


# GenomicScores: efficient storage and retrieval of genomewide position-specific scores

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joint work with

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- Genomewide position-specific scores are ubiquitous in genomic analyses, specially for the filtering and interpretation of single nucleotide variants.
- Some of the most popular score sets are:
  - **phastCons** Siepel et al. *Genome Res.*, 15:1034-1050, 2005.
  - **phyloP** Pollard et al. *Genome Res.*, 20:110-121, 2010.
  - **CADD** Kircher et al. *Nat Genet.*, 46:310-315, 2014.
  - **fitCons** Gulko et al. *Nat. Genet.*, 47:276-283, 2015.
  - **M-CAP** Jagadeesh et al. *Nat. Genet.*, 48:1581-1586, 2016.
- The size of some of them, e.g., ( $\approx 2.5\text{Gb}$  phastCons,  $\approx 80\text{Gb}$  CADD), derived from storing double-precision numbers for millions of nucleotides along the genome, makes it difficult to use them interactively or integrate them into R workflows.

- Sometimes, measurements and statistical models generate false precision, i.e., values that are meaningless or not that useful from the scientific point of view (sometimes this is application-dependent).
- Using **lossy compression**, also known as **quantization**, we can trade off precision for compression without compromising the scientific integrity of the data (Zender, 2016).
- Lossy compression leads to a subset of *quantized* values, much smaller than the original set of genomic scores.
- Quantized values often lead to runs of identical values along the genome that can be further compressed with run-length encoding (RLE) vectors.

# The GenomicScores package

- Efficient storage and retrieval of genomewide position-specific scores.
- Supports annotation packages such as `phastCons100way.UCSC.hg19`, but can be also used to fetch further score sets as AnnotationHub resources.
- Defines the *GScores* class of objects, inspired by the former *SNPlocs* class, and some of its accessors are (see help page for full list):
  - `scores(object, ranges, scores.only=FALSE, summaryFun=mean, quantized=FALSE, caching=TRUE)`
  - `name(x)`: name of the set of scores, e.g., `phastCons100way.UCSC.hg19`.
  - `type(x)`: type of scores, e.g., `phastCons100way`.
  - `provider(x)`: provider of the score data, e.g., UCSC.
  - `providerVersion(x)`: version of the data given by the provider.
  - `organism(x)`: organism on which the scores are defined.
  - `seqinfo(x)`: information about the genome sequence.
  - `qfun(x)`: quantization function.
  - `dqfun(x)`: dequantization function.
  - `citation(x)`: *bibentry* object on how to cite these data.

# GScores objects through annotation packages

```
> library(phastCons100way.UCSC.hg19)
> gsco <- phastCons100way.UCSC.hg19
> gsco
```

```
GScores object
# organism: Homo sapiens (UCSC, hg19)
# provider: UCSC
# provider version: 09Feb2014
# download date: Mar 17, 2017
# loaded sequences: chr19_gl000208_random
# maximum abs. error: 0.05
```

```
> scores(gsco, GRanges(seqnames="chr7", IRanges(start=117232380, width=1)))
```

```
GRanges object with 1 range and 1 metadata column:
```

seqnames	ranges	strand	scores
<Rle>	<IRanges>	<Rle>	<numeric>
[1] chr7	[117232380, 117232380]	*	0.8

```
-----
seqinfo: 1 sequence from an unspecified genome; no seqlengths
```

```
> gsco
```

```
GScores object
# organism: Homo sapiens (UCSC, hg19)
# provider: UCSC
# provider version: 09Feb2014
# download date: Mar 17, 2017
# loaded sequences: chr19_gl000208_random, chr7
# maximum abs. error: 0.05
```

# GScores objects through the AnnotationHub

```
> library(GenomicScores)
> availableGScores()
```

```
snapshotDate(): 2017-07-11
```

```
[1] "cadd.v1.3.hg19"           "fitCons.UCSC.hg19"
[3] "mcap.v1.0.hg19"          "phastCons100way.UCSC.hg19"
[5] "phastCons100way.UCSC.hg38" "phastCons60way.UCSC.mm10"
[7] "phastCons7way.UCSC.hg38"  "phyloP100way.UCSC.hg19"
[9] "phyloP100way.UCSC.hg38"
```

```
> cadd <- getGScores("cadd.v1.3.hg19")
```

```
> citation(cadd)
```

```
Martin Kircher, Daniela M. Witten, Preti Jain, Brian J. O'Roak, Gregory
M. Cooper and Jay Shendure (2014). "A general framework for estimating
the relative pathogenicity of human genetic variants." Nature
Genetics, *46*, pp. 310-315. doi: 10.1038/ng.2892 (URL:
http://doi.org/10.1038/ng.2892).
```

```
> makeGScoresPackage(cadd, maintainer="me", author="me <me@example.com>", version="1.0.0")
```

```
Creating package in ./cadd.v1.3.hg19
```

- Current compression ratios, are:

Score set	Original	Compressed	Ratio
fitCons.UCSC.hg19	76 Mb	25 Mb	$\approx 3$
phyloP100way.UCSC.hg19	5.1 Gb	1.2 Gb	$\approx 4$
phastCons100way.UCSC.hg19	2.5 Gb	233 Mb	$\approx 10$
mcap.v1.0.hg19	729 Mb	61 Mb	$\approx 12$
cadd.v1.3.hg19	80 Gb	716 Mb	$\approx 114$

Can they be improved? Do we need different lossy compression for different applications?

- Current *GScores* class is based on the “older” *SNPlocs* class. This should probably change to the newer *ODLT\_SNPlocs* class.

- Should we integrate the *MafDb* class, as a subclass of *GScores*?

```
> library(MafDb.gnomAD.r2.0.1.hs37d5)
> mafdb <- MafDb.gnomAD.r2.0.1.hs37d5
> mafdb
```

Minor allele frequency Db (MafDb) object

```
# organism: Homo sapiens
# provider: BroadInstitute
# provider version: r2.0.1
# download date: Apr 10, 2017
# loaded sequences (SNVs): none
# loaded sequences (nonSNVs): none
# loaded populations (SNVs): none
# loaded populations (nonSNVs): none
# nr. of variants: 241056551
```

```
> populations(mafdb)
```

```
[1] "AF"           "AF_AFR"       "AF_AMR"       "AF_ASJ"       "AF_EAS"       "AF_Female"
[7] "AF_FIN"       "AF_Male"      "AF_NFE"       "AF_OTH"
```

```
> mafByOverlaps(mafdb, "15:28356859", populations(mafdb))
```

GRanges object with 1 range and 10 metadata columns:

	seqnames	ranges	strand	AF	AF_AFR	AF_AMR			
	<Rle>	<IRanges>	<Rle>	<numeric>	<numeric>	<numeric>			
[1]	15	[28356859, 28356859]	*	0.44	0.13	0.22			
	AF_ASJ	AF_EAS	AF_Female	AF_FIN	AF_Male	AF_NFE	AF_OTH		
	<numeric>	<numeric>	<numeric>	<numeric>	<numeric>	<numeric>	<numeric>		
[1]	0.46	0.001	0.42	0.12	0.47	0.2	0.32		

```
-----
seqinfo: 1 sequence from an unspecified genome; no seqlengths
```



# Comments, bugs, issues and acknowledgments

- Comments to `robert.castelo@upf.edu`
- Bugs and issues to <https://github.com/rcastelo/GenomicScores/issues>
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