

BioC 2016 Developer Day

Core team updates

Welcome and Project Update

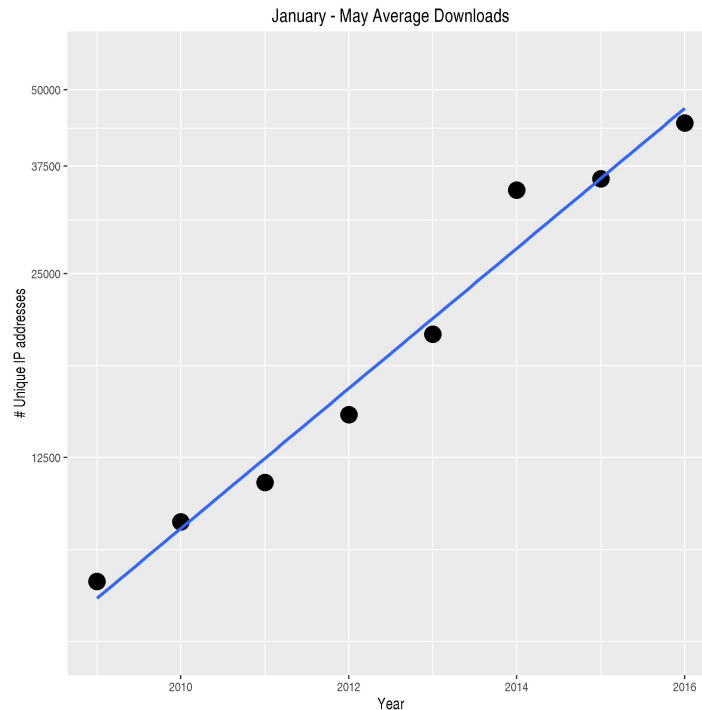
Thanks!



- Pam Jarrett, Ellen Sanders Noonan, Ellen Van Stone
- Susan Holmes, Sean Davis
- Speakers and Workshop presenters
- Bioc developers!

The project since last year

- 2 Releases with 187 new packages
- Lots of activity on the support site
- Steadily growing user base
- Move to Roswell Park



Activities and opportunities

Core team activities

- *GenomicRanges* infrastructure
- *AnntotationHub* and *ExperimentHub*
- *BiocParallel* / *GenomicFiles*
- Progress on *MultiAssayExperiment*
- On-disk / lazy evaluation of large data
- Public new package submissions
- User and developer support

Keeping up with the burgeoning R community

- Package development best practices
- Approaches to version control and testing

Increasingly cloud-based computing

- Efficient access to cloud-based resources
- Participation in cloud-based bioinformatics initiatives
- Computation in the cloud

Career opportunities!

- [Senior Programmer / Analyst](#) -- creative web / system administration / development -- <https://goo.gl/2s26pp>

Acknowledgements

Core team (current & recent): Valerie Obenchain, Hervé Pagès, Dan Tenenbaum, Lori Shepherd, Marcel Ramos, Jim Hester, Jim Java, Brian Long, Sonali Arora, Nate Hayden, Paul Shannon, Marc Carlson

Technical advisory board: Vincent Carey, Wolfgang Huber, Robert Gentleman, Rafael Irizzary, Levi Waldron, Michael Lawrence, Sean Davis, Aedin Culhane

Scientific advisory board: Simon Tavaré (CRUK), Paul Flicek (EMBL/EBI), Simon Urbanek (AT&T), Vincent Carey (Brigham & Women's), Wolfgang Huber (EBI), Rafael Irizzary (Dana Farber), Robert Gentleman (23andMe)



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Lori Shepherd

GenomicFiles / VcfStack / RangedVcfStack

disjoin() in IRanges / GenomicRanges

GenomicFiles

VcfStack / RangedVcfStack

VcfStack / RangedVcfStack

The VcfStack class is a vector of related VCF files, for instance each file representing a separate chromosome. The class helps manage these files as a group.

The RangedVcfStack class extends VcfStack by associating genomic ranges of interest to the collection of VCF files.

VcfStack / RangedVcfStack

`VcfStack(files=NULL, seqinfo=NULL, colData=NULL)`

`files`: A character vector of files paths pointing to VCF files. The character vector must be named, with names correspond to `seqnames` in each VCF file.

`seqinfo`: A `Seqinfo` object describing the levels genome and circularity of each sequence.

`colData`: An optional `DataFrame` describing each sample in the `VcfStack`. When present, row names must correspond to sample names in the VCF file.

`RangedVcfStack(vs=NULL, rowRanges=NULL)`

`vs`: A `VcfStack` object.

`rowRanges`: An optional `GRanges` object associating the genomic ranges of interest to the collection of VCF files. The `seqnames` of `rowRanges` are a subset of `seqnames(vs)`. If missing, a default is created from the `seqinfo` object of the provided `VcfStack`

VcfStack / RangedVcfStack

Accessors

- `dim(x)`
- `dimnames(x)`
- `rownames(x)`
- `colnames(x)`

As well as your typical getters and setters for object attributes:

- `files(x)`
- `seqinfo(x)`
- `colData(x)`
- `rowRanges(x)`

VcfStack / RangedVcfStack Methods

`assay(x, i, ...)`

Get matrix of genotype calls from VCF files

`readVcfStack(x, i, j=colnames(x))`

Get content of VCF files in the VcfStack

`show(x)`

Display abbreviated information about VcfStack / RangedVcfStack

- i: indicated which files to read
is a GRanges object, character() vector of seqnames, numeric() vector, logical() vector, or can be missing. For a RangedVcfStack object, assay and readVcfStack will use the associated rowRanges object for i.
- j: indicates which samples to read
can be missing or a character() vector of sample names

VcfStack / RangedVcfStack Subsetting

`x[i, j]`

Get elements from ranges `i` and samples `j` as a `VcfStack` or `RangedVcfStack` object

`x`: is a `VcfStack` or `RangedVcfStack` object

`i`: indicated which files to subset

can be missing, a `character()` vector of seqnames, `numeric()` vector of indexes, or `logical()` vector.
When `x` is a `VcfStack` instance, `i` can also be a `GRanges` object; `seqnames(i)` is then used to subset the files in the `VcfStack`.

`j`: indicated which samples to subset.

can be missing, a `character()` vector of sample names, a `numeric()` vector, or `logical()` vector.

IRanges / GenomicRanges

`disjoin()`

IRanges / GenomicRanges

`disjoin(x, with.revmap=FALSE)`

- Ranges
- RangesList
- CompressedIRangesList

`disjoin(x, with.revmap=FALSE, ignore.strand=FALSE)`

- GenomicRanges
- GRangesList

`with.revmap`

TRUE or FALSE. Should the mapping from output to input ranges be stored in the returned object? If yes, then it is stored as metadata column `revmap` of type `IntegerList`

GenomicRanges 'GRanges' Example

```
> gr <- GRanges(Rle(c("chr1", "chr3"), c(2, 2)),  
                IRanges(c(8,6,8,6),c(11,15,11,15)), names=c("k","l","m","n")),  
                Rle(strand(c("-", "-", "+", "*"))),  
                score=11:14, GC=c(.2,.3,.3,.1))
```

> gr

GRanges object with 4 ranges and 2 metadata columns:

seqnames	ranges	strand	score	GC
<Rle>	<IRanges>	<Rle>	<integer>	<numeric>
k	chr1 [8, 11]	-	11	0.2
l	chr1 [6, 15]	-	12	0.3
m	chr3 [8, 11]	+	13	0.3
n	chr3 [6, 15]	*	14	0.1

seqinfo: 2 sequences from an unspecified genome; no
seqlengths

> dgr <- disjoint(gr, with.revmap=TRUE)

> dgr

GRanges object with 5 ranges and 1 metadata column:

seqnames	ranges	strand	revmap
<Rle>	<IRanges>	<Rle>	<IntegerList>
[1]	chr1 [6, 7]	-	2
[2]	chr1 [8, 11]	-	1,2
[3]	chr1 [12, 15]	-	2
[4]	chr3 [8, 11]	+	3
[5]	chr3 [6, 15]	*	4

seqinfo: 2 sequences from an unspecified genome; no seqlengths

To Get Original Metadata Values:

```
> revmap <- mcols(dgr)$revmap  
> score <- extractList(mcols(gr)$score, revmap)  
> GC <- extractList(mcols(gr)$GC, revmap)  
> mcols(dgr)$score <- score  
> mcols(dgr)$GC <- GC  
> dgr
```

GRanges object with 5 ranges and 3 metadata columns:

seqnames	ranges	strand	revmap	score	GC
<Rle>	<IRanges>	<Rle>	<IntegerList>	<IntegerList>	<NumericList>
[1]	chr1 [6, 7]	-	2	12	0.3
[2]	chr1 [8, 11]	-	1,2	11,12	0.2,0.3
[3]	chr1 [12, 15]	-	2	12	0.3
[4]	chr3 [8, 11]	+	3	13	0.3
[5]	chr3 [6, 15]	*	4	14	0.1

seqinfo: 2 sequences from an unspecified genome; no seqlengths

GenomicRanges 'GRangesList' Example

```
gr <- GRanges(Rle(c("chr1", "chr3"), c(2, 2)),
              IRanges(c(8,6,8,6),c(11,15,11,15)), names=c("k","l","m","n")),
              Rle(strand(c("-", "-", "+", "*"))),
              score=11:14, GC=c(.2,.3,.3,.1))
grl <- GRangesList(gr, gr)
```

> grl

GRangesList object of length 2:

[[1]]

GRanges object with 4 ranges and 2 metadata columns:

seqnames	ranges	strand	score	GC
<Rle>	<IRanges>	<Rle>	<integer>	<numeric>
k	chr1 [8, 11]	-	11	0.2
l	chr1 [6, 15]	-	12	0.3
m	chr3 [8, 11]	+	13	0.3
n	chr3 [6, 15]	*	14	0.1

[[2]]

GRanges object with 4 ranges and 2 metadata columns:

seqnames	ranges	strand	score	GC
k	chr1 [8, 11]	-	11	0.2
l	chr1 [6, 15]	-	12	0.3
m	chr3 [8, 11]	+	13	0.3
n	chr3 [6, 15]	*	14	0.1

seqinfo: 2 sequences from an unspecified genome; no seqlengths

> disjoint(grl, with.revmap=TRUE)

GRangesList object of length 2:

[[1]]

GRanges object with 5 ranges and 1 metadata column:

seqnames	ranges	strand	revmap
<Rle>	<IRanges>	<Rle>	<IntegerList>
[1]	chr1 [6, 7]	-	2
[2]	chr1 [8, 11]	-	1,2
[3]	chr1 [12, 15]	-	2
[4]	chr3 [8, 11]	+	3
[5]	chr3 [6, 15]	*	4

[[2]]

GRanges object with 5 ranges and 1 metadata column:

seqnames	ranges	strand	revmap
[1]	chr1 [6, 7]	-	2
[2]	chr1 [8, 11]	-	1,2
[3]	chr1 [12, 15]	-	2
[4]	chr3 [8, 11]	+	3
[5]	chr3 [6, 15]	*	4

seqinfo: 2 sequences from an unspecified genome; no seqlengths

Valerie Obenchain

ExperimentHub

ExperimentHub

Resource to house curated data from experiments, publications or courses

Similar interface as AnnotationHub except ...

- Parent package documentation
- List resources by package
- Interface with the data through the package or ExperimentHub
- All data stored in AWS S3; no web downloads

ExperimentHub: parent package documentation

```
> library(ExperimentHub)
```

```
> eh = ExperimentHub()  
snapshotDate(): 2016-06-08
```

```
> eset = eh[[100]]
```

```
see ?curatedMetagenomicData and browseVignettes('curatedMetagenomicData') for documentation  
downloading from 'https://experimenthub.bioconductor.org/fetch/100'  
retrieving 1 resource
```

```
|=====| 100%
```

```
> ?curatedMetagenomicData
```

ExperimentHub: list resources by package

```
> head(package(eh), 3)
```

EH1	EH2	EH3
"GSE62944"	"curatedMetagenomicData"	"curatedMetagenomicData"

```
> table(package(eh))
```

curatedMetagenomicData	GSE62944
162	1

ExperimentHub: interface with data via package

```
> eh["EH100"]
ExperimentHub with 1 record
# snapshotDate(): 2016-06-08
# package(): curatedMetagenomicData
# $dataprovder: Human Microbiome Project Consortium
# $species: Homo sapiens
# $title: hmp.r_retroauricular_crease.marker_ab.eset.rda
...

> ?hmp.r_retroauricular_crease.marker_ab.eset ## package man page
> hmp.r_retroauricular_crease.marker_ab.eset() ## loads the data
> hmp.r_retroauricular_crease.marker_ab.eset(metadata = TRUE) ## loads the metadata
```

ExperimentHubData

Information on adding resources to ExperimentHub is found in the ExperimentHubData [vignette](#).

Marcel Ramos

MultiAssayExperiment

MultiAssayExperiment

A package to manage multiple assays on sets of samples or specimens

- A container class for handling overlapping sets of samples
- User-friendly operations (subsetting)
- Mapping scheme for relating samples to participants or experiment results to specimen data
- Set up for common genomic computations across diverse assays
- On-disk representation of data (moving to lazy eval with `HDF5Array`)

Hierarchy of information:

Study

└ Experiment

└ Biological Unit



Datasets will
soon be
accessible via
ExperimentHub

MultiAssayExperiment: Structure Overview

- **MultiAssayExperiment** class
 - **Elist** class and slot - *workhorse container*
 - Any class that has a `[` bracket method, ``colnames``, ``rownames`` and ``dim``.
 - *RangedRaggedAssay*
 - *SummarizedExperiment, RangedSummarizedExperiment*
 - *ExpressionSet*
 - *matrix*
 - **pData** (of class *DataFrame*) - *specimen description*
 - Each row is a patient or specimen
 - Includes demographics and/or other specimen-wide variables
 - **sampleMap** (of class *DataFrame*) - *mapping scheme*
 - Maps sample identifiers to participants/specimen in a table
 - **metadata** (*ANY* class)
 - Include additional study level information

MultiAssayExperiment: Quick Example

```
> library(MultiAssayExperiment)
```

```
> example("MultiAssayExperiment")
```

```
> myMultiAssayExperiment
```

A "MultiAssayExperiment" object of 3 listed experiments with user-defined names and respective classes.

Containing an "Elist" class object of length 3:

[1] Affy: "ExpressionSet" - 2 rows, 4 columns

[2] Methyl450k: "matrix" - 2 rows, 5 columns

[3] CNVgistic: "RangedRaggedAssay" - 5 rows, 3 columns

To access slots use:

elist() - to obtain the "Elist" of experiment instances

pData() - for the primary/phenotype "DataFrame"

sampleMap() - for the sample availability "DataFrame"

metadata() - for the metadata object of "ANY" class

See also: subsetByAssay(), subsetByRow(), subsetByColumn()

MultiAssayExperiment: Thorough Example

An in-depth example on how to build your own **MultiAssayExperiment** can be found in the package [vignette](#)

Hervé Pagès

Recent developments:

- GPos class
- HDF5Array, DelayedArray

What's next?

GPos

A very light GRanges-like container for storing a set of *positions* along the genome.

Particularly memory-efficient when the object contains long runs of adjacent positions.

Can be put on a SummarizedExperiment object (as rowRanges).

```
> gpos
GPos object with 12162995 positions and 0 metadata columns:
      seqnames      pos strand
      <Rle> <integer> <Rle>
[1]      chrI         1      *
[2]      chrI         2      *
[3]      chrI         3      *
...
[12162993] 2micron     6316     *
[12162994] 2micron     6317     *
[12162995] 2micron     6318     *
-----
seqinfo: 18 sequences (2 circular) from sacCer2 genome
```

All the single positions along the Yeast genome are represented.

```
> object.size(gpos)
14000 bytes
```

GPos

Metadata columns need to be light too.

Good candidates:

- Rle (e.g. coverage)
- DNASTring
- sparse object (e.g. Matrix)
- on-disk object (e.g. HDF5Array)
- ?

Current limitation: length of a GPos object cannot exceed 2^{31} (2 billions).

See ?GPos in the GenomicRanges package for more information.

```
> gpos
GPos object with 12162995 positions and 2 metadata columns:
      seqnames      pos strand |      cov      dna
      <Rle> <integer> <Rle> | <Rle> <DNASTring>
[1]      chrI         1      * |      0      C
[2]      chrI         2      * |      0      C
[3]      chrI         3      * |      0      A
[4]      chrI         4      * |      0      C
[5]      chrI         5      * |      0      A
...      ...      ...      ...      ...
[12162991] 2micron     6314      * |      0      A
[12162992] 2micron     6315      * |      0      A
[12162993] 2micron     6316      * |      0      C
[12162994] 2micron     6317      * |      0      G
[12162995] 2micron     6318      * |      0      A
-----
seqinfo: 18 sequences (2 circular) from sacCer2 genome
```

HDF5Array / DelayedArray

Convenient access and manipulation of HDF5 datasets.

Can be used inside a SummarizedExperiment object (assay data).

A dataset with coverage for 6 samples along Human chr 16:

```
> cov0 <- HDF5Array(tally_file, "/ExampleStudy/16/Coverages")
> cov0
HDF5Array object of 6 x 2 x 90354753 integers:
, , 1
      [,1] [,2]
[1,]    0    0
[2,]    0    0
...     .     .
[5,]    0    0
[6,]    0    0
...
, , 90354753
      [,1] [,2]
[1,]    0    0
[2,]    0    0
...     .     .
[5,]    0    0
[6,]    0    0
```

HDF5Array / DelayedArray

Support delayed operations.

Result is a DelayedArray object.

as `.array()` would **realize it in memory**. Don't do that!

Instead **realize it on disk** (if you really need to) with `writeHDF5Dataset()`.

```
Compute unstranded coverage:
```

```
> pcov <- drop(cov0[ , 1, ]) # delayed
> mcov <- drop(cov0[ , 2, ]) # delayed
> cov <- pcov + mcov         # delayed
> cov
```

```
DelayedMatrix object of 6 x 90354753 integers:
```

```
          [,1]      [,2]      [,3]      . [,90354751]
[1,]          0          0          0      .          0
[2,]          0          0          0      .          0
[3,]          0          0          0      .          0
[4,]          0          0          0      .          0
[5,]          0          0          0      .          0
[6,]          0          0          0      .          0
          [,90354752] [,90354753]
[1,]          0          0
[2,]          0          0
[3,]          0          0
[4,]          0          0
[5,]          0          0
[6,]          0          0
```

HDF5Array / DelayedArray

Block-processing:

- Operations that cannot be delayed (e.g. `rowSums()` or matrix multiplication) process the `DelayedArray` object block-by-block, one block at a time.
- Each block is *realized* (i.e. all delayed operations are executed) and the current operation (e.g. `rowSums`) applied to the result.

See `?DelayedArray` in the `HDF5Array` package for more information.

```
> sum_cov <- rowSums(cov) # block-processing
> sum_cov
[1] 39807797 45246576 18405376 36487401 17218497 36681571

> gc()
      used (Mb) gc trigger (Mb) max used (Mb)
Ncells 2947878 157.5   4703850 251.3  4703850 251.3
Vcells 3765245  28.8   67472700 514.8 58464312 446.1
```

Loading the full dataset at once in memory would use 4 Gb of RAM!

What's next?

- ❖ **HDF5Array:**
 - Support more operations on DelayedArray objects
 - Vignette
 - Integration of HDF5Array to some common workflows (e.g. `summarizeOverlaps`)
- ❖ Support **long Vector derivatives** (e.g. long Rle, long DataFrame, long GRanges, long Hits, long DNASTring, long DNASTringSet, etc). Will require important changes to the internals of several core packages (S4Vectors, IRanges, GenomicRanges, Biostrings, and more...)
- ❖ **On-disk GRanges objects.** Indexed for fast extraction of elements that overlap a set of regions of interest (i.e. `fastSubsetByOverlaps`). Analog to `scanBam` “which” feature. An immediate use case for this is to speed up `snpsByOverlaps`.
- ❖ Support **easy creation of standalone BSgenome objects** (from 2bit, FASTA, and maybe other sources).
- ❖ Maybe other **"genomic Views"** objects (in addition to `BSgenomeViews`).
- ❖ Build system: **incremental builds.**