThreshold	CNV regions with a confidence threshold below this value are excluded from analysis results.	35	True	True
CopyNeutralLOHOnly	If set to true, detects regions of extended homozygosity only if they are copy neutral	True	True	False
DetectExtendedHomozygosity	Detect regions of extended homozygosity (regions exhibiting LOH but no change in copy number)	True	True	True

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 Technical Note available at [illumina.com](http://illumina.com). 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 found regions.

GapSizeThreshold	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
GcWaveAdjustLRR	Set this flag to true if you want to adjust Log R Ratios for GC waves	False	True	False
GcWaveAdjustmentWindow	The GC wave adjustment window	115000	True	False

Parameter Name	Description	Default Value	Mandatory	Visible in GUI?
Include Mitochondria	Set this flag to True if you want to include mitochondrial chromosomes in this analysis. NOTE: KaryoStudio excludes mitochondrial chromosomes from analysis.	False	True	False
IncludeSex Chromosomes	Set this flag to True if you want to include X, Y, and XY (pseudoautosomal) chromosomes in this analysis. NOTE: KaryoStudio excludes pseudoautosomal regions from analysis.	False	True	True
LogDiagnosticInfo	Log diagnostic info to a file in the application's temp file directory. The log directory location on Windows XP machines is: C:\Documents and Settings\<username> \Local Settings\Application Data\Illumina\cnvPartition	False	True	False
MinHomozygoteCount	Minimum number of homozygotes needed to detect a region of extended homozygosity  See the DNA Copy Number Analysis Technical Note for more details.	50	True	True
MinHomozygous RegionSize	Homozygous regions smaller than this are not detected	10 Mb	True	True
MinProbeCount	Regions with probe counts smaller than this are removed from analysis results.	3	True	False
SmoothingMoving AveragePeriod	The smoothing moving average period	2	True	True
SmoothLRR	Set this flag to true if you want to smooth the Log R Ratio	True	True	True

## 6. Technical Support

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

## 7. Version History

Build	Date
v2.4.4 for GenomeStudio and KaryoStudio Software	11/11/09
<ul style="list-style-type: none"> <li>Improved consistency between 32-bit and 64-bit PCs—Fixed an occasional rounding issue with 32-bit PCs.</li> <li>Improved consistency between GenomeStudio software and KaryoStudio software—The upcoming release of KaryoStudio also includes this fix.</li> </ul>	

- 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 `AdjustYLR`
- 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
<b>v2.3.4 for GenomeStudio and KaryoStudio Software</b>	<b>03/09/09</b>

- 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
<b>v2.2.1 for GenomeStudio and KaryoStudio Software</b>	<b>01/22/09</b>

- `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
<b>v1.2.0 for BeadStudio</b>	<b>10/10/08</b>
<ul style="list-style-type: none"> <li>Added configuration file</li> <li>All chromosomes starting with letter "M" are now recognized as mitochondrial.</li> <li>B Allele Frequency is now ignored for Intensity Only probes.</li> <li>Added configuration option to detect extended regions of homozygosity such as copy-neutral LOH (default = True)</li> <li>Added configuration option for the minimum size of a detected region of homozygosity</li> <li>Added configuration option to ignore CNV regions with less than a minimum number of probes defined by the user (default=3)</li> </ul>	
Build	Date
<b>v1.0.2 for BeadStudio</b>	<b>3/11/08</b>
<ul style="list-style-type: none"> <li>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.</li> <li>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.</li> <li>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.</li> </ul>	
Build	Date
<b>v1.0.1 for BeadStudio</b>	<b>1/29/08</b>
<ul style="list-style-type: none"> <li>Improved detection of smaller CNVs</li> <li>Both Log R Ratio and B Allele Frequency are used as inputs.</li> <li>Mitochondrial SNPs can be included in an analysis (optionally).</li> <li>The CNV Confidence score is now calculated.</li> </ul>	
Build	Date
<b>v0.9.3 for BeadStudio</b>	<b>09/04/07</b>
<ul style="list-style-type: none"> <li>Improved classification of CN = 0 regions (homozygous deletions)</li> <li>Lowered the Min SNPs Per Bin parameter default to ten (from 30) to improve detection of CN = 0 regions (homozygous deletions)</li> </ul>	
Build	Date
<b>v0.9.2 for BeadStudio</b>	<b>07/23/07</b>
<ul style="list-style-type: none"> <li>First release</li> </ul>	

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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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