

# Package ‘HiSpaR’

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**Type** Package

**Title** Hierarchical Inference of Spatial Positions from Hi-C Data

**Version** 1.0.0

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**Description** Provides R bindings for HiSpa, a hierarchical Bayesian model for inferring three-dimensional chromatin structures from Hi-C contact matrices using Markov Chain Monte Carlo (MCMC) sampling. The package implements a cluster-based hierarchical approach that efficiently handles large-scale Hi-C datasets. It uses Rcpp and RcppArmadillo for efficient C++ integration with the original HiSpa C++ implementation, enabling fast computation of chromatin structure inference through parallel MCMC sampling.

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**Depends** R (>= 4.5.0)

**Imports** Rcpp (>= 1.0.0), utils, stats, Matrix, HiCExperiment

**biocViews** Software, Epigenetics, HiC, StructuralPrediction, Bayesian, Spatial

**LinkingTo** Rcpp, RcppArmadillo

**SystemRequirements** C++17, GNU make, Armadillo (>= 9.0), OpenMP

**URL** <https://github.com/masterStormtrooper/HiSpaR>

**BugReports** <https://github.com/masterStormtrooper/HiSpaR/issues>

**Encoding** UTF-8

**LazyData** false

**RoxygenNote** 7.3.3

**Suggests** testthat (>= 3.0.0), knitr, rmarkdown, BiocStyle, rgl, HiContactsData, HiContacts, plotly, callr

**VignetteBuilder** knitr

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HiSpaR-package	<i>HiSpaR: Hierarchical Inference of Spatial Positions from Hi-C Data</i>
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## Description

HiSpaR provides R bindings for the HiSpa C++ library, enabling hierarchical Bayesian inference of 3D chromatin structures from Hi-C contact matrices.

## Details

The package provides functions to:

- Analyze Hi-C contact matrices using MCMC sampling
- Infer 3D chromatin structures
- Use prior information from other datasets
- Perform cluster-based hierarchical analysis

Main functions:

- [hispa\\_analyze](#): Run complete HiSpa analysis

## Author(s)

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## See Also

Useful links:

- <https://github.com/masterStormtrooper/HiSpa>
- Report bugs at <https://github.com/masterStormtrooper/HiSpa/issues>

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hispa_analyze	<i>Run HiSpa MCMC Analysis</i>
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### Description

Performs hierarchical Bayesian inference of 3D chromatin structure from Hi-C contact matrix using MCMC sampling. This function follows the exact workflow from the HiSpa C++ implementation.

### Usage

```
hispa_analyze(  
  hic_experiment,  
  output_dir,  
  mcmc_iterations = 6000L,  
  num_clusters = 0L,  
  mcmc_burn_in = 0L,  
  mcmc_initial_sd = 0.1,  
  mcmc_sd_floor = 1e-04,  
  mcmc_sd_ceil = 0.3,  
  use_cluster_init = FALSE,  
  cluster_init_iterations = 1000L,  
  cluster_initial_sd = 0.1,  
  save_samples = FALSE,  
  sample_interval = 50L,  
  verbose = TRUE,  
  filter_quantile = -1,  
  safe_mode = TRUE  
)
```

### Arguments

hic_experiment	A Bioconductor 'HiCExperiment' object or a numeric matrix containing Hi-C contact data. If a 'HiCExperiment' object, the function extracts the contact matrix using 'gi2cm()' from the interactions and converts it to a numeric matrix for analysis. If a matrix, it is used directly.
output_dir	Character string specifying the output directory path.
mcmc_iterations	Integer, number of MCMC iterations (default: 6000).
num_clusters	Integer, number of clusters for hierarchical analysis. If 0 (default), automatically determined as sqrt(n).
mcmc_burn_in	Integer, number of burn-in iterations to discard (default: 0).
mcmc_initial_sd	Numeric, initial standard deviation for MCMC proposals (default: 0.1).
mcmc_sd_floor	Numeric, minimum allowed standard deviation (default: 0.0001).
mcmc_sd_ceil	Numeric, maximum allowed standard deviation (default: 0.3).

<code>use_cluster_init</code>	Logical, use cluster-based initialization instead of random initialization (default: FALSE).
<code>cluster_init_iterations</code>	Integer, number of iterations for cluster initialization MCMC (default: 1000).
<code>cluster_initial_sd</code>	Numeric, initial standard deviation for cluster initialization MCMC (default: 0.1).
<code>save_samples</code>	Logical, whether to save MCMC trace samples (default: FALSE).
<code>sample_interval</code>	Integer, save samples every n iterations (default: 50).
<code>verbose</code>	Logical, enable verbose output (default: TRUE).
<code>filter_quantile</code>	Numeric, quantile threshold for filtering loci by contact counts (default: -1, no filtering). If $\geq 0$ , loci with row sums below this quantile are removed. For example, 0.1 removes loci in the bottom 10% of contact counts.
<code>safe_mode</code>	Logical, whether to run analysis in a safe subprocess using callr (default: TRUE). If TRUE and callr is available, analysis runs in an isolated subprocess to prevent R crashes from affecting the parent session. Set to FALSE to run inline.

## Details

This function implements the complete HiSpa workflow:

1. Filter loci by contact count (optional)
2. Load contact matrix from file
3. Assign loci to clusters (k-means)
4. Build cluster relationships
5. Initialize structure (random or cluster-based)
6. Assemble global structure
7. Run main MCMC algorithm
8. Save results to output directory

**Locus Filtering:** By default, no filtering is applied (`filter_quantile = -1`). If `filter_quantile`  $\geq 0$ , loci with contact counts below the specified quantile are removed before analysis. For example, `filter_quantile = 0.1` removes loci in the bottom 10% of contact counts. This improves computational efficiency and focuses analysis on loci with sufficient data.

All results are automatically saved to the output directory:

- **final\_positions.txt** - Final inferred 3D coordinates (n x 3 matrix)
- **initial\_positions.txt** - Initial positions before MCMC (n x 3 matrix)

Read results using standard R functions: `final_pos <- read.table("output_dir/final_positions.txt")`

**Value**

A list containing:

- **positions** - A numeric matrix of dimensions  $n \times 3$  containing the final inferred 3D coordinates of loci. Rows correspond to loci, columns are (x, y, z).
- **beta0** - The final intercept parameter of the log-distance relationship.
- **beta1** - The final slope parameter of the log-distance relationship.

If filtering was applied, the positions matrix has an attribute 'filtered\_locus\_indices' containing the original indices of the retained loci (before filtering). Additionally, all analysis results are saved as text files in the output directory.

**Examples**

```
# Load example contact matrix
data(su1_contact_mat)

# Check dimensions
dim(su1_contact_mat)

# Example 1: Run analysis with matrix input
su_res <- hispa_analyze(
  hic_experiment = su1_contact_mat,
  output_dir = tempdir(),
  mcmc_iterations = 100,
  mcmc_burn_in = 10,
  use_cluster_init = FALSE,
  verbose = TRUE
)

# check results
dim(su_res$positions) # Should be n x 3
```

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su1\_contact\_mat

*Example Hi-C Contact Matrix*

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**Description**

Hi-C contact matrix of Human Chromosome 21, collected from <https://zenodo.org/records/3928890>. This dataset is provided as an example for testing and demonstrating the HiSpaR package functionality.

**Usage**

```
su1_contact_mat
```

**Format**

A symmetric numeric matrix with 649 rows and 649 columns, where entry (i,j) represents the normalized contact frequency between genomic loci i and j. The matrix is:

**Dimensions** 649 x 649

**Type** Numeric matrix

**Symmetry** Symmetric (contact\_matrix[i,j] = contact\_matrix[j,i])

**Diagonal** Zero or near-zero (self-contacts)

**Range** Non-negative contact frequencies

**Details**

This contact matrix represents chromatin interaction frequencies derived from Hi-C experiments on Human Chromosome 21. Higher values indicate more frequent spatial proximity between genomic loci in the 3D nuclear space.

The data can be used directly with [hispa\\_analyze](#)

**Source**

Human Hi-C data, chromosome 21, collected from <https://zenodo.org/records/3928890>

**See Also**

[hispa\\_analyze](#) for running the analysis

**Examples**

```
# Load the example data
data(su1_contact_mat)

# Check dimensions
dim(su1_contact_mat)

# Check if matrix is symmetric
isSymmetric(su1_contact_mat)

# Summary statistics
summary(as.vector(su1_contact_mat))

# Visualize contact matrix
image(su1_contact_mat,
      main = "Hi-C Contact Matrix (SU1)",
      xlab = "Genomic Locus",
      ylab = "Genomic Locus")
```

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