

# Package ‘CNVrd2’

April 5, 2014

**Type** Package

**Title** CNVrd2: a read depth-based method to detect and genotype complex common copy number variants from next generation sequencing data.

**Version** 1.0.0

**Date** 2014-03-28

**Author** Hoang Tan Nguyen, Tony R Merriman and MA Black

**Depends** R (>= 3.0.0), DNACopy, methods, Rsamtools, VariantAnnotation, parallel, rjags, ggplot2, gridExtra

**VignetteBuilder** knitr

**Suggests** knitr

**Maintainer** Hoang Tan Nguyen <hoangtannguyenvn@gmail.com>

**Description** CNVrd2 uses next-generation sequencing data to measure human gene copy number for multiple samples, identify SNPs tagging copy number variants and detect copy number polymorphic genomic regions.

**License** GPL-2

**Imports** IRanges

**biocViews** High Throughput Sequencing, CNV, SNP.

**Collate** AllClasses.R AllGenerics.R countReadInWindow.R  
segmentSamples.R segmentSamplesUsingPopInformation.R  
identifyPolymorphicRegion.R plotPolymorphicRegion.R  
emnormalCNV.R groupCNVs.R searchGroupCNVs.R groupBayesianCNVs.R  
plotCNVrd2.R calculateLDSNPandCNV.R

**URL** <https://github.com/hoangtn/CNVrd2>

**R topics documented:**

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CNVrd2-package	<i>CNVrd2</i>
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**Description**

CNVrd2 uses next-generation sequencing data to measure human gene copy number for multiple samples and identify SNPs/INDELs which are in linkage disequilibrium with the gene copy number variation.

**Details**

Package:	CNVrd2
Type:	Package
Version:	1.0
Date:	2013-03-26
License:	GPL-2

Depends: methods

### Author(s)

Maintainer: Hoang Tan Nguyen <hoangtannguyenvn@gmail.com>

---

calculateLDSNPandCNV *calculateLDSNPandCNV*

---

### Description

Identifying SNPs/INDELs being in linkage disequilibrium with CNV.

### Usage

```
calculateLDSNPandCNV(sampleCNV = NULL, vcfFile = NULL,
matrixGenotype = NULL, cnvColumn = NULL, popColumn = NULL,
population = NULL, chr = NULL, hg = "hg19",
st = NULL, en = NULL, nChunkForVcf = 10,
codeSNP = c("Two", "Three"), codeCNV = c("CN", "ThreeGroup"),
typeTest = c("All", "Dup", "Del"), parallel = FALSE)
```

### Arguments

sampleCNV	A data frame with no missing data; The first column is samples, the other columns are copy number, population names. This object can be obtained from the clustering step (allGroups).
vcfFile	Name of zipped vcf file including SNPs/INDELs.
matrixGenotype	A matrix of SNPs/INDELs coded: 0 for 0 0 or 0/0; 1 for 0/1, 1/0, 0 1, 1 0; 2 for 1/1, 1 1. Rows are SNPs/INDELs and columns are samples. If users use this argument then the argument vcfFile is not necessary.
cnvColumn	A number indicating the column of CNV.
popColumn	A number indicating the column of a population being calculated LD values.
population	A character() vector indicating names of populations.
chr	A character string indicating a chromosome of genes/SNPs/INDELs.
hg	A character string indicating the version of a reference genome (default: hg19).
st	A number indicating a starting coordinate to read the vcf file.
en	A number indicating an ending coordinate to read the vcf file.
nChunkForVcf	A number indicating how many chunks users would like to divide the vcf file to read into R. It depends on users' computers. We usually use 10 to 50 for this argument.



```
tagSNPandINDELofMXL[1:3,]  
nChunkForVcf = 5, chr = "1",  
st = 161600000, en = 161611000,  
codeSNP= "Three", codeCNV = "ThreeGroup")
```

---

ccl3l1data

*Data of CCL3L1 gene (The 1000 Genomes Project)*

---

### Description

This data set includes: segmentation results, population information and CCL3L1 CN.

### Usage

```
data(ccl3l1data)
```

### Format

This is a data frame including four columns: *Name* (names of samples), *Pop* (names of populations), *SS* (segmentation scores of samples at the gene) and *CN* (CCL3L1 CN obtained by using a Bayesian clustering approach with European-ancestry as prior information).

### References

[www.1000genomes.org](http://www.1000genomes.org)

---

clusteringCNVs-class

*Class "clusteringCNVs"*

---

### Description

This class is used to cluster segmentation scores into copy-number groups.

### Objects from the Class

Objects can be created by calls of the form `new("clusteringCNVs", ...)`.

**Slots**

**x:** Object of class "numeric".  
**k:** Object of class "numeric" indicating a number of groups.  
**p:** Object of class "numericOrNULL" indicating groups' proportions.  
**m:** Object of class "numericOrNULL" indicating groups' means.  
**sigma:** Object of class "numericOrNULL" indicating groups' standard deviations.  
**small:** Object of class "numeric" indicating the value to stop the iteration process of the EM algorithm.  
**nMax:** Object of class "numeric" indicating a maximum number of iterations.  
**EV:** Object of class "logical" indicating whether all groups having equal variances or not (default).  
**eee:** Object of class "numeric" indicating a pseudo value of 0.  
**nmaxInit:** Object of class "numeric" indicating a number of iterations to obtain initial values.  
**nChangeVariance:** Object of class "numeric" indicating a number of times to change from unequal variances to equal variances (*"this option is used to avoid the EM algorithm being broken down if there is one (or a few) sample in a group"*).  
**verbose:** Object of class "logical" indicating whether printing out all loops.  
**groupDistance:** Object of class "numericOrNULL" indicating the distance between groups.

**Methods**

**emnormalCNV** signature(Object = "clusteringCNVs"): run the EM algorithm.  
**groupCNVs** signature(Object = "clusteringCNVs"): cluster segmentation scores into groups.  
**searchGroupCNVs** signature(Object = "clusteringCNVs"): identify a number of groups.

**Author(s)**

Hoang Tan Nguyen, Tony R Merriman and MA Black. <hoangtannguyenvn@gmail.com>

**Examples**

```
showClass("clusteringCNVs")
```

---

 CNVrd2-class

 Class "CNVrd2"
 

---

**Description**

A class of reading BAM files into R and grouping read-count windows into similar segments.

**Objects from the Class**

Objects can be created by calls of the form `new("CNVrd2", ...)`.

**Slots**

**windows:** Object of class "numeric" indicating a window size.  
**chr:** Object of class "character" indicating the chromosome of the region.  
**st:** Object of class "numeric" indicating the starting coordinate of the region.  
**en:** Object of class "numeric" indicating the ending coordinate of the region.  
**dirBamFile:** Object of class "character" indicating a directory of BAM files.  
**dirCoordinate:** Object of class "character" indicating a directory where all the positions of mapped reads will be written out to prepare for the segmentation process.  
**genes:** Object of class "numeric" indicating gene coordinates.  
**geneNames:** Object of class "character" indicating names of genes.

**Methods**

**countReadInWindow** signature(Object = "CNVrd2"): Count reads in windows.  
**plotCNVrd2** signature(Object = "CNVrd2"): Plot traces of samples.  
**segmentSamples** signature(Object = "CNVrd2"): Cluster windows of read counts into regions having similar signal values.

**Author(s)**

Hoang Tan Nguyen, Tony R Merriman and MA Black. <hoangtannguyenvn@gmail.com>

**Examples**

```
showClass("CNVrd2")
```

---

countReadInWindow      *Obtain read counts in constant windows.*

---

**Description**

Counting, transferring and standardizing read counts for all windows of samples. If correctGC = TRUE then all read-count windows will be corrected by the method of Yoon et al. (2009).

**Usage**

```
countReadInWindow(Object, ...)
```

**Arguments**

Object            An object of class CNVrd2.  
...                Further arguments.

**Value**

readCountMatrix: a matrix of read counts for all samples (rows).

**Author(s)**

Hoang Tan Nguyen, Tony R Merriman and MA Black. <hoangtannguyenvn@gmail.com>

**References**

Yoon, S., Xuan, Z., Makarov, V., Ye, K., Sebat, J., 2009. Sensitive and accurate detection of copy number variants using read depth of coverage. *Genome research* 19 (9), 1586-1592.

**Examples**

```
## Not run:
data(fcgr3bMXL)
bamFiles <- dir("Bam", pattern = ".bam$")
objectCNVrd2 <- new("CNVrd2", windows = 1000, chr = "chr1",
                  st = 161100001, en = 162100000,
                  dirBamFile = "Bam",
                  genes = c(161592986, 161601753),
                  geneNames = "3B")

readCountMatrix <- countReadInWindow(Object = objectCNVrd2, correctGC = TRUE)
readCountMatrix[1:3, 1:3]

## End(Not run)
```

---

countReadInWindow-methods

*Method* countReadInWindow

---

**Description**

Method to count reads in windows

**Methods**

signature(Object = "CNVrd2") Count, transfer and standardize read count in windows of samples

**See Also**

[countReadInWindow](#)



## Examples

```
##data(fcgr3bMXL)
##readCountMatrix <- countReadInWindow(Object = objectCNVrd2, correctGC = TRUE)
##readCountMatrix[1:3, 1:3]
```

---

emnormalCNV

*Implement the EM algorithm*

---

## Description

This function is used to obtain the maximization likelihood estimation of normal mixture model by using the EM algorithm (Demster et al., 1977).

## Usage

```
emnormalCNV(Object, ...)
```

## Arguments

Object	An object of class clusteringCNVs.
...	Optional arguments

## Value

loglk	Value of the likelihood function.
p	Proportions of groups.
m	Means of groups.
sigma	Standard deviations of groups.
count	A number of iteration to obtain convergence stage.
bic	See <a href="#">searchGroupCNVs</a> .
z	Data frame of proportions of data in mixture components.

## Note

In the package, the distance between two initial means of the two nearest neighbor groups was set `groupDistance = 0.25` as a default value to obtain initial values (using the `kmeans` function in R).

## Author(s)

Hoang Tan Nguyen, Tony R Merriman and MA Black. <hoangtannguyenvn@gmail.com>

## References

Dempster, A. P., Laird, N. M., Rubin, D. B., 1977. Maximum likelihood from incomplete data via the em algorithm. *Journal of the Royal Statistical Society. Series B (Methodological)*, 1-38.

**See Also**

[searchGroupCNVs](#), [groupCNVs](#)

**Examples**

```
data(fcgr3bMXL)

sS <- resultSegment$segmentationScores
#####Histogram#####
###View segmentation scores#####
hist(sS[, 1], 100)
#####
###Number of components#####
###Make an object of clusteringCNVs class#####
objectCluster <- new("clusteringCNVs",
                     x = sS[, 1], k = 4, EV = TRUE)

set.seed(123)
copynumberGroups <- groupCNVs(Object = objectCluster)
```

---

emnormalCNV-methods      *Method* emnormalCNV

---

**Description**

Implement the Expectation Maximization

**Methods**

```
signature(Object = "clusteringCNVs")
```

---

fcgr3bMXL      *MXL population data (The 1000 Genomes Project)*

---

**Description**

This data set includes: segmentation results “resultSegment”, information copy number “copynumberGroups” of *FCGR3B* gene.

**Usage**

```
data(fcgr3bMXL)
```

**Format**

All results analysed by the CNVrd2 package.

**References**

[www.1000genomes.org](http://www.1000genomes.org)

---

groupBayesianCNVs      *groupBayesianCNVs*

---

**Description**

Cluster segmentation scores into different groups by using prior information from one population.

**Usage**

```
groupBayesianCNVs(xData, nGroups, lambda0, sd0, alpha0, distanceBetweenGroups, inits = NULL,
precisionOfGroupMeans = 3000, sdOftau = NULL, n.adapt = 100,
nUpdate = 1000, n.iter = 20000, thin = 5, n.chains = 1,
heidel.diag = FALSE, leftLimit = NULL, rightLimit = NULL)
```

**Arguments**

xData	a numeric vector of observations (segmentation scores).
nGroups	an integer indicating a number of groups.
lambda0	Prior means of groups.
sd0	Prior standard deviations of groups.
alpha0	Prior parameters for mixing proportions.
distanceBetweenGroups	Prior value for the distance between groups.
inits	A list of initial values of parameters.
precisionOfGroupMeans	Prior parameter of group means (default = 3000).
sdOftau	Prior parameter of the standard deviations of group precisions.
n.adapt	the number of iterations for adaptation (rjags's parameter)
nUpdate	the number of iterations for burn-in process.
n.iter	the number of iterations for sampling (rjags's parameter)
thin	thinning interval for monitors (rjags's parameter)
n.chains	the number of parallel chains for the model (rjags's parameter, default = 1)
heidel.diag	If heidel.diag = TRUE then Heidelberg and Welch's convergence diagnostic is used.
leftLimit	Values which are less than this value will be allocated to the smallest group.
rightLimit	Values which are larger than this value will be allocated to the largest group.

**Details**

This function assumes that users already know the information of groups' means, standard deviations; the distances between groups.

**Value**

mcmcChains	A list of marray objects for means, standard deviations, proportions
m1	Means of groups
s1	Standard deviations of groups
p1	Proportions of groups
allGroups	A data.frame includes samples and their corresponding groups
hTest	Results of Heidelberger and Welch's convergence diagnostic

**Note**

#####

**Author(s)**

Hoang Tan Nguyen, Tony R Merriman and MA Black. <hoangtannguyenvn@gmail.com>

**References**

Martyn Plummer (2013). rjags: Bayesian graphical models using MCMC. R package version 3-10. <http://CRAN.R-project.org/package=rjags>.

Lunn, David J., et al. WinBUGS-a Bayesian modelling framework: concepts, structure, and extensibility. Statistics and Computing 10.4 (2000): 325-337.

**See Also**

[groupCNVs](#)

**Examples**

```
## Not run:
data(cc13l1data)

xyEuro <- cc13l1data[grep("CEU|TSI|IBS|GBR|FIN", cc13l1data[, 2]), ]

names(yEuro) <- rownames(xyEuro)

##Clustering European segmentation scores into group: 5 groups were chosen

objectClusterEuroCCL3L1 <- new("clusteringCNVs", x = yEuro, k = 5)

europeanCCL3L1Groups <- groupCNVs(Object = objectClusterEuroCCL3L1)

##Obtain prior information
#Means
```



---

`groupCNVs`*Cluster segmentation scores into groups.*

---

**Description**

Use the EM algorithm (Dempster et al., 1977) to cluster segmentation scores into various groups.

**Usage**

```
groupCNVs(Object, ...)
```

**Arguments**

Object	An object of class <code>clusteringCNVs</code> .
...	Further arguments.

**Details**

Users can set limits of segmentation scores: values being smaller than the left limit will be assigned to the smallest group and values being larger than right limit will be assigned to the largest group.

**Value**

<code>allGroups</code>	Samples and their corresponding groups
<code>means</code>	Means of groups.
<code>sigma</code>	Variances of groups.
<code>p</code>	Proportions of groups in all data set.
<code>loglk</code>	Value of loglikelihood function.

**Author(s)**

Hoang Tan Nguyen, Tony R Merriman and MA Black. <hoangtannguyenvn@gmail.com>

**References**

Dempster, A. P., Laird, N. M., Rubin, D. B., 1977. Maximum likelihood from incomplete data via the em algorithm. *Journal of the Royal Statistical Society. Series B (Methodological)*, 1-38.

**See Also**

[emnormalCNV](#), [searchGroupCNVs](#)

**Examples**

```

data("fcgr3bMXL")
#resultSegment <- segmentSamples(Object = objectCNVrd2, stdCntMatrix = readCountMatrix)
objectCluster <- new("clusteringCNVs",
                    x = resultSegment$segmentationScores[, 1], k = 4, EV = TRUE)

#searchGroupCNVs(Object = objectCluster)
copynumberGroups <- groupCNVs(Object = objectCluster)

```

---

groupCNVs-methods	<i>Method</i> groupCNVs
-------------------	-------------------------

---

**Description**

Method groupCNVs

**Methods**

```
signature(Object = "clusteringCNVs")
```

---

identifyPolymorphicRegion	<i>Identify polymorphic regions.</i>
---------------------------	--------------------------------------

---

**Description**

Using quantile values to identify polymorphic regions.

**Usage**

```
identifyPolymorphicRegion(Object, ...)
```

**Arguments**

Object	An object of class CNVrd2
...	polymorphicRegionObject An object obtained from the process of identifying polymorphic regions. Optional arguments.





---

identifyPolymorphicRegion-methods

*Methods for Function* identifyPolymorphicRegion

---

### **Description**

Methods for function identifyPolymorphicRegion

### **Methods**

signature(Object = "CNVrd2")

---

numericOrNULL-class    *Class "numericOrNULL"*

---

### **Description**

Auxiliary classes; may contain either a numeric vector or NULL [or a call / data.frame or NULL, respectively].

### **Objects from the Class**

A virtual Class: No objects may be created from it.

### **Methods**

No methods defined with class "numericOrNULL" in the signature.

### **Author(s)**

Hoang Tan Nguyen, Tony R Merriman and MA Black. <hoangtannguyenvn@gmail.com>

---

plotCNVrd2                      *Plot traces of samples.*

---

**Description**

Plot traces of samples.

**Usage**

```
plotCNVrd2(Object, ...)
```

**Arguments**

Object	An object of class CNVrd2.
...	Optional arguments.

**Value**

Plot

**Note**

Users can plot multiple samples simultaneously.

**Author(s)**

Hoang Tan Nguyen, Tony R Merriman and MA Black. <hoangtannguyenvn@gmail.com>

**Examples**

```
data(fcgr3bMXL)
##Obtain all information of CNVs
allGroups <- copynumberGroups$allGroups
###Obtain names of duplicate samples
duplicatedSamples <- rownames(allGroups[allGroups[, 2] > 2,])
###Plot the first duplicate samples
par(mfrow = c(3, 2))
for (ii in duplicatedSamples[1:6])
plotCNVrd2(Object = objectCNVrd2,
            segmentObject = resultSegment,
            sampleName = ii)
```

---

plotCNVrd2-methods      *Method* plotCNVrd2

---

**Description**

Method plotCNVrd2

**Methods**

signature(Object = "CNVrd2")

---

plotPolymorphicRegion      *Plot polymorphic regions.*

---

**Description**

Plot polymorphic regions based on coordinates set by users.

**Usage**

plotPolymorphicRegion(Object, ...)

**Arguments**

Object	An object of class CNVrd2
...	polymorphicRegionObject An object obtained from the process of identifying polymorphic regions. Optional arguments.

**Value**

putativeBoundary  
Putative boundaries of polymorphic regions based on quantile values.

**Note**

Users can choose various quantile values and adjust different thresholds to obtain polymorphic regions.

**Author(s)**

Hoang Tan Nguyen, Tony R Merriman and MA Black. <hoangtannguyenvn@gmail.com>

**See Also**

[identifyPolymorphicRegion](#)

**Examples**

```
## Not run:

plotPolymorphicRegion(Object = objectCNVrd2, polymorphicRegionObject = fcgr3PolymorphicRegion,
  xlim = c(161300000, 161800000), drawThresholds = TRUE,
  thresholdForPolymorphicRegions = c(0.75, 0.25))

##Change thresholds
plotPolymorphicRegion(Object = objectCNVrd2, polymorphicRegionObject = fcgr3PolymorphicRegion,
  xlim = c(161300000, 161800000), drawThresholds = TRUE,
  thresholdForPolymorphicRegions = c(0.9, 0.1))

##Plot standard deviation

plotPolymorphicRegion(Object = objectCNVrd2, polymorphicRegionObject = fcgr3PolymorphicRegion,
  xlim = c(161300000, 161800000), typePlot = "SD",
  thresholdForPolymorphicRegions = c(0.75, 0.25))

## End(Not run)
```

---

plotPolymorphicRegion-methods

*Methods for Function plotPolymorphicRegion*

---

**Description**

Methods for function plotPolymorphicRegion

**Methods**

signature(Object = "CNVrd2")

---

searchGroupCNVs

*Choose a number of CN groups*

---

**Description**

Choose a number of CN groups by using Bayesian Information Criterion (Schwarz, 1978).

**Usage**

```
searchGroupCNVs(Object, ...)
```

**Arguments**

Object	An object of class <i>clusteringCNVs</i> .
...	Optional arguments.

**Value**

Groups	General information.
nComponents	A suitable number of components.

**Author(s)**

Hoang Tan Nguyen, Tony R Merriman and MA Black. <hoangtannguyenvn@gmail.com>

**References**

Schwarz, G. , 1978. Estimating the dimension of a model. The Annals of Statistics 6(2), 461-464.

---

```
searchGroupCNVs-methods
      Method searchGroupCNVs
```

---

**Description**

Method searchGroupCNVs

**Methods**

```
signature(Object = "clusteringCNVs")
```

---

```
segmentSamples      Implement the segmentation process
```

---

**Description**

Segment read-count windows into region having similar signal values by using the DNACopy package (Venkatraman and Olshen, 2007) and refine this process to obtain segmentation scores at genes.

**Usage**

```
segmentSamples(Object, ...)
```

**Arguments**

Object            An object of class CNVrd2.  
...                Optional arguments.

**Value**

segmentResults   All results of the segmentation process.  
segmentationScores        Segmentation scores of the gene(s) being measured.  
observedReadCountRatios    Observed read-count ratios of genes. This value is a matrix of observed read-count ratios at genes if (only inputBamFile = TRUE).  
stdCntMatrix        Matrix of read counts (standardized).

**Author(s)**

Hoang Tan Nguyen, Tony R Merriman and MA Black. <hoangtannguyenvn@gmail.com>

**References**

Venkatraman, E., Olshen, A. B., 2007. A faster circular binary segmentation algorithm for the analysis of array chg data. *Bioinformatics* 23 (6), 657-663.

**See Also**

[countReadInWindow](#), DNACopy

**Examples**

```
data(fcgr3bMXL)
## Not run: resultSegment <- segmentSamples(Object = objectCNVrd2, stdCntMatrix = readCountMatrix)
```

---

segmentSamples-methods

*Method* segmentSamples

---

**Description**

Method segmentSamples

**Methods**

signature(Object = "CNVrd2")

---

`segmentSamplesUsingPopInformation`*Implement the segmentation process for multiple populations*

---

**Description**

Segment read-count windows into region having similar signal values by using the DNACopy package (Venkatraman and Olshen, 2007) and refine this process to obtain segmentation scores at genes. Then, the function adjusts segmentation scores for multiple populations using a linear regression model.

**Usage**

```
segmentSamplesUsingPopInformation(Object, ...)
```

**Arguments**

Object	An object of class CNVrd2.
...	Optional arguments.

**Value**

segmentationScores	All adjusted results of the segmentation process.
segmentationScoresFromSinglePops	Segmentation scores of single populations.
segmentResults	Un-adjusted segmentation scores
observedReadCountRatios	Observed read-count ratios of genes. This value is a matrix of observed read-count ratios at genes if (only inputBamFile = TRUE).
stdCntMatrix	Matrix of read counts (standardized).

**Author(s)**

Hoang Tan Nguyen, Tony R Merriman and MA Black. <hoangtannguyenvn@gmail.com>

**References**

Venkatraman, E., Olshen, A. B., 2007. A faster circular binary segmentation algorithm for the analysis of array chg data. *Bioinformatics* 23 (6), 657-663.

**See Also**

[countReadInWindow](#), DNACopy

segmentSamplesUsingPopInformation-methods  
*Method* segmentSamplesUsingPopInformation

---

**Description**

Method segmentSamplesUsingPopInformation

**Methods**

signature(Object = "CNVrd2")

---

vectorORfactor-class *Class* "vectorORfactor"

---

**Description**

Auxiliary class

**Objects from the Class**

A virtual Class: No objects may be created from it.

**Methods**

No methods defined with class "vectorORfactor" in the signature.

**Author(s)**

Hoang Tan Nguyen, Tony Merriman and Mik Black. <hoangtannguyenvn@gmail.com>



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