

# HOWARD Help Parameters Databases

## Contents

<b>1</b>	<b>Introduction</b>	<b>3</b>
<b>2</b>	<b>assembly</b>	<b>5</b>
<b>3</b>	<b>genomes_folder</b>	<b>5</b>
<b>4</b>	<b>genome</b>	<b>5</b>
<b>5</b>	<b>genomes</b>	<b>5</b>
5.1	download_genomes . . . . .	5
5.2	download_genomes_provider . . . . .	6
5.3	download_genomes_contig_regex . . . . .	6
<b>6</b>	<b>snpeff</b>	<b>6</b>
6.1	download_snpeff . . . . .	6
<b>7</b>	<b>annovar</b>	<b>6</b>
7.1	download_annovar . . . . .	6
7.2	download_annovar_files . . . . .	6
7.3	download_annovar_url . . . . .	6
<b>8</b>	<b>refseq</b>	<b>6</b>
8.1	download_refseq . . . . .	7
8.2	download_refseq_url . . . . .	7
8.3	download_refseq_prefix . . . . .	7
8.4	download_refseq_files . . . . .	7
8.5	download_refseq_format_file . . . . .	7
8.6	download_refseq_include_utr5 . . . . .	7
8.7	download_refseq_include_utr3 . . . . .	7
8.8	download_refseq_include_chrM . . . . .	7
8.9	download_refseq_include_non_canonical_chr . . . . .	7
8.10	download_refseq_include_non_coding_transcripts . . . . .	8
8.11	download_refseq_include_transcript_version . . . . .	8
<b>9</b>	<b>dbnsfp</b>	<b>8</b>
9.1	download_dbnsfp . . . . .	8
9.2	download_dbnsfp_url . . . . .	8
9.3	download_dbnsfp_release . . . . .	8
9.4	download_dbnsfp_parquet_size . . . . .	8
9.5	download_dbnsfp_subdatabases . . . . .	8
9.6	download_dbnsfp_parquet . . . . .	8
9.7	download_dbnsfp_vcf . . . . .	9
9.8	download_dbnsfp_no_files_all . . . . .	9
9.9	download_dbnsfp_add_info . . . . .	9
9.10	download_dbnsfp_only_info . . . . .	9

9.11	download_dbnsfp_uniquify . . . . .	9
9.12	download_dbnsfp_row_group_size . . . . .	9
<b>10</b>	<b>alphamissense</b>	<b>9</b>
10.1	download_alphamissense . . . . .	9
10.2	download_alphamissense_url . . . . .	9
<b>11</b>	<b>exomiser</b>	<b>10</b>
11.1	download_exomiser . . . . .	10
11.2	download_exomiser_application_properties . . . . .	10
11.3	download_exomiser_url . . . . .	10
11.4	download_exomiser_release . . . . .	10
11.5	download_exomiser_phenotype_release . . . . .	10
11.6	download_exomiser_remm_release . . . . .	10
11.7	download_exomiser_remm_url . . . . .	10
11.8	download_exomiser_cadd_release . . . . .	11
11.9	download_exomiser_cadd_url . . . . .	11
11.10	download_exomiser_cadd_url_snv_file . . . . .	11
11.11	download_exomiser_cadd_url_indel_file . . . . .	11
<b>12</b>	<b>dbSNP</b>	<b>11</b>
12.1	download_dbSNP . . . . .	11
12.2	download_dbSNP_releases . . . . .	11
12.3	download_dbSNP_release_default . . . . .	11
12.4	download_dbSNP_url . . . . .	12
12.5	download_dbSNP_url_files . . . . .	12
12.6	download_dbSNP_url_files_prefix . . . . .	12
12.7	download_dbSNP_assemblies_map . . . . .	12
12.8	download_dbSNP_vcf . . . . .	12
12.9	download_dbSNP_parquet . . . . .	12
<b>13</b>	<b>hgmd</b>	<b>12</b>
13.1	convert_hgmd . . . . .	12
13.2	convert_hgmd_file . . . . .	13
13.3	convert_hgmd_basename . . . . .	13
<b>14</b>	<b>from_Annovar</b>	<b>13</b>
14.1	input_annovar . . . . .	13
14.2	output_annovar . . . . .	13
14.3	annovar_code . . . . .	13
14.4	annovar_to_parquet . . . . .	13
14.5	annovar_reduce_memory . . . . .	13
14.6	annovar_multi_variant . . . . .	14
<b>15</b>	<b>from_extann</b>	<b>14</b>
15.1	input_extann . . . . .	14
15.2	output_extann . . . . .	14
15.3	refgene . . . . .	14
15.4	transcripts . . . . .	14
15.5	param_extann . . . . .	14
15.6	mode_extann . . . . .	14
<b>16</b>	<b>Parameters</b>	<b>15</b>
16.1	generate_param . . . . .	15
16.2	generate_param_description . . . . .	15
16.3	generate_param_releases . . . . .	15
16.4	generate_param_formats . . . . .	15
16.5	generate_param_bcftools . . . . .	15

# 1 Introduction

HOWARD Parameters JSON file defines parameters for databases' downloads.

Examples:

Example of simple databases parameters JSON file for downloads

```
{
  "databases": {
    "genomes": {
      "download_genomes": "~/howard/databases/genomes/current",
      "download_genomes_contig_regex": "chr[0-9XYM]+$"
    },
    "snpeff": {
      "download_snpeff": "~/howard/databases/snpeff/current"
    },
    "annovar": {
      "download_annovar": "~/howard/databases/annovar/current",
      "download_annovar_files": "refGene,cosmic70,nci60"
    },
    "refseq": {
      "download_refseq": "~/howard/databases/refseq/current"
    },
    "dbnsfp": {
      "download_dbnsfp": "~/howard/databases/dbnsfp/current",
      "download_dbnsfp_release": "4.4a"
    },
    "alphamissense": {
      "download_alphamissense": "~/howard/databases/alphamissense/current"
    },
    "exomiser": {
      "download_exomiser": "~/howard/databases/exomiser/current"
    },
    "dbSNP": {
      "download_dbSNP": "~/howard/databases/dbSNP/current",
      "download_dbSNP_releases": "b156",
      "download_dbSNP_vcf": true,
      "download_dbSNP_parquet": true
    },
    "assemblies": [
      "hg19"
    ]
  }
}
```

Example of a full Databases parameters JSON file for downloads

```
{
  "databases": {
    "genomes_folder": "~/howard/databases/genomes/current",
    "genome": "~/howard/databases/genomes/current/hg19/hg19.fa",
    "genomes": {
      "download_genomes": "~/howard/databases/genomes/current",
      "download_genomes_provider": "UCSC",
      "download_genomes_contig_regex": "chr[0-9XYM]+$"
    },
    "snpeff": {
      "download_snpeff": "~/howard/databases/snpeff/current"
    }
  }
}
```

```

},
"annovar": {
  "download_annovar": "~/howard/databases/annovar/current",
  "download_annovar_files": "refGene,cosmic70,nci60",
  "download_annovar_url": "http://www.openbioinformatics.org/annovar/download"
},
"refseq": {
  "download_refseq": "~/howard/databases/refseq/current",
  "download_refseq_url": "http://hgdownload.soe.ucsc.edu/goldenPath",
  "download_refseq_prefix": "ncbiRefSeq",
  "download_refseq_files": "ncbiRefSeq.txt,ncbiRefSeqLink.txt",
  "download_refseq_format_file": "ncbiRefSeq.txt",
  "download_refseq_include utr5": false,
  "download_refseq_include utr3": false,
  "download_refseq_include chrM": false,
  "download_refseq_include_non_canonical_chr": false,
  "download_refseq_include_non_coding_transcripts": false,
  "download_refseq_include_transcript_version": false
},
"dbnsfp": {
  "download_dbnsfp": "~/howard/databases/dbnsfp/current",
  "download_dbnsfp_url": "https://dbnsfp.s3.amazonaws.com",
  "download_dbnsfp_release": "4.4a",
  "download_dbnsfp_parquet_size": 100,
  "download_dbnsfp_subdatabases": true,
  "download_dbnsfp_parquet": false,
  "download_dbnsfp_vcf": false,
  "download_dbnsfp_no_files_all": false,
  "download_dbnsfp_add_info": false,
  "download_dbnsfp_uniquify": false,
  "download_dbnsfp_row_group_size": 100000
},
"alphamissense": {
  "download_alphamissense": "~/howard/databases/alphamissense/current",
  "download_alphamissense_url": "https://storage.googleapis.com/dm_alphamissense"
},
"exomiser": {
  "download_exomiser": "~/howard/databases/exomiser/current",
  "download_exomiser_url": "http://data.monarchinitiative.org/exomiser",
  "download_exomiser_remm_url": "https://kircherlab.bihealth.org/download/ReMM",
  "download_exomiser_cadd_url": "https://kircherlab.bihealth.org/download/CADD",
  "download_exomiser_cadd_url_snv_file": "whole_genome_SNVs.tsv.gz",
  "download_exomiser_cadd_url_indel_file": "InDels.tsv.gz"
},
"dbsnp": {
  "download_dbsnp": "~/howard/databases/dbsnp/current",
  "download_dbsnp_releases": "b156",
  "download_dbsnp_url": "https://ftp.ncbi.nih.gov/snp/archive",
  "download_dbsnp_url_files_prefix": "GCF_000001405",
  "download_dbsnp_assemblies_map": {
    "hg19": "25",
    "hg38": "40"
  },
  "download_dbsnp_vcf": true,
  "download_dbsnp_parquet": false
},

```

```

        "parameters": {
            "generate_param_releases": "current",
            "generate_param_formats": "parquet",
            "generate_param_bcftools": false
        },
        "assemblies": [
            "hg19"
        ]
    }
}

```

## 2 assembly

Genome Assembly (e.g. 'hg19', 'hg38').

Type: `str`

Default: `hg19`

Examples:

Default assembly for all analysis tools

```

{
    "assembly": "hg19"
}

```

List of assemblies for databases download tool

```

{
    "assembly": "hg19,hg38"
}

```

## 3 genomes\_\_folder

Folder containing genomes. (e.g. '~/howard/databases/genomes/current')

Type: `Path`

Default: `~/howard/databases/genomes/current`

## 4 genome

Genome file in fasta format (e.g. 'hg19.fa', 'hg38.fa').

Type: `Path`

Default: `~/howard/databases/genomes/current/hg19/hg19.fa`

## 5 genomes

Genomes download.

### 5.1 download\_\_genomes

Path to genomes folder with Fasta files, indexes, and all files generated by pygenome module. (e.g. '~/howard/databases/genomes/current').

Type: `Path`

Default: `None`

## 5.2 download\_genomes\_provider

Download Genome from an external provider. Available: GENCODE, Ensembl, UCSC, NCBI.

Type: `str`

Choices: ['GENCODE', 'Ensembl', 'UCSC', 'NCBI']

Default: UCSC

## 5.3 download\_genomes\_contig\_regex

Regular expression to select specific chromosome (e.g 'chr[0-9XYM]+\$').

Type: `str`

Default: `None`

# 6 snpeff

snpEff download.

## 6.1 download\_snpeff

Download snpEff databases within snpEff folder

Type: `Path`

Default: `None`

# 7 annovar

Annovar download.

## 7.1 download\_annovar

Path to Annovar databases (e.g. '~/howard/databases/annovar/current').

Type: `Path`

Default: `None`

## 7.2 download\_annovar\_files

Download Annovar databases for a list of Annovar file code (see Annovar Doc). Use `None` to download all available files, or Annovar keyword (e.g. 'refGene', 'cosmic70', 'clinvar\_202\*'). Note that refGene will at least be downloaded, and only files that not already exist or changed will be downloaded.

Type: `str`

Default: `None`

## 7.3 download\_annovar\_url

Annovar databases URL (see Annovar Doc).

Type: `str`

Default: `http://www.openbioinformatics.org/annovar/download`

# 8 refseq

refSeq download.

## 8.1 download\_refseq

Path to refSeq databases (e.g. '~/howard/databases/refseq/current').

Type: `Path`

Default: `None`

## 8.2 download\_refseq\_url

refSeq databases URL (see refSeq WebSite) (e.g. 'http://hgdownload.soe.ucsc.edu/goldenPath') • /n

Type: `str`

Default: `http://hgdownload.soe.ucsc.edu/goldenPath`

## 8.3 download\_refseq\_prefix

Check existing refSeq files in refSeq folder.

Type: `str`

Default: `ncbiRefSeq`

## 8.4 download\_refseq\_files

List of refSeq files to download.

Type: `str`

Default: `ncbiRefSeq.txt,ncbiRefSeqLink.txt`

## 8.5 download\_refseq\_format\_file

Name of refSeq file to convert in BED format (e.g. 'ncbiRefSeq.txt'). Process only if not `None`.

Type: `str`

Default: `None`

## 8.6 download\_refseq\_include\_utr5

Formating BED refSeq file including 5'UTR.

Default: `False`

## 8.7 download\_refseq\_include\_utr3

Formating BED refSeq file including 3'UTR.

Default: `False`

## 8.8 download\_refseq\_include\_chrM

Formating BED refSeq file including Mitochondiral chromosome 'chrM' or 'chrMT'.

Default: `False`

## 8.9 download\_refseq\_include\_non\_canonical\_chr

Formating BED refSeq file including non canonical chromosomes.

Default: `False`

## 8.10 `download_refseq_include_non_coding_transcripts`

Formating BED refSeq file including non coding transcripts.

Default: `False`

## 8.11 `download_refseq_include_transcript_version`

Formating BED refSeq file including transcript version.

Default: `False`

# 9 `dbnsfp`

dbNSFP download.

## 9.1 `download_dbnsfp`

Download dbNSFP databases within dbNSFP folder(e.g. `'~/howard/databases'`).

Type: `Path`

Default: `None`

## 9.2 `download_dbnsfp_url`

Download dbNSFP databases URL (see dbNSFP website) (e.g. `https://dbnsfp.s3.amazonaws.com'`).

Type: `str`

Default: `https://dbnsfp.s3.amazonaws.com`

## 9.3 `download_dbnsfp_release`

Release of dbNSFP to download (see dbNSFP website) (e.g. `'4.4a'`).

Default: `4.4a`

## 9.4 `download_dbnsfp_parquet_size`

Maximum size (Mb) of data files in Parquet folder. Parquet folder are partitioned (hive) by chromosome (sub-folder), which contain N data files.

Type: `int`

Default: `100`

## 9.5 `download_dbnsfp_subdatabases`

Generate dbNSFP sub-databases. dbNSFP provides multiple databases which are split onto multiple columns. This option create a Parquet folder for each sub-database (based on columns names).

Default: `False`

## 9.6 `download_dbnsfp_parquet`

Generate a Parquet file for each Parquet folder.

Default: `False`



## 9.7 download\_dbnsfp\_vcf

Generate a VCF file for each Parquet folder. Need genome FASTA file (see --download-genome).

Default: **False**

## 9.8 download\_dbnsfp\_no\_files\_all

Not generate database Parquet/VCF file for the entire database ('ALL'). Only sub-databases files will be generated. (see '--download-dbnsfp-subdatabases').

Default: **False**

## 9.9 download\_dbnsfp\_add\_info

Add INFO column (VCF format) in Parquet folder and file. Useful for speed up full annotation (all available columns). Increase memory and space during generation of files.

Default: **False**

## 9.10 download\_dbnsfp\_only\_info

Add only INFO column (VCF format) in Parquet folder and file. Useful for speed up full annotation (all available columns). Decrease memory and space during generation of files. Increase time for partial annotation (some available columns).

Default: **False**

## 9.11 download\_dbnsfp\_uniquify

Uniquify values within column (e.g. "D,D" to "D", "D,,T" to "D,T"). Remove transcripts information details. Useful to reduce size of the database. Increase memory and space during generation of files.

Default: **False**

## 9.12 download\_dbnsfp\_row\_group\_size

Minimum number of rows in a parquet row group (see duckDB doc). Lower can reduce memory usage and slightly increase space during generation, speed up highly selective queries, slow down whole file queries (e.g. aggregations).

Type: **int**

Default: 100000

# 10 alphamissense

AlphaMissense download.

## 10.1 download\_alphamissense

Path to AlphaMissense databases

Type: **Path**

Default: **None**

## 10.2 download\_alphamissense\_url

Download AlphaMissense databases URL (see AlphaMissense website) (e.g. 'https://storage.googleapis.com/dm\_alphamissense').

Type: **str**

Default: **https://storage.googleapis.com/dm\_alphamissense**

## 11 exomiser

Exomiser download.

### 11.1 download\_exomiser

Path to Exomiser databases (e.g. ~/howard/databases/exomiser/current).

Type: Path

Default: None

### 11.2 download\_exomiser\_application\_properties

Exomiser Application Properties configuration file (see Exomiser website). This file contains configuration settings for the Exomiser tool. If this parameter is not provided, the function will attempt to locate the application properties file automatically based on the Exomiser. Configuration information will be used to download expected releases (if no other parameters). CADD and REMM will be downloaded only if 'path' are provided.

Type: Path

Default: None

### 11.3 download\_exomiser\_url

URL where Exomiser database files can be downloaded from (e.g. 'http://data.monarchinitiative.org/exomiser').

Type: str

Default: <http://data.monarchinitiative.org/exomiser>

### 11.4 download\_exomiser\_release

Release of Exomiser data to download. If "default", "auto", or "config", retrieve from Application Properties file. If not provided (None), from Application Properties file (Exomiser data-version) or default '2109'.

Type: str

Default: None

### 11.5 download\_exomiser\_phenotype\_release

Release of Exomiser phenotype to download. If not provided (None), from Application Properties file (Exomiser Phenotype data-version) or Exomiser release.

Type: str

Default: None

### 11.6 download\_exomiser\_remm\_release

Release of ReMM (Regulatory Mendelian Mutation) database to download. If "default", "auto", or "config", retrieve from Application Properties file.

Type: str

Default: None

### 11.7 download\_exomiser\_remm\_url

URL where ReMM (Regulatory Mendelian Mutation) database files can be downloaded from (e.g. 'https://kircherlab.bihealth.org/d

Type: str

Default: <https://kircherlab.bihealth.org/download/ReMM>

## 11.8 download\_exomiser\_cadd\_release

Release of CADD (Combined Annotation Dependent Depletion) database to download. If "default", "auto", or "config", retrieve from Application Properties file.

Type: `str`

Default: `None`

## 11.9 download\_exomiser\_cadd\_url

URL where CADD (Combined Annotation Dependent Depletion) database files can be downloaded from (e.g. 'https://kircherlab.bihealth.org/download/CADD').

Type: `str`

Default: `https://kircherlab.bihealth.org/download/CADD`

## 11.10 download\_exomiser\_cadd\_url\_snv\_file

Name of the file containing the SNV (Single Nucleotide Variant) data for the CADD (Combined Annotation Dependent Depletion) database.

Type: `str`

Default: `whole_genome_SNVs.tsv.gz`

## 11.11 download\_exomiser\_cadd\_url\_indel\_file

Name of the file containing the INDEL (Insertion-Deletion) data for the CADD (Combined Annotation Dependent Depletion) database.

Type: `str`

Default: `InDels.tsv.gz`

# 12 dbsnp

dbSNP download.

## 12.1 download\_dbsnp

Path to dbSNP databases (e.g. '~/howard/databases/exomiser/dbsnp').

Type: `Path`

Default: `None`

## 12.2 download\_dbsnp\_releases

Release of dbSNP to download (e.g. 'b152', 'b152,b156').

Type: `str`

Default: `b156`

## 12.3 download\_dbsnp\_release\_default

Default Release of dbSNP ('default' symlink) (e.g. 'b156'). If `None`, first release to download will be assigned as default only if it does not exists.

Type: `str`

Default: `None`

## 12.4 download\_dbsnp\_url

URL where dbSNP database files can be downloaded from. (e.g. 'https://ftp.ncbi.nih.gov/snp/archive').

Type: `str`

Default: `https://ftp.ncbi.nih.gov/snp/archive`

## 12.5 download\_dbsnp\_url\_files

Dictionary that maps assembly names to specific dbSNP URL files. It allows you to provide custom dbSNP URL files for specific assemblies instead of using the default file naming convention.

Type: `str`

Default: `None`

## 12.6 download\_dbsnp\_url\_files\_prefix

String that represents the prefix of the dbSNP file name for a specific assembly. It is used to construct the full URL of the dbSNP file to be downloaded.

Type: `str`

Default: `GCF_000001405`

## 12.7 download\_dbsnp\_assemblies\_map

dictionary that maps assembly names to their corresponding dbSNP versions. It is used to construct the dbSNP file name based on the assembly name.

Type: `str`

Default: `{'hg19': '25', 'hg38': '40'}`

## 12.8 download\_dbsnp\_vcf

Generate well-formatted VCF from downloaded file:

- Add and filter contigs associated to assembly
- Normalize by splitting multiallelics
- Need genome (see `--download-genome`)

Default: `False`

## 12.9 download\_dbsnp\_parquet

Generate Parquet file from VCF.

Default: `False`

# 13 hgmd

HGMD convert.

## 13.1 convert\_hgmd

Convert HGMD databases. Folder where the HGMD databases will be stored. Fields in VCF, Parquet and TSV will be generated. If the folder does not exist, it will be created.

Type: `Path`

Default: `None`

## 13.2 convert\_hgmd\_file

File from HGMD. Name format 'HGMD\_Pro\_\_\_\_.vcf.gz'.

Type: Path

Default: None

## 13.3 convert\_hgmd\_basename

File output basename. Generated files will be prefixed by basename (e.g. 'HGMD\_Pro\_MY\_RELEASE') By default (None), input file name without '.vcf.gz'.

Type: str

Default: None

# 14 from\_\_Annovar

Annovar convert.

## 14.1 input\_annovar

Input Annovar file path. Format file must be a Annovar TXT file, associated with '.idx'.

Type: Path

Default: None

## 14.2 output\_annovar

Output Annovar file path. Format file must be either VCF compressed file '.vcf.gz'.

Type: Path

Default: None

## 14.3 annovar\_code

Annovar code, or database name. Usefull to name databases columns.

Type: str

Default: None

## 14.4 annovar\_to\_parquet

Parquet file conversion.

Type: Path

Default: None

## 14.5 annovar\_reduce\_memory

Reduce memory option for Annovar convert, either 'auto' (auto-detection), 'enable' or 'disable'.

Type: str

Choices: ['auto', 'enable', 'disable']

Default: auto

## 14.6 annovar\_\_multi\_\_variant

Variant with multiple annotation lines on Annovar file. Either 'auto' (auto-detection), 'enable' or 'disable'.

Type: `str`

Choices: ['auto', 'enable', 'disable']

Default: `auto`

## 15 from\_\_extann

Extann convert (gene annotation).

### 15.1 input\_\_extann

Input Extann file path. Format file must be a Extann TXT file or TSV file. File need to have at least the genes column.

Type: `Path`

Default: `None`

### 15.2 output\_\_extann

Output Extann file path. Output extann file, should be BED or BED.gz.

Type: `Path`

Default: `None`

### 15.3 refgene

Path to refGene annotation file.

Type: `Path`

Default: `None`

### 15.4 transcripts

Transcripts TSV file, with Transcript in first column, optional Gene in second column.

Type: `Path`

Default: `None`

### 15.5 param\_\_extann

Param extann file path. Param containing configuration, options to replace chars and bedlike header description, conf vcf specs. (e.g. '~/howard/config/param.extann.json')

Type: `Path`

Default: `None`

### 15.6 mode\_\_extann

Mode extann selection. How to pick transcript from ncbi, keep all, keep the longest, or keep the chosen one (transcript\_extann).

Type: `str`

Choices: ['all', 'longest', 'chosen']

Default: `longest`

## 16 Parameters

Parameters generation.

### 16.1 `generate__param`

Parameter file (JSON) with all databases found. Databases folders scanned are defined in config file. Structure of databases follow this structure (see doc): `...///*.[parquet|vcf.gz|...]`

Type: `Path`

Default: `None`

### 16.2 `generate__param__description`

Description file (JSON) with all databases found. Contains all databases with description of format, assembly, fields...

Type: `Path`

Default: `None`

### 16.3 `generate__param__releases`

List of database folder releases to check (e.g. `'current'`, `'latest'`).

Type: `str`

Default: `current`

### 16.4 `generate__param__formats`

List of database formats to check (e.g. `'parquet'`, `'parquet,vcf,bed,tsv'`).

Type: `str`

Default: `parquet`

### 16.5 `generate__param__bcftools`

Generate parameter JSON file with BCFTools annotation for allowed formats (i.e. `'vcf'`, `'bed'`).

Default: `False`