Database mining with biomaRt

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Overview

- The BioMart software suite
- biomaRt package
- Workshop style discussion to show the variety of different data types that can be retrieved for many organisms

BioMart 0.7

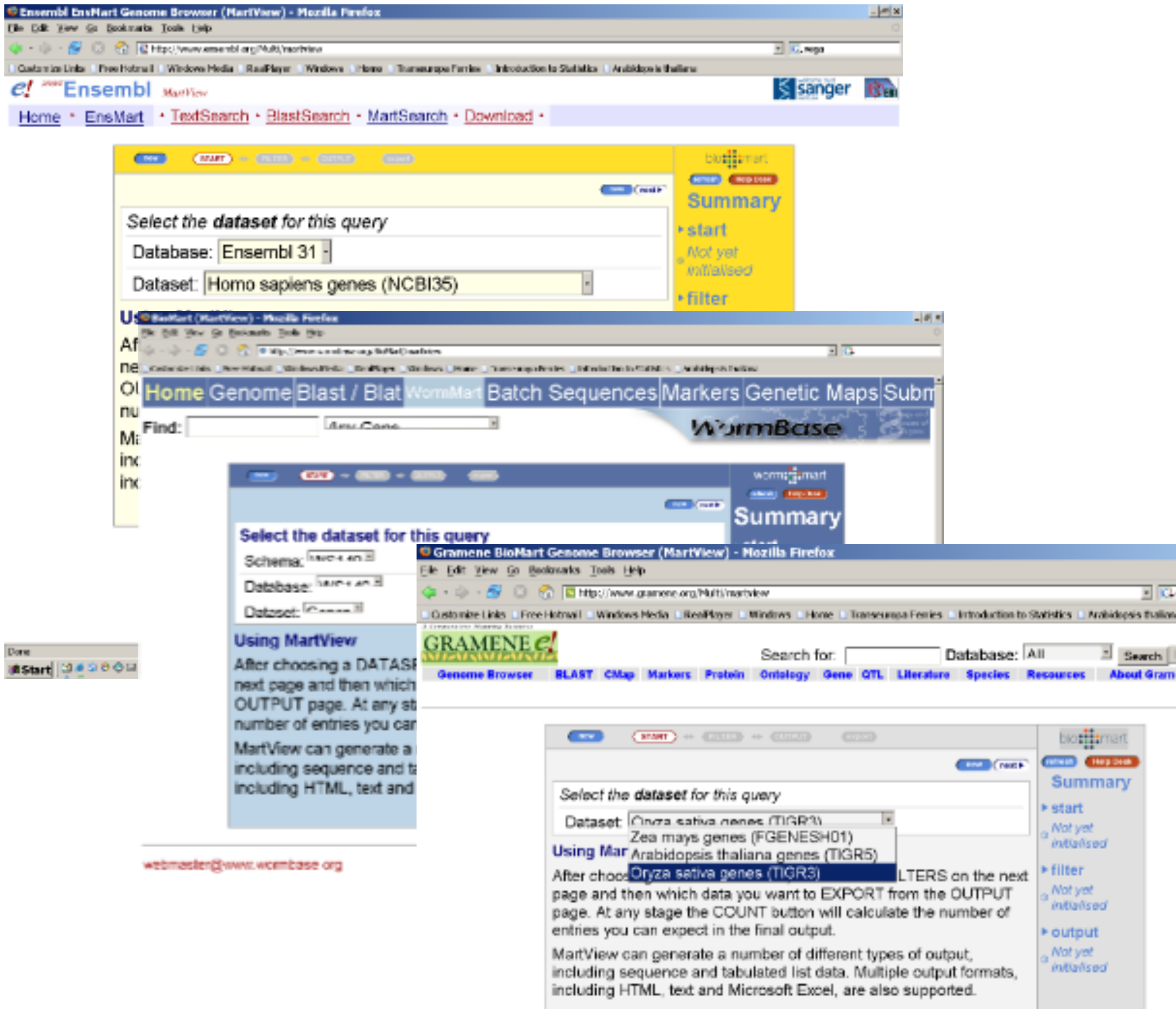
- BioMart is a query-oriented data management system developed jointly by the European Bioinformatics Institute (EBI) and Cold Spring Harbor Laboratory (CSHL).
- Originally developed for the Ensembl project but has now been generalized

BioMart 0.7

- BioMart data can be accessed using either web, graphical, or text based applications, or programmatically using web services or software libraries written in Perl and Java.
- http://www.biomart.org

Example BioMart databases

- Ensembl
- Wormbase
- Reactome
- Gramene
- .....



Ensembl EnsMart Genome Browser (MartView) - Mozilla Firefox

Ensembl MartView

Home · EnsMart · TextSearch · BlastSearch · MartSearch · Download ·

Select the **dataset** for this query

Database: Ensembl 31

Dataset: Homo sapiens genes (NCBI35)

Summary
- start
Not yet initialised
- filter

WormMart (MartView) - Mozilla Firefox

Home Genome Blast / Blat WormMart Batch Sequences Markers Genetic Maps Subm

Find: Any Gene

WormBase

Summary

Select the dataset for this query

Schema:

Database:

Dataset:

Using MartView

After choosing a DATASE
next page and then which
OUTPUT page. At any st
number of entries you can

MartView can generate a
including sequence and ta
including HTML, text and

webmaster@www.wormbase.org

Gramene BioMart Genome Browser (MartView) - Mozilla Firefox

http://www.gramene.org/Multi/martview

GRAMENE

Search for: Database: All Search

Genome Browser BLAST CMap Markers Protein Ontology Gene QTL Literature Species Resources About Gram

Select the **dataset** for this query

Dataset: Oryza sativa genes (TIGR3)
Zea mays genes (FGENESH01)
Arabidopsis thaliana genes (TIGR5)
Oryza sativa genes (TIGR3)

Using Mar

After choo LTERS on the next page and then which data you want to EXPORT from the OUTPUT page. At any stage the COUNT button will calculate the number of entries you can expect in the final output.

MartView can generate a number of different types of output, including sequence and tabulated list data. Multiple output formats, including HTML, text and Microsoft Excel, are also supported.

Summary
- start
Not yet initialised
- filter
Not yet initialised
- output
Not yet initialised

BioMart databases

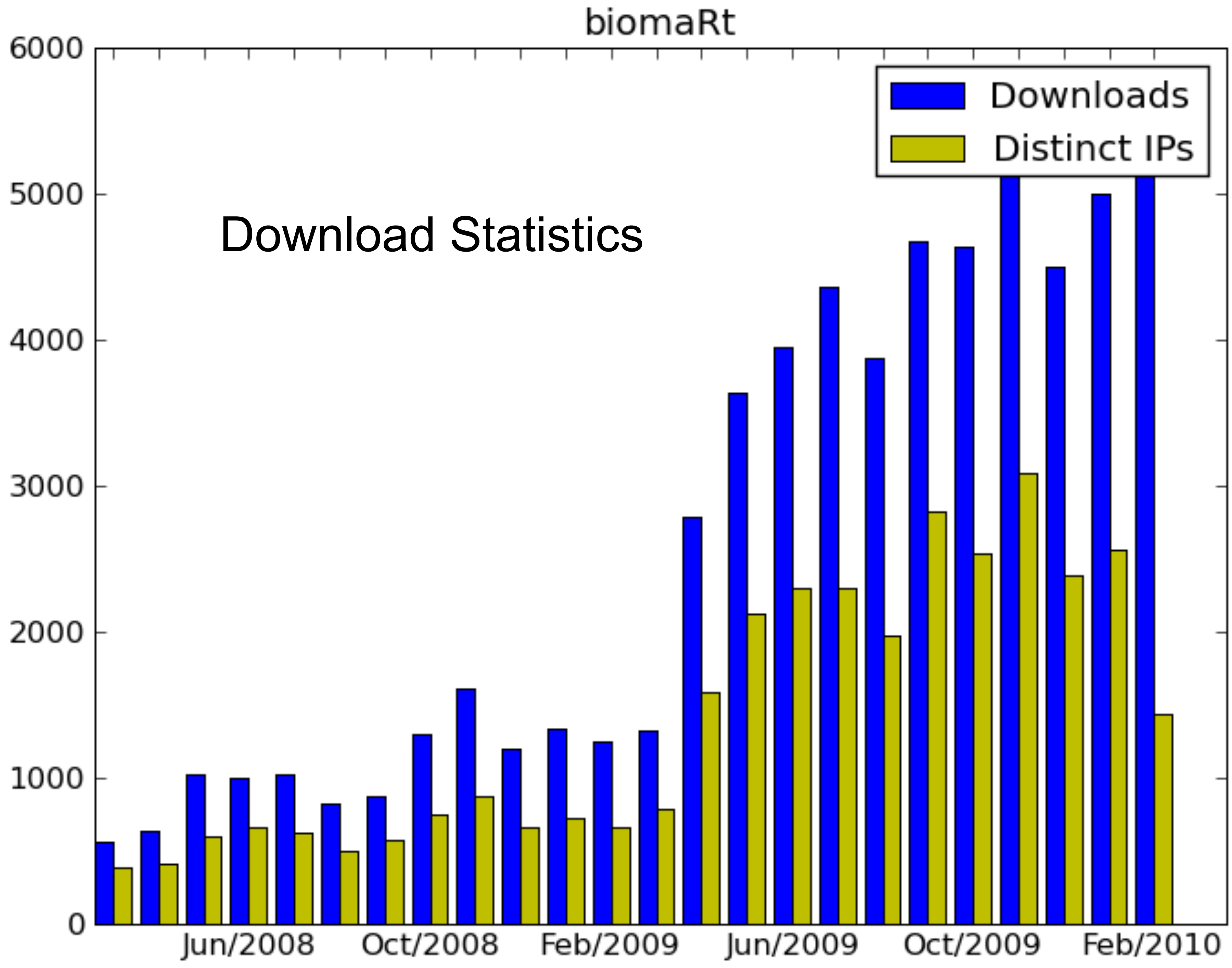
- De-normalized
- Tables with ‘redundant’ information
- Query optimized
- Fast and flexible

- Well suited for batch querying

biomaRt

- R interface to BioMart databases
- Performs online queries
- Current release version 2.2.0
- Depends on Rcurl and XML packages

Download Statistics



List available BioMart databases

```
> library(biomaRt)
Loading required package: XML
Loading required package: Rcurl
> listMarts()
```

List available BioMarts

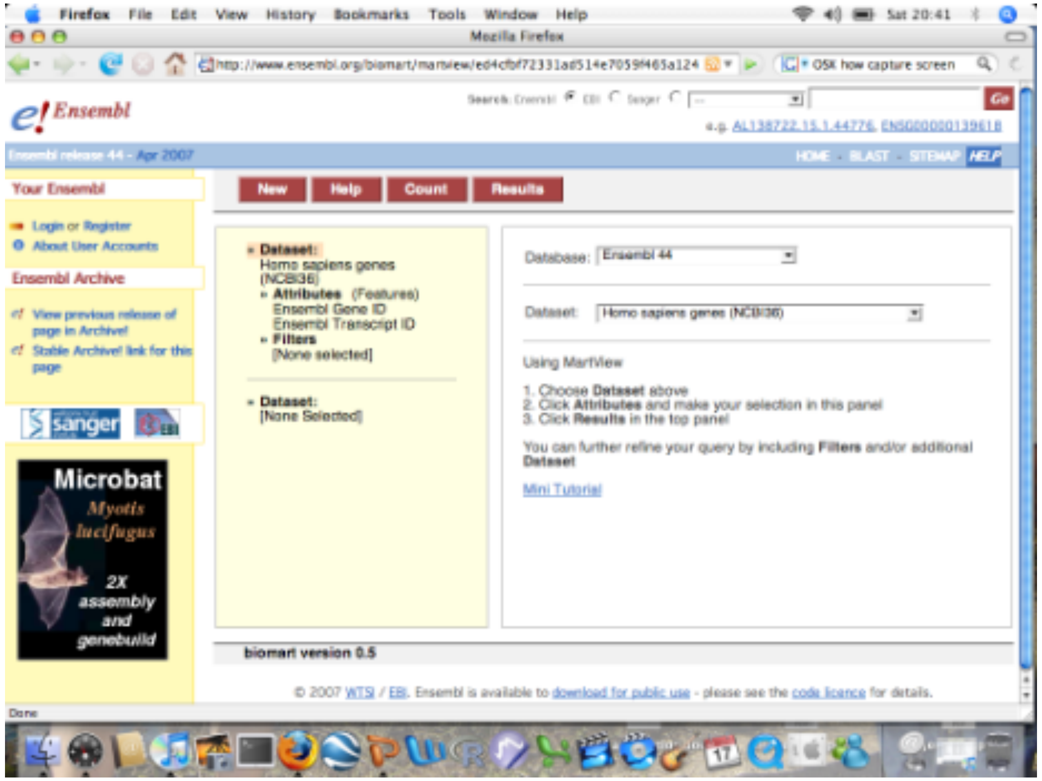
```
      biomart                        version
1       ensembl              ENSEMBL 55 GENES (SANGER UK)
2     snp                         ENSEMBL 55 VARIATION (SANGER UK)
3    functional_genomics          ENSEMBL 55 FUNCTIONAL GENOMICS
4     vega                       VEGA 35 (SANGER UK)
5    msd                          MSD PROTOTYPE (EBI UK)
6    htgt                HIGH THROUGHPUT GENE TARGETING AND TRAPPING
7     QTL_MART                   GRAMENE 29 QTL DB (CSHL US)
8     ENSEMBL_MART_ENSEMBL         GRAMENE 29 GENES
9 ENSEMBL_MART_SNP                   GRAMENE 29 SNPs
10 GRAMENE_MARKER_29               GRAMENE 29 MARKERS
....
```

Ensembl

- Ensembl is a joint project between EMBL - European Bioinformatics Institute (EBI) and the Wellcome Trust Sanger Institute (WTSI)
- A software system which produces and maintains automatic annotation on selected eukaryotic genomes.
- http://www.ensembl.org

Ensembl - BioMart

```
> ensembl=useMart("ensembl")
```


Firefox File Edit View History Bookmarks Tools Window Help
Sat 20:41
Mozilla Firefox
http://www.ensembl.org/biomart/martview/ed4cfbf72331ad514e7059f465a124
OSX how capture screen
Ensembl
Go
e.g. AL138722.15.1.44776, ENSG00000139618
Ensembl release 44 - Apr 2007
HOME - BLAST - SITEMAP HELP
Your Ensembl
Login or Register
About User Accounts
Ensembl Archive
View previous release of page in Archive!
Stable Archive! link for this page
sanger
EBI
Microbat Myotis lucifugus 2X assembly and genebuild
New
Help
Count
Results

Dataset:
Homo sapiens genes (NCBI36)
Attributes (Features)
Ensembl Gene ID
Ensembl Transcript ID
Filters
[None selected]

Dataset:
[None Selected]

Database: Ensembl 44

Dataset: Homo sapiens genes (NCBI36)

Using MartView

1. Choose **Dataset** above
2. Click **Attributes** and make your selection in this panel
3. Click **Results** in the top panel

You can further refine your query by including **Filters** and/or additional **Dataset**

Mini Tutorial

biomart version 0.5

© 2007 WTSI / EBI. Ensembl is available to download for public use - please see the code licence for details.

Ensembl - Datasets

```
> listDatasets(ensembl)
```

Returns:

- name: *hsapiens_gene_ensembl*
- description: *Homo sapiens genes*
- version: *(GRCh37)*

Ensembl currently contains 50 datasets~species

Ensembl - Datasets

A dataset can be selected using the useMart function

```
> ensembl = useMart("ensembl", dataset=
"hsapiens_gene_ensembl)
```

```
Checking attributes ... ok
Checking filters ... ok
```

biomaRt query: Attributes

- Attributes define the values which the user is interested in.
- Conceptually equal to output of the query
- Example attributes:
  - chromosome_name
  - band

biomaRt query: Filters

- Filters define restrictions on the query
- Conceptually filters are inputs

- Example filters:
  - entrezgene
  - chromosome_name

biomaRt query

Attributes (e.g., chromosome and band)

Filters (e.g., “entrezgene”)

Values (e.g., EntrezGene identifiers)

$\underbrace{\hspace{10em}}$

biomaRt query

Three main biomaRt functions

- *listFilters*
  - Lists the available filters
- *listAttributes*
  - Lists the available attributes
- *getBM*
  - Performs the actual query and returns a data.frame

Microarrays & Ensembl

- Ensembl does an independent mapping of array probe sequences to genomes (Affymetrix, Illumina, Agilent, …)
- If there is no clear match then that probe is not assigned to a gene

TASK 1 - Ensembl

- Annotate the following Affymetrix probe identifiers from the human u133plus2 platform with hugo gene nomenclature symbol (hgnc_symbol) and chromosomal location information:

211550_at, 202431_s_at, 206044_s_at

TASK 1 - Ensembl

- Filters: affy_hg_u133_plus_2
- Attributes:

affy_hg_u133_plus_2, chromosome_name, start_position, end_position, band, strand

- Values:

211550_at, 202431_s_at, 206044_s_at

TASK 1 - Ensembl

```
> affyids = c("211550_at","202431_s_at","206044_s_at")
> annotation = getBM(attributes=c("affy_hg_u133_plus_2","ensembl_gene_id","hgnc_symbol","chromosome_name","start_position","end_position","band","strand"), filters="affy_hg_u133_plus_2", values=affyids, mart = ensembl)
```

TASK 1 - Ensembl

```
>annotation

  affy_hg_u133_plus_2 ensembl_gene_id hgnc_symbol chromosome_name
1        202431_s_at    ENSG00000136997        MYC               8
2          211550_at    ENSG00000146648        EGFR              7
3        206044_s_at   ENSG00000157764         BRAF              7

     start_position     end_position   band     strand
1       128747680       128753674      q24.21       1
2        55086714        55324313      p11.2        1
3       140424943       140624564      q34         -1
```

TASK 1* - Ensembl

Retrieve GO annotation for the following Illumina human_wg6_v2 identifiers:

ILMN_1728071, ILMN_1662668

```
> illuminaIDs = c("ILMN_1728071","
ILMN_1662668")
> goAnnot = getBM(c("illumina_humanwg_6_v2",
"go_biological_process_id","
go_biological_process_linkage_type"), filters="
illumina_humanwg_6_v2", values=illuminaIDs, mart
= ensembl)
```

TASK 1* - Ensembl

```
illumina_humanwg_6_v2      go_biological_process_id
1 ILMN_1662668                 GO:0000281
2 ILMN_1662668                 GO:0006461
3 ILMN_1662668                 GO:0006974
4 ILMN_1662668                 GO:0007026
5 ILMN_1662668                 GO:0007050

go_biological_process_linkage_type
IMP
IDA
IDA
IDA
IDA
```

Using more than one filter

- getBM can be used with more than one filter
- Filters should be given as a vector
- Values should be a list of vectors where the position of each vector corresponds with the position of the associated filter in the filters argument

TASK 2 - Ensembl

Retrieve all genes that are involved in Diabetes Mellitus Type I or Type II and have transcription factor activity

TASK 2 - Ensembl

1. Diabetes Mellitus type I MIM accession: 222100
2. Diabetes Mellitus type II MIM accession:

125853

3. GO id for “transcription factor activity”: GO: 0003700

TASK 2 - Ensembl

```
diab=getBM(c("ensembl_gene_id","hgnc_symbol"),
filters=c("mim_morbid_accession","go"),
values=list(c("125853","222100"),"GO:0003700"),
mart=ensembl)
```

TASK 2 - Ensembl

```
  ensembl_gene_id      hgnc_symbol
1 ENSG00000139515          PDX1
2 ENSG00000108753          HNF1B
3 ENSG00000148737          TCF7L2
4 ENSG00000106331          PAX4
5 ENSG00000162992          NEUROD1
6 ENSG00000135100          HNF1A
```

Boolean filters

- Filters can be either numeric, string or boolean
- Boolean filters should have either TRUE or FALSE as values
  - TRUE: return all information that comply with the given filter (e.g. return only genes that have a hgnc_symbol)
  - FALSE: return all information that doesn’t comply with the given filter (e.g. with no hgnc_symbol)

Boolean filters/ *filterType*

The function *filterType* allows you to figure out which type each filter is (this function is currently only available in the devel version of biomaRt)

```
> filterType("affy_hg_u133_plus_2", mart=ensembl)
[1] “id_list

>filterType("with_affy_hg_u133_plus_2", mart=ensembl)
[1] "boolean_list"
```

TASK 3 - Ensembl

Retrieve all miRNAs known on chromosome 13 and their chromosomal locations

TASK 3 - Ensembl

```
>miRNA = getBM(c("mirbase","ensembl_gene_id","
start_position",
"chromosome_name"), filters=c("chromosome_name","
with_mirbase"), values=list(13,TRUE), mart=ensembl)
> miRNA[1:5,]
```

TASK 3 - Ensembl

```
    mirbase    ensembl_gene_id   start_position   chromosome_name
1 MI0008190    ENSG00000211491      41301964             13
2 MI0003635    ENSG00000207652      41384902             13
3 MI0000070    ENSG00000208006      50623109             13
4 MI0000069    ENSG00000207718      50623255             13
5 MI0003636    ENSG00000207858      90883436             13
```

TASK 4 - Ensembl

Retrieve all entrezgene identifiers on chromosome 22 that have a non-synonymous coding SNP

TASK 4 - Ensembl

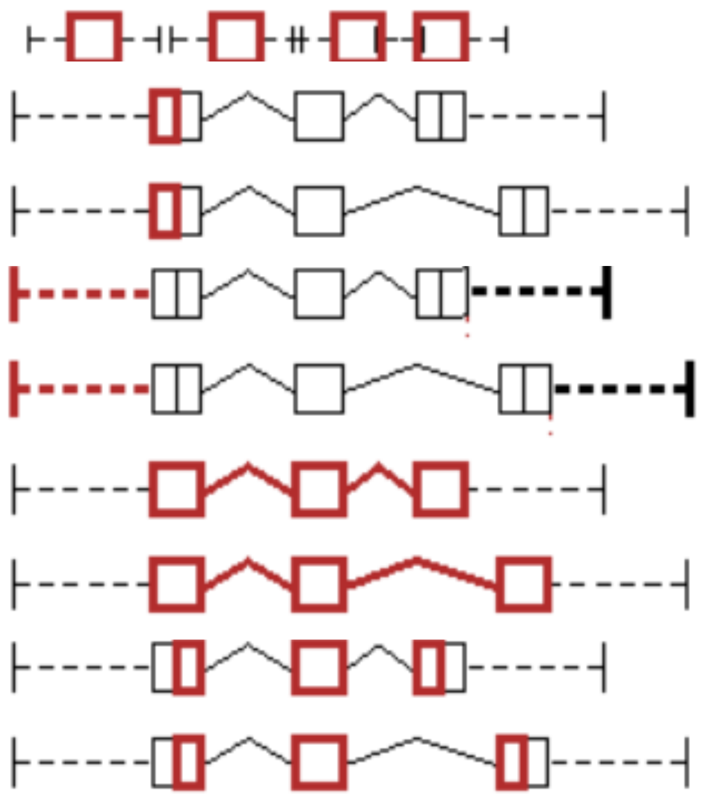
```
> filterOptions("snptype_filters",ensembl)
[1] "[STOP_GAINED,STOP_LOST,COMPLEX_INDEL,FRAMESHIFT_CODING,
NON_SYNONYMOUS_CODING,STOP_GAINED,SPLICE_SITE,STOP_LOST,
SPLICE_SITE,FRAMESHIFT_CODING,SPLICE_SITE,
NON_SYNONYMOUS_CODING,SPLICE_SITE,SYNONYMOUS_CODING,
SPLICE_SITE,SYNONYMOUS_CODING,5PRIME_UTR,SPLICE_SITE,
5PRIME_UTR,3PRIME_UTR,SPLICE_SITE,3PRIME_UTR,INTRONIC,
ESSENTIAL_SPLICE_SITE,INTRONIC,SPLICE_SITE,INTRONIC,UPSTREAM,
DOWNSTREAM]“

> entrez = getBM("entrezgene",filters=c("chromosome_name","
snptype_filters"), values=list(22,"NON_SYNONYMOUS_CODING"),
mart=ensembl)

> entrez[1:5,]
> [1] 23784 81061 150160 150165 128954
```

getSequence

- Retrieving sequences from Ensembl can be done using the *getBM* function or the *getSequence* wrapper function
- Output of *getSequence* can be exported to FASTA file using the *exportFASTA* function

getSequence

- Available sequences in Ensembl:
  - Exon
  - 3’UTR
  - 5’UTR
  - Upstream sequences
  - Downstream sequences
  - Unspliced transcript/gene
  - Coding sequence
  - Protein sequence



getSequence

- Arguments of getSequence:
  - *id* : identifier
  - *type* : type of identifier used e.g. hgnc_symbol or affy_hg_u133_plus_2
  - *seqType* : sequence type that needs to be retrieved e.g. gene_exon, coding, 3utr, 5utr,
  - *upstream/downstream* : specify number of base pairs upstream/downstream that need to be retrieved

TASK 5 - Ensembl

Retrieve all exons of CDH1

TASK 5 - Ensembl

```
> seq = getSequence(id="CDH1", type="hgnc_symbol",seqType="
gene_exon", mart = ensembl)
> seq[1,]
gene_exon
1
TACAAGGGTCAGGTGCCTGAGAACGAGGCTAACGTCGTAATCACCA
CACTGAAAGTGACTGATGCTGATGCCCCCAATACCCCAGCGTGGGA
GGCTGTATACACCATATTGAATGATGATGGTGGACAATTTGTCGTCA
CCACAAATCCAGTGAACAACGATGGCATTTTGAAAACAGCAAAG
hgnc_symbol
1 CDH1
```

TASK 6 - Ensembl

Retrieve 2000bp sequence upstream of the APC and CUL1 translation start site

TASK 6 - Ensembl

```
>promoter=getSequence(id=c("APC","CUL1"),type="hgnc_symbol",
seqType="coding_gene_flank",upstream =2000, mart=ensembl)

>  promoter
coding_gene_flank
1 TTGTTCATCTGAAGAGTTGATTTTTTTATTCCTGTAATA………………
2 TCCGTAGCAGTTGAATGTG …………………..

hgnc_symbol
1 APC
2 CUL1
```

Homology - Ensembl

- The different species in Ensembl are interlinked
- biomaRt takes advantage of this to provide homology mappings between different species

Linking two datasets

- Two datasets (e.g. two species in Ensembl) can be linked to each other by using the *getLDS* (get linked dataset) function
- One has to connect to two different datasets and specify the linked dataset using *martL* , *filtersL* , *attributesL* , *valuesL* arguments

TASK 7 - Ensembl

Retrieve human gene symbol and affy identifiers of their homologs in chicken for the following two identifiers from the human affy_hg_u95av2 platform: 1434_at, 1888_s_at

TASK 7 - Ensembl

```
> human=useMart("ensembl", dataset="hsapiens_gene_ensembl")
Checking attributes and filters ... ok
> chicken=useMart("ensembl", dataset="ggallus_gene_ensembl")
Checking attributes and filters ... ok

>out = getLDS(attributes=c("affy_hg_u95av2","hgnc_symbol"), filters="
affy_hg_u95av2", values=c("1888_s_at",“1434_at"),mart=human,
attributesL="affy_chicken", martL=chicken)
> out
V1 V2 V3
1 1434_at PTEN GgaAffx.25913.1.S1_a
2 1888_s_at KIT Gga.606.1.S1_at
```

Variation BioMart

- dbSNP mapped to Ensembl

```
> snp = useMart(“snp”, dataset=“hsapiens_snp”))
```

TASK 8 - Variation

Retrieve all refsnp_ids and their alleles and position that are located on chromosome 8 and between bp 148350 and 158612.

TASK 8 - Variation

```
>out=getBM(attributes=c("refsnp_id","allele","chrom_start"),
filters=c("chr_name","chrom_start","chrom_end"), values=list
(8,148350, 158612), mart=snp)
```

```
> out[1:5,]
refsnp_id              allele          chrom_start
1 ENSSNP4490669        C/G               148729
2 ENSSNP5558526        T/C               148909
3 ENSSNP4089737        T/A               149060
4 ENSSNP9060169        C/T               149245
5 ENSSNP4351891        C/G               149250
```

Ensembl Archives

- Provide alternate host

```
>listMarts(host="may2009.archive.ensembl.
org/biomart/martservice/")
biomart version
1 ENSEMBL_MART_ENSEMBL Ensembl 54
2 ENSEMBL_MART_SNP Ensembl Variation 54
3 ENSEMBL_MART_VEGA Vega 35
4 REACTOME Reactome(CSHL US)
5 wormbase_current WormBase (CSHL US)
6 pride PRIDE (EBI UK)

>ensembl54=useMart(“ENSEMBL_MART_ENSEMBL”, host="
may2009.archive.ensembl.org/biomart/martservice/")
```

Ensembl Archives

- Access to archives by setting archive=TRUE or connect to specific host (Note that this is currently not up to date in the central repository)

```
>listMarts(archive=TRUE)
    biomart             version
1 ensembl_mart_51     Ensembl 51
2 snp_mart_51         SNP 51
3 vega_mart_51        Vega 32
4 ensembl_mart_50     Ensembl 50
5 snp_mart_50         SNP 50

> ensembl51 = useMart("ensembl_mart_51", archive=TRUE, dataset="
hsapiens_gene_ensembl")
```

Gramene

- Gramene is a curated, open-source, data resource for comparative genome analysis in the grasses.
- Rice, Maize and Arabidopsis

TASK 9 - Gramene

Retrieve affy ATH1 ids and CATMA ids that map to the *Arabidopsis thaliana* chromosome 1 between basepair 30.000 and 41.000

TASK 9 - Gramene

```
>gramene = useMart
("ENSEMBL_MART_ENSEMBL", dataset="
athaliana_gene_ensembl")

>getBM(c("affy_ath1_id","catma_tigr5_id"),
filters=c("chromosome_name","start","end"),
values=list("1", "30000","41000"),
mart=gramene)
```

TASK 9 - Gramene

```
  affy_ath1_id    catma_tigr5_id
1 261579_at      CATMA1a00040
2 261569_at      CATMA1a00045
3 261569_at      CATMA1a00045
4 261569_at      CATMA1a00045
5 261576_at      CATMA1a00050
6 261576_at      CATMA1a00050
```

Wormbase

- Database on the genetics of C elegans and related nematodes.

TASK 10 - Wormbase

Determine the RNAi ids and the observed phenotypes for the gene with wormbase gene id: WBGene00006763

TASK 10 - Wormbase

```
> worm = useMart("wormbase176",
dataset="wormbase_rnai")

> pheno = getBM(c(“rnai”,”
phenotype_primary_name”), filters=“gene”, values=
“WBGene00006763”, mart=worm)
```

TASK 10 - Wormbase

```
>pheno
              rnai                phenotype_primary_name
1 WBRNAi00021278                  slow_growth
2 WBRNAi00021278 postembryonic_development_abnormal
3 WBRNAi00021278               embryonic_lethal
4 WBRNAi00021278                  larval_lethal
5 WBRNAi00021278                  larval_arrest
6 WBRNAi00021278                maternal_sterile
7 WBRNAi00021278                     Abnormal
8 WBRNAi00021278               sterile_progeny
9 WBRNAi00026915                 slow_growth
```

Discussion

- Using biomaRt to query public web services gets you started quickly, is easy and gives you access to a large body of metadata in a uniform way
- Need to be online
- Online metadata can change behind your back; although there is possibility of connecting to a particular, immutable version of a dataset

Reporting bugs

- Check with MartView if you get the same output
  - Yes: contact database e.g. helpdesk@ensembl.org
  - No: contact me - sdurinck@lbl.gov

Acknowledgements

- EBI
  - Rhoda Kinsella
  - Arek Kasprzyk
  - Ewan Birney
- EMBL
  - Wolfgang Huber

Bioconductor users