

Programmatic retrieval of information from DAS servers using the **DASiR** package

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1 Introduction

Distributed Annotation System (DAS) is a protocol for information exchange between a server and a client. Is widely used in bioinformatics and the most important repositories include a DAS server parallel to their main front-end. Few examples are "UCSC", "Ensembl" or "UniProt".

The DASiR package provides a convenient R-DAS interface to programmatically access DAS servers available from your network. It supports the main features of DAS 1.6 protocol providing a convenient interface to R users to a huge amount of biological information. DAS uses XML and HTTP protocols, so the server deployment and client requirements are significantly less than MySQL or BioMart based alternatives. You can find an browsable list with more than 1500 on-line DAS servers in the url <http://www.dasregistry.org>.

Despite the DAS protocol supports querying different kinds of data, DASiR has been designed with ranges-features in mind. Querying genomic sequences and protein structures is also supported, but you probably will find better ways to access such data in R if you require an intensive use of them (Biostrings genomes or Bio3dD package for PDB structure, for example).

Here you have a brief summary of the main functions of DASiR:

- Set/get the DAS server: `setDasServer`, `getDasServer`
- Retrieve the data sources: `getDasSource`, `getDasDsn`
- Retrieve the entry points and types: `getDasEntries`, `getDatTypes`
- Retrieve information about the features: `getDasFeature`
- Nucleotide/amino acid sequence retrieval: `getDasSequence`
- Protein 3D structure retrieval: `getDasStructure`

For detailed information about these functions and how to use them refer to the DASiR manual or give a look to the following sections for an overview.

2 DAS metadata information handling

As an important part of the dialog between the client and the server consists on knowing which information has every server, DASiR provides the following functions to query metadata from a DAS server.

The first step before start quering and retrieving information is, of course, set the DAS server we will use during this session. Notice that DASiR only supports one active DAS session per R instance.

To set the server we will use the function `setDasServer`:

```
> setDasServer(server="http://genome.ucsc.edu/cgi-bin/das")
> getDasServer()
```

```
[1] "http://genome.ucsc.edu/cgi-bin/das"
```

The function `getDasSource()` will return the id's, the titles and the capabilities of the data sources available in the server in the form of a data frame. This function is important since it is necessary to use the exact name ("id" or "title" depending on the server) as reference name in the other functions of the package.

```
> #sources = getDasSource() #This will fail for UCSC (but no for ENSEMBL)
> sources = getDasDsn() #This will fail for ENSEMBL (but no for UCSC)
> head(sources)
```

```
[1] "hg38"      "hg19"      "hg18"      "hg17"      "hg16"      "panTro4"
```

We should also take into account that the values in capabilities of each data source returned by this function. If we query an unknown name or we query for a capability that is not implemented in the server (for example we ask for a atomic structure to a sequence server) DASiR will return a NULL value, but due to the nature of HTTP based queries, we cannot detect the origin of this error without overloading the server with cross-calls.

Despite "sources" is the common way to recover server features, some servers (as UCSC) are still using the deprecated "dsn" option to get the ids of the different datasets. The rule of a thumb is that if the first don't work, try the second.

Once we have the name of the database we want to query, we need to know where we can look. This is called "entry point" and could be from a protein ID to a chromosome number (depending on the type of server, of course). Notice that output will be a GRanges by default (if the server supplies start, stop and id values). If this is not possible or `textttas.GRanges=FALSE`, the output will be a `data.frame`.

```
> source = "sacCer3"
> entries = getDasEntries(source, as.GRanges=TRUE)
> head(entries)
```

GRanges object with 6 ranges and 2 metadata columns:

	seqnames	ranges	strand	orientation	subparts
	<Rle>	<IRanges>	<Rle>	<factor>	<factor>
[1]	IV	[1, 1531933]	*	+	no
[2]	XV	[1, 1091291]	*	+	no
[3]	VII	[1, 1090940]	*	+	no
[4]	XII	[1, 1078177]	*	+	no
[5]	XVI	[1, 948066]	*	+	no
[6]	XIII	[1, 924431]	*	+	no

seqinfo: 17 sequences from an unspecified genome; no seqlengths

Finally, the different attributes we can ask for, called "types" could be obtained with the function `getDasTypes`.

```
> types = getDasTypes(source)
> head(types)
```

[1]	"blastHg18KG"	"est"	"intronEst"	"mrna"
[5]	"ensGene"	"esRegGeneToMotif"		

Think about Sources as the name of the database, Entries are the tables of this database and finally Types are the columns on this table.

In general a `character` vector is returned for most of the functions, except for `getDasSource` and `getDasEntries` which return a `data.frame` with the name of the entry the ranges of the elements and possibly other attributes depending on the server.

3 Querying features

The `getDasFeature` function queries the DAS server and returns the available information for the type(s) at the given range(s).

```
> ranges=entries[c(1,2)]
> types=c("sgdGene", "mrna")
> features = getDasFeature(source, ranges, types)
> head(features)
```

	segment.range	id	label	type	method	start	end	score
1	1 AY169693.chrIV.84188.0	AY169693	mrna	BLAT	84189	85450	990	
2	1 AY169693.chrIV.84188.1	AY169693	mrna	BLAT	520477	520627	990	
3	1 AY169693.chrIV.84188.2	AY169693	mrna	BLAT	520628	520633	990	
4	1 AY169693.chrIV.84188.3	AY169693	mrna	BLAT	520634	520643	990	
5	1 AY169693.chrIV.84188.4	AY169693	mrna	BLAT	540324	540328	990	
6	1 AY169693.chrIV.84188.5	AY169693	mrna	BLAT	593167	593177	990	

orientation phase group

```

1      +      - Link to UCSC BrowserAY169693
2      +      - Link to UCSC BrowserAY169693
3      +      - Link to UCSC BrowserAY169693
4      +      - Link to UCSC BrowserAY169693
5      +      - Link to UCSC BrowserAY169693
6      +      - Link to UCSC BrowserAY169693

```

A `data.frame` is returned with the contents of the specific annotation for the given ranges and types in the server (again, note that servers could provide different/additional information for types with the same name).

4 Querying nucleotide or amino acid sequence

The `getDasSequence` function queries the DAS server and retrieves the nucleotide or amino acid sequence for the given ranges.

```

> #Now we will retrieve sequences from VEGA server
> setDasServer("http://vega.sanger.ac.uk/das")
> source = "Homo_sapiens.VEGA51.reference"
> ranges = GRanges(c("1","2"), IRanges(start=10e6, width=1000))
> #Returning character vector, we only ask 50 first bases in the range
> sequences = getDasSequence(source, resize(ranges, fix="start", 50))
> print(sequences)

```

```

[1] "caggtggatcatgaggtcaggagttcaagaccagcctggccaacatggtg"
[2] "tttagagatggtttcactctatcgcccaggctggagtacagtgggtgcaat"

```

An `character` vector is returned (the default class) containing the nucleotide or amino acid sequences that match the content of the annotation for the given ranges in the server. Automatic conversion to `Biostring` classes is supported with the `class` attribute:

```

> #Now we specify we want a AAStringSet (Biostring class for AminoAcids strings)
> #and query for the whole sequence length
> sequences = getDasSequence(source, ranges, class="AAStringSet")
> print(sequences)

```

```

A AAStringSet instance of length 2
width seq

```

```

[1] 1000 caggtggatcatgaggtcaggagttcaagaccag...ctcgtgatccacccgccttggcctcccaaagtg
[2] 1000 tttagagatggtttcactctatcgcccaggctgg...aaactttattccaagagttaacagagtctctgg

```

5 Query a protein 3D structure

The `getDasStructure` function queries the DAS server and retrieves the 3D structure, including metadata and coordinates for the given query (ID of the reference structure) using the data source id (or title).

```
> #On 2013-03-05 there are 2 structure servers in dasregistry.org...
> setDasServer(server="http://das.sanger.ac.uk/das")
> #Get the sources with "structure" capability...
> sources = getDasSource()
> sources[grep("structure", sources$capabilities),]
```

```
      id      title  capabilities
300 structure structure das1:structure
```

```
> source="structure" #...which name is also "structure"
> query="1HCK" #PDB code
> structure=getDasStructure(source,query)
> head(structure)
```

	atomID	atomName	x	y	z	type	groupID	name
1	1	N	102.329	111.862	92.452	amino	1	MET
2	2	CA	103.332	112.165	93.516	amino	1	MET
3	3	C	103.877	113.584	93.255	amino	1	MET
4	4	O	103.802	114.075	92.129	amino	1	MET
5	5	CB	104.437	111.099	93.495	amino	1	MET
6	6	CG	105.176	110.881	94.812	amino	1	MET

An `data.frame` is returned with the information of every atom of the reference structure of the given query. Notice that a single residue (identified by `groupID` and `name`) has few atoms inside. Depending on your purposes, you can find this way to represent the structural information inconvenient (for example, if you are used to work with PDB format). Structure query in DAS seems a secondary feature of the protocol (as only 2 servers out of >1500 are supporting it) but anyway we wanted to support the maximum amount of features that DAS protocol implement. We realize that are better options to work with PDB files, but maybe this one can help you for quick structural analysis.

6 Plotting of obtained features

The `plotFeatures` function creates a basic plot with the features retrieved by `getDasFeature` or adds them to an existing plot.

```
> #Let's retrieve some genes from UCSC Genome Browser DAS Server now
> setDasServer(server="http://genome.ucsc.edu/cgi-bin/das")
> #Official yeast genes and other annotated features in the range I:22k-30k
> source = "sacCer3" #Saccharomices Cerevisiae
> range = GRanges(c("I"), IRanges(start=22000, end=30000))
> type = c("sgdGene", "sgdOther") #This is also the name of the UCSC tracks
> features = getDasFeature(source, range, type)
> #Only the main columns
> head(features[,c("id", "label", "type", "start", "end")])
```

	id	label	type	start	end
1	YAL063C-A.chrI.22394.0	YAL063C-A	sgdGene	22395	22685
2	YAL063C.chrI.23999.0	YAL063C	sgdGene	24000	27968
3	YALWdelta1.chrI.22230	YALWdelta1	sgdOther	22231	22552
4	FL09.chrI.24000	FL09	sgdOther	24001	27968

```
> plotFeatures(features, box.height=10, box.sep=15, pos.label="top", xlim=c(22000,30000))
```

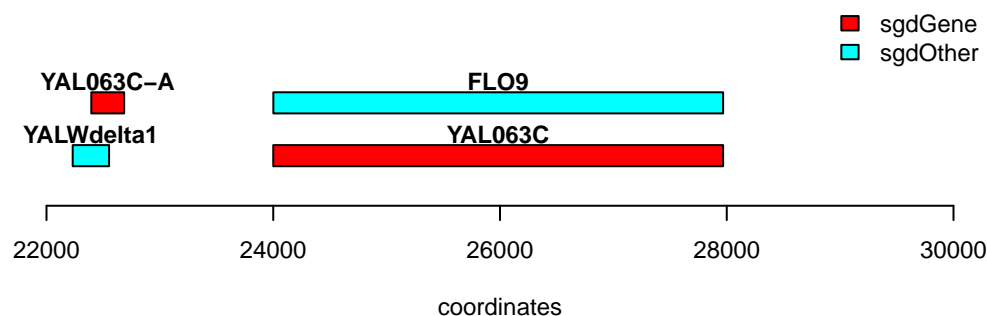


Figure 1: Basic feature plot generated with `getDasFeature` and `plotFeatures`

The `plotFeatures` function is a simple way of drawing text boxes in a new or an existing plot with the features retrieved. Notice that when overplotting to a already open graphical device, the x-coordinates must match.

And this is all. You can find more detailed information and examples of each function in the R manpages for DASiR. We hope this package helps you in your data mining.