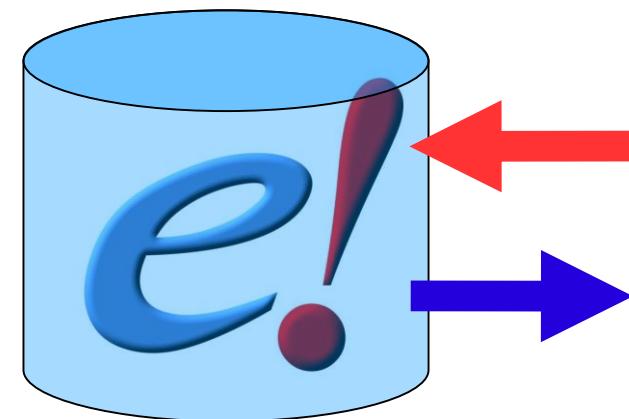
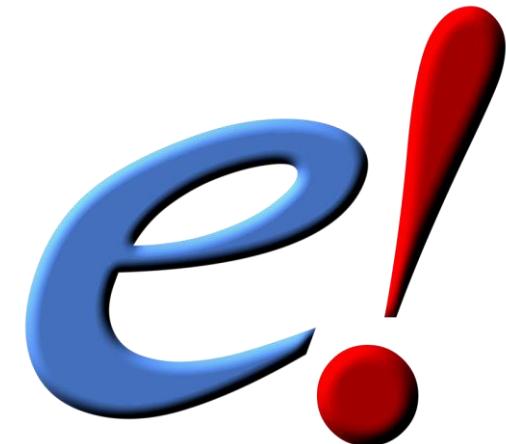




Ensembl Core API



EMBL – European Bioinformatics Institute
Wellcome Trust Genome Campus
Hinxton, Cambridge, CB10 1SD, UK



Outline

- a. Introduction
- b. Data objects & object adaptors
- c. Ensembl documentation
- d. The Registry & Ensembl API script design
- e. Coordinate systems & slices
- f. Features
- g. Genes, transcripts, exons & translations
- h. External references

Ensembl API

- Written in Object-Oriented Perl.
- Used to retrieve data from and to store data in Ensembl databases.
- Foundation for the Ensembl Pipeline and Ensembl Web interface.



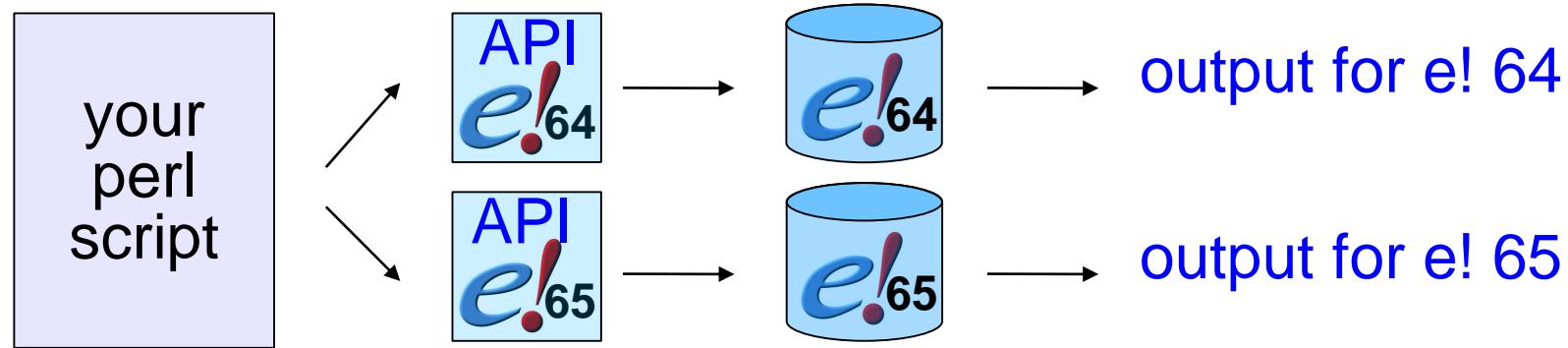
```
my $slice = $slice_adaptor->  
fetch_by_region("chromosome", "13",  
                31786617, 31872809);  
  
my $genes = $slice->get_all_Genes();  
  
foreach my $this_gene (@$genes) {  
  
    print $this_gene->stable_id, ": ",  
          $this_gene->start, " - ",  
          $this_gene->end, "\n";  
  
}  
}
```

Why use an API?

- Uniform method of access to the data.
- Avoid writing the same thing twice: reusable in different systems.
- Reliable: lots of hard work, testing and optimisation already done.
- Insulates developers from underlying changes at a lower level (i.e. the database).

Using the correct API version

API version **must** match database version. Old scripts using the API *should* continue working with a newer API.



Run script `ensembl/misc-scripts/ping_ensembl.pl` to test if you can contact the Ensembl database server. The script will help you resolve issues with your setup.

An Alternative - REST

[Endpoints](#)[User Guide](#)[Change Log](#)[About the Ensembl Project](#)[Contact Ensembl](#)

Sequences

Resource	Description
GET sequence/id/:id	Request multiple types of sequence by stable identifier.
GET sequence/region/:species/:region	Returns the genomic sequence of the specified region of the given species.

Variation

Resource	Description
GET variation/:species/:id	Uses a variation identifier (e.g. rsID) to return the variation features
GET vep/:species/id/:id	Fetch variant consequences based on a variation identifier
POST vep/:species/id/	Fetch variant consequences for multiple ids

<http://rest.ensembl.org>

Installing the Perl API from FTP

```
# cd to a location to install Ensembl to
mkdir src
cd src

# Get the latest API from FTP (always the live version) and BioPerl 1.2.3
wget ftp://ftp.ensembl.org/pub/ensembl-api.tar.gz
wget http://bioperl.org/DIST/old_releases/bioperl-1.2.3.tar.gz

# untar both
tar zxvf ensembl-api.tar.gz
tar zxvf bioperl-1.2.3.tar.gz

# open up .bashrc or .profile and add the following
PERL5LIB=${PERL5LIB}:$HOME/src/bioperl-1.2.3
PERL5LIB=${PERL5LIB}:$HOME/src/ensembl/modules
PERL5LIB=${PERL5LIB}:$HOME/src/ensembl-compara/modules
PERL5LIB=${PERL5LIB}:$HOME/src/ensembl-variation/modules
PERL5LIB=${PERL5LIB}:$HOME/src/ensembl-functgenomics/modules
export PERL5LIB

# Checking your installation
perl $HOME/src/ensembl/misc-scripts/ping_ensembl.pl
```

Alternative Methods of Installation

- Git clone from <https://github.com/Ensembl/>
- Ensembl Virtual Machine
 - ftp://ftp.ensembl.org/pub/current_virtual_machine
 - 64bit only in OVA format

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Ensembl API – Object Types

We have two main object types in Ensembl API:

1. Data Objects

Talk to a particular row in a data table, such as the BRCA2 gene to get (or set) information related to this gene only.

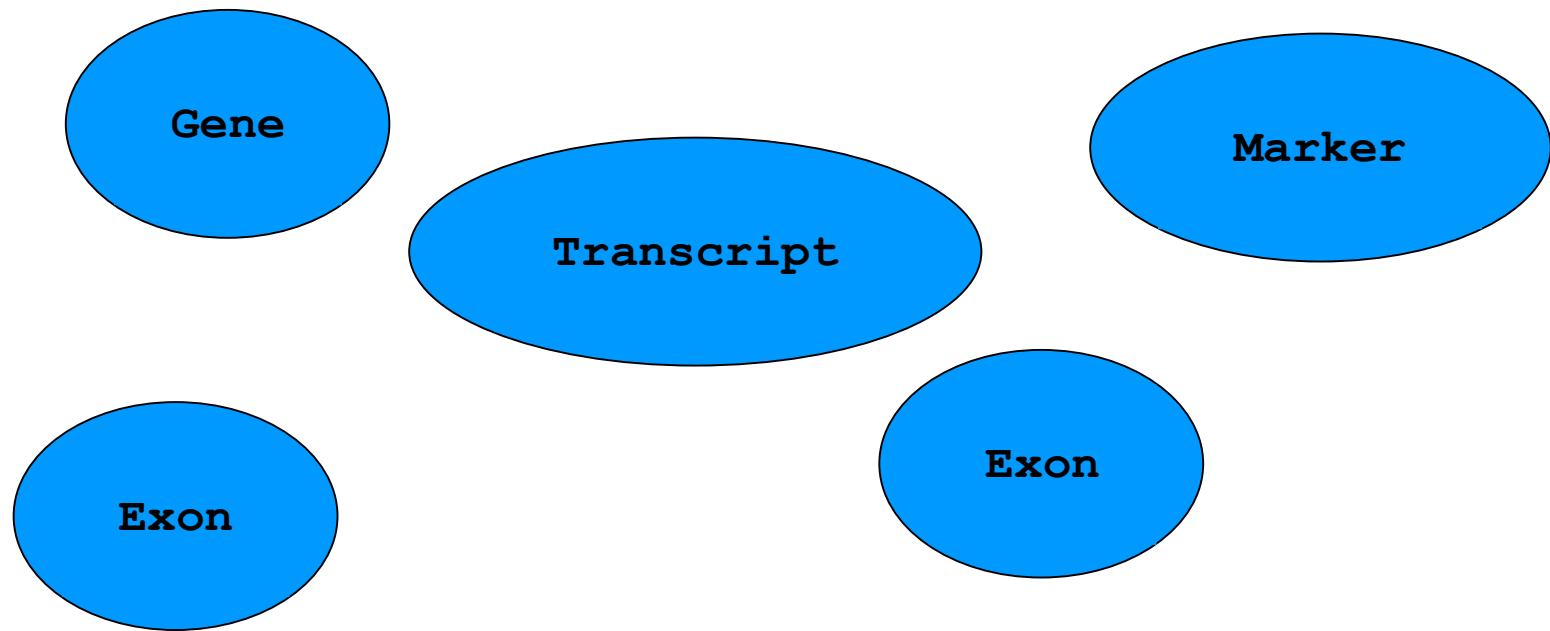
2. Object Adaptors

Talk to a particular data table, such as the gene table to retrieve or store genes in the gene table.

Data Objects

Data objects model biological entities, e.g. genes, transcripts, exons...

A *Data Object* represents a piece of data that is (or can be) stored in the database.



Object Adaptors

Data Objects are retrieved from and stored in the database using **Object Adaptors**.

Each *Object Adaptor* is responsible for creating objects of only one particular type. For instance:

- The **Gene**Adaptor is used to fetch **Gene** objects
- The **Exon**Adaptor is used to fetch **Exon** objects

Object Adaptor *fetch*, *store*, and *remove* methods are used to retrieve, save, and delete information in the database.

Two types of methods:

- **fetch_by_....** returns 1 object (or undef)
- **fetch_all_by_...** returns a ref. to an array of objects (or ref. to an empty array)

Object methods in Ensembl API

An Object has attributes and methods.

We avoid accessing object attributes directly, we use methods instead.

Methods are called using the “arrow” (->) operator:

```
my $exons = $gene->get_all_Exons();
```

Many methods can be used to either get or set an attribute value:

GET (no arg.):

```
my $gene_id = $gene->stable_id();
```

SET (new value):

```
$gene->stable_id("ENSG0000000123152");
```

Object methods and adaptors

- The API deals with objects representing database entities
- Adaptors are “**factories**” for generating objects
 - Adaptors are retrieved from the Registry

```
use strict;
use warnings
use Bio::EnsEMBL::Registry;

my $reg = 'Bio::EnsEMBL::Registry';

$reg->load_registry_from_db(
    -host => 'ensembldb.ensembl.org',
    -user => 'anonymous'
);

my $ga = $reg->get_adaptor('human', 'core', 'gene');
...
my $gene= $ga->fetch_by_stable_id('ENSG00000139618');
```

The diagram illustrates the components of the adaptor creation code. Three colored boxes with arrows point to specific parts of the line: 'species' points to 'human', 'group' points to 'core', and 'object name' points to 'gene'.

Object methods and adaptors

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);

my $ga = $reg->get_adaptor('human', 'core', 'gene');

...
my $gene= $ga->fetch_by_stable_id('ENSG00000139618');
```

The diagram consists of two main parts. On the left, there is a dashed rectangular box containing Perl code. On the right, there is a light blue arrow pointing from the explanatory text to the first line of code ('use strict;'). Below the code, three colored boxes (red, blue, and green) have arrows pointing upwards to specific parts of the code: 'species' points to 'human', 'group' points to 'core', and 'object name' points to 'gene'.

Use 'strict' and 'warnings'

species group object name

Object methods and adaptors

- The API deals with objects representing database entities
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 - Adaptors are retrieved from the Registry

```
use strict;
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use Bio::EnsEMBL::Registry;

my $reg = 'Bio::EnsEMBL::Registry';

$reg->load_registry_from_db(
    -host => 'ensembldb.ensembl.org',
    -user => 'anonymous'
);

my $ga = $reg->get_adaptor('human', 'core', 'gene');

...
my $gene= $ga->fetch_by_stable_id('ENSG00000139618');
```

The diagram illustrates the structure of the arguments passed to the `get_adaptor` method. It shows three colored boxes with arrows pointing to specific parts of the code:

- A red box labeled "species" has an arrow pointing to the first argument "human".
- A blue box labeled "group" has an arrow pointing to the second argument "core".
- A green box labeled "object name" has an arrow pointing to the third argument "gene".
- A large blue arrow points to the `-host` argument with the text "Change your host and port".

Object methods and adaptors

- The API deals with objects representing database entities
- Adaptors are “**factories**” for generating objects
 - Adaptors are retrieved from the Registry

```
use strict;
use warnings
use Bio::EnsEMBL::Registry;

my $reg = 'Bio::EnsEMBL::Registry';

$reg->load_registry_from_db(
    -host => 'ensembldb.ensembl.org',
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);

my $ga = $reg->get_adaptor('human', 'core', 'gene');
...
my $gene= $ga->fetch_by_stable_id('ENSG00000139618');
```

The diagram illustrates the components of the adaptor creation code. Three colored boxes with arrows point to specific parts of the code: a red box labeled 'species' points to 'human', a blue box labeled 'group' points to 'core', and a green box labeled 'object name' points to 'gene'.

Object retrieval

- Using adaptors
 - **Fetch** object(s) according to some property e.g. name, location
 - “fetch_all_...” -> returns a list reference of items
 - “fetch_by_...” usually returns only 1 item
 - Check documentation which methods the adaptor provides
- Using API objects: e.g. **Slice**, **Gene**, **Transcript**...
 - **Get** other object(s) from an API object
 - e.g. `$gene->get_all_Transcripts()`
returns a list reference of Ensembl **Transcript** objects
 - Usually the object is written with a upper case in the method
 - e.g. `get_all_Transcripts()`

Data Objects & Object Adaptors

```
# fetch a gene by its stable identifier using a gene adaptor

my $gene =
    $gene_adaptor->fetch_by_stable_id('ENSG00000139618');

# print out the name of a gene and its stable identifier

print $gene->external_name(), "\n";
print $gene->stable_id, "\n";
```

Ensembl Core modules

Name space for the modules:

- Object modules start with **Bio::EnsEMBL**
 - Bio::EnsEMBL::Gene for gene objects
 - Bio::EnsEMBL::Exon for exon objects
- ObjectAdaptors start with **Bio::EnsEMBL::DBSQL**
 - Bio::EnsEMBL::DBSQL::GeneAdaptor
 - Bio::EnsEMBL::DBSQL::ExonAdaptor

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Ensembl API Documentation (1)

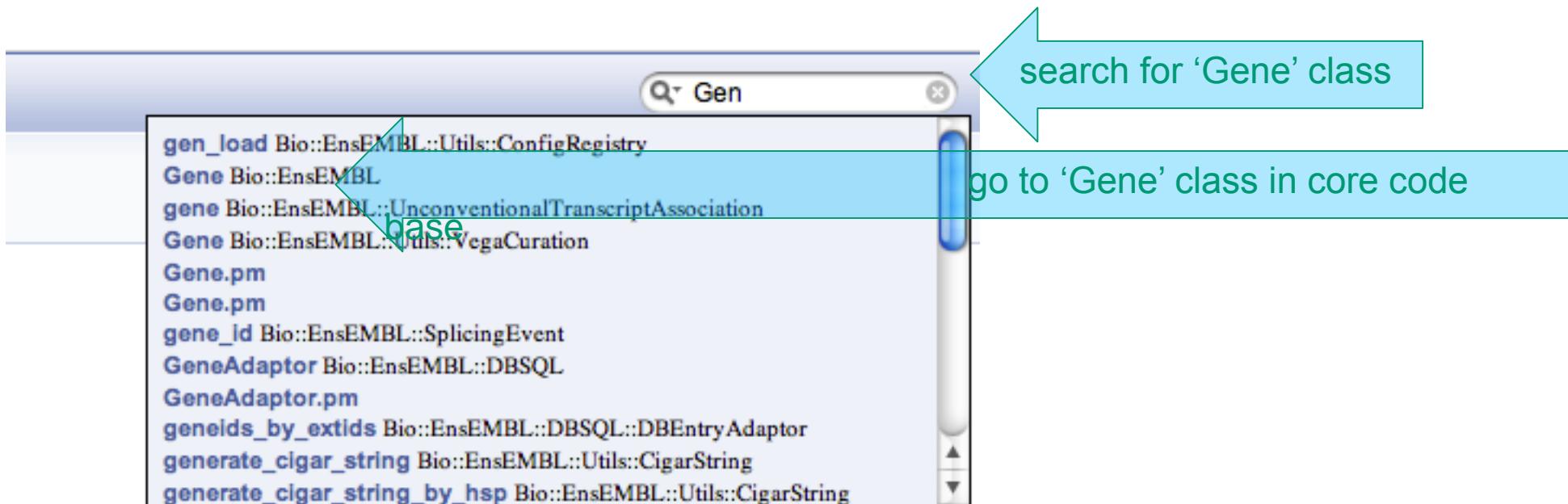
Go to <http://www.ensembl.org/info/docs/Doxygen/index.html>

The screenshot shows the Ensembl website's navigation bar with links for BLAST/BLAT, BioMart, Tools, Downloads, and Help & Documentation. Below the navigation bar, a breadcrumb trail shows the user has navigated from the homepage to Help & Documentation and then to Doxygen Perl documentation. The main content area is titled "Doxygen perl module documentation". A sub-section title "Core code base" is highlighted with a teal arrow pointing to the list of modules. The list includes:

- [Ensembl](#) - Ensembl core database API
- [Ensembl-analysis](#)
- [Ensembl-hive](#)
- [Ensembl-compara](#) - Ensembl comparative genomics API
- [Ensembl-external](#)
- [Ensembl-functgenomics](#) - Ensembl functional genomics API
- [Ensembl-pipeline](#) - Ensembl gene build pipeline*
- [Ensembl-variation](#) - Ensembl variation data API
- [BioPerl](#)

Ensembl API Documentation (2)

Search for classes or methods



Ensembl API Documentation (3)

Breadcrumbs help you keep track of which code base you're in.

Help & Documentation > API & Software > Doxygen Perl documentation

Overview Classes Namespaces Files Directory Browser Related Pages

Class Hierarchy Class Index Full Class List Methods from all packages

Bio::EnsEMBL::IdMapping::InternalIdMapper::Entry
Bio::EnsEMBL::IdMapping::Entry
Bio::EnsEMBL::Utils::Eprof
Bio::EnsEMBL::Utils::EprofStack
Bio::EnsEMBL::Utils::Exception
Bio::EnsEMBL::Exon
Bio::EnsEMBL::DBSQL::ExonAdaptor
Bio::EnsEMBL::IdMapping::ExonScoreBuilder
Bio::EnsEMBL::External::ExternalFeatureAdaptor
Bio::EnsEMBL::DB::ExternalFeatureFactoryI
Bio::EnsEMBL::Utils::IO::FASTASerializer
Bio::EnsEMBL::Feature
Bio::EnsEMBL::FeaturePair
Bio::EnsEMBL::Utils::IO::FeatureSerializer
Bio::EnsEMBL::DBFile::FileAdaptor
Bio::EnsEMBL::DBSQL::Support::FullIdCache
Bio::EnsEMBL::Mapper::Gap
Bio::EnsEMBL::Gene
Bio::EnsEMBL::Utils::VegaCuration::Gene
Bio::EnsEMBL::DBSQL::GeneAdaptor
Bio::EnsEMBL::IdMapping::GeneScoreBuilder
Bio::EnsEMBL::DBSQL::GenomeContainer
Bio::EnsEMBL::Utils::IO::GFFParser
Bio::EnsEMBL::Utils::IO::GFFSerializer
Bio::EnsEMBL::DBSQL::GOTermAdaptor

Bio::EnsEMBL::Gene Class Reference

Inheritance diagram for Bio::EnsEMBL::Gene:
List of all members.

Class Summary

Synopsis

```
my $gene = Bio::EnsEMBL::Gene->new(  
    -START  => 123,  
    -END    => 1045,  
    -STRAND => 1,  
    -SLICE   => $slice  
);  
  
# print gene information  
print("gene start:end:strand is "  
    . join( ":", map { $gene->$_ } qw(start end strand) )  
    . "\n" );  
  
# set some additional attributes  
$gene->stable_id('ENSG000001');  
$gene->description('This is the gene description');
```

Description

A representation of a Gene within the Ensembl system. A gene is a set of one or more alternative transcripts.

Bio > EnsEMBL > Gene

Ensembl API Documentation (4)

Classes can *inherit* attributes and methods from other classes. For instance a Gene is also a Feature as it can be located on a region of DNA so it inherits from the **Bio::EnsEMBL::Feature** object.

The screenshot shows a web-based API documentation interface for the Ensembl Perl API. The URL in the address bar is [http://www.ensembl.org/Help/Documentation/Doxygen_Perl_documentation/Ensembl/Bio/EnsEMBL/Gene](#). The page title is "Bio::EnsEMBL::Gene Class Reference".

The navigation menu at the top includes links for Overview, Classes (which is selected), Namespaces, Files, Directory Browser, and Related Pages. Below the menu, there are links for Class Hierarchy, Class Index, Full Class List, and Methods from all packages.

The main content area displays the "Bio::EnsEMBL::Gene Class Reference". It includes sections for Inheritance diagram for Bio::EnsEMBL::Gene, List of all members, Class Summary, and Synopsis. The Synopsis section contains the following Perl code:

```
my $gene = Bio::EnsEMBL::Gene->new(
    -START  => 123,
    -END    => 1045,
    -STRAND => 1,
    -SLICE  => $slice
);

# print gene information
print("gene start:end:strand is "
    . join( ":", map { $gene->$_ } qw(start end strand) )
    . "\n");
```

A large blue arrow points from the text "expand to view classes which 'Gene' inherits from" towards the "Inheritance diagram for Bio::EnsEMBL::Gene" link. The "Bio::EnsEMBL::Gene" class name is highlighted in the sidebar under the "Classes" tab, and the inheritance diagram link is visible above it.

expand to view classes
which 'Gene' inherits from

Ensembl API Documentation (5)

Scroll down to see a list of available methods in the ‘Gene’ class. Can you find a method to retrieve all transcripts for a gene? Where possible, this list shows the returned data types for each method.

Help & Documentation > Doxygen Perl documentation > Ensembl > Bio > EnsEMBL > Gene

Overview	Classes	Namespaces	Files	Directory Browser	Related Pages																																		
Class Hierarchy	Class Index	Full Class List	Methods from all packages	Definition at line 5 for file Gene.pm																																			
Available Methods																																							
<table border="0"><tbody><tr><td>protected</td><td>_deprecated_transform ()</td></tr><tr><td>public Bio::EnsEMBL::DBSQL::BaseAdaptor</td><td>adaptor ()</td></tr><tr><td>public void</td><td>add_Attributes ()</td></tr><tr><td>public void</td><td>add_DBEntry ()</td></tr><tr><td>public DEPRECATED</td><td>add_DBLink ()</td></tr><tr><td>public</td><td>add_sub_SeqFeature ()</td></tr><tr><td>public void</td><td>add_Transcript ()</td></tr><tr><td>public void</td><td>add_unconventional_transcript_association ()</td></tr><tr><td>public Bio::EnsEMBL::Analysis</td><td>analysis ()</td></tr><tr><td>public String</td><td>biotype ()</td></tr><tr><td>public String</td><td>canonical_annotation ()</td></tr><tr><td>public Bio::EnsEMBL::Transcript</td><td>canonical_transcript ()</td></tr><tr><td>public</td><td>chr_name ()</td></tr><tr><td>public</td><td>confidence ()</td></tr><tr><td>public String</td><td>contig ()</td></tr><tr><td>public String</td><td>coord_system_name ()</td></tr><tr><td>public String</td><td>created_date ()</td></tr></tbody></table>						protected	_deprecated_transform ()	public Bio::EnsEMBL::DBSQL::BaseAdaptor	adaptor ()	public void	add_Attributes ()	public void	add_DBEntry ()	public DEPRECATED	add_DBLink ()	public	add_sub_SeqFeature ()	public void	add_Transcript ()	public void	add_unconventional_transcript_association ()	public Bio::EnsEMBL::Analysis	analysis ()	public String	biotype ()	public String	canonical_annotation ()	public Bio::EnsEMBL::Transcript	canonical_transcript ()	public	chr_name ()	public	confidence ()	public String	contig ()	public String	coord_system_name ()	public String	created_date ()
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public Bio::EnsEMBL::Analysis	analysis ()																																						
public String	biotype ()																																						
public String	canonical_annotation ()																																						
public Bio::EnsEMBL::Transcript	canonical_transcript ()																																						
public	chr_name ()																																						
public	confidence ()																																						
public String	contig ()																																						
public String	coord_system_name ()																																						
public String	created_date ()																																						

Ensembl API Documentation (6)

Clicking on a method takes you to a description with associated arguments, return types and exceptions.

public Bio::EnsEMBL::Slice Bio::EnsEMBL::Feature::slice ()

Arg [1] : (optional) **Bio::EnsEMBL::Slice** \$slice
Example :

```
$seqname = $feature->slice()->name();
```

Description: Getter/Setter for the **Slice** that is associated with this feature. The slice represents the underlying sequence that this feature is on. Note that this method call is analogous to the old **SeqFeature** methods **contig()**, **entire_seq()**, **attach_seq()**, etc.

Returntype : **Bio::EnsEMBL::Slice**

Exceptions : thrown if an invalid argument is passed

Caller : general

Status : Stable

▶Code:

[click to view](#)

Reimplemented in **Bio::EnsEMBL::Exon**, and **Bio::EnsEMBL::Map::DitagFeature**.

Ensembl API Documentation (7)

Clicking on **Code**: shows the method's implementation

▼Code:

```
sub slice {
    my ( $self, $slice ) = @_;
    if ( defined($slice) ) {
        if ( !check_ref( $slice, 'Bio::EnsEMBL::Slice' )
            && !check_ref( $slice, 'Bio::EnsEMBL::LRGSlice' ) )
        {
            throw('slice argument must be a Bio::EnsEMBL::Slice');
        }
        $self->{'slice'} = $slice;
    } elsif ( @_ > 1 ) {
        delete($self->{'slice'});
    }
    return $self->{'slice'};
}
```

Reimplemented in [Bio::EnsEMBL::Exon](#), and [Bio::EnsEMBL::Map::DitagFeature](#).

Ensembl Core DB Documentation (1)

Go to http://www.ensembl.org/info/docs/api/core/core_schema.html

Ensembl Core - Schema documentation

This document gives a high-level description of the tables that make up the EnsEMBL core schema. Tables are grouped into logical groups, and the purpose of each table is explained. It is intended to allow people to familiarise themselves with the schema when encountering it for the first time, or when they need to use some tables that they've not used before.

This document refers to version **74** of the EnsEMBL core schema.

The core database schema is available in several diagrams (PDF format) here:



List of the tables:

Assembly Tables	External References	Features
<ul style="list-style-type: none">assemblyassembly exceptioncoord systemdata filedna	<ul style="list-style-type: none">associated groupassociated xrefdependent xrefexternal dbexternal synonym	<ul style="list-style-type: none">density featuredensity typeditagditag featureintron supporting evidenceprediction transcriptrepeat consensusrepeat featuresimple featuretranscript intron supporting evidence

Ensembl Core DB Documentation (2)

Scroll down to the list of Fundamental Tables and click on the gene table.

■ Fundamental Tables

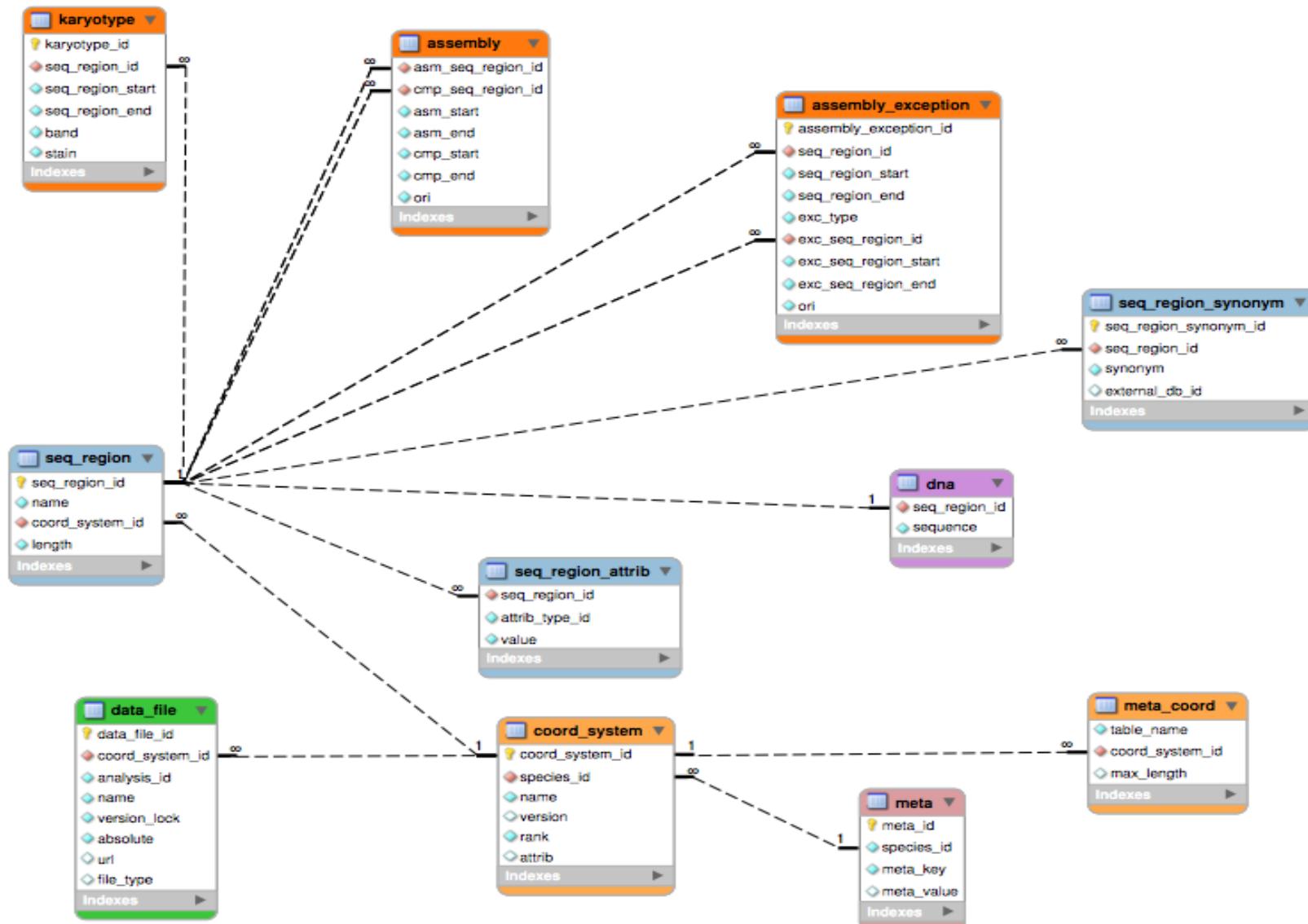
- [alt_allele](#)
- [alt_allele_attrib](#)
- [alt_allele_group](#)
- [analysis](#)
- [analysis_description](#)
- [attrib_type](#)
- [dna_align_feature](#)
- [exon](#)
- [exon_transcript](#)
- [gene](#)
- [gene_attrib](#)
- [protein_align_feature](#)
- [protein_feature](#)
- [splicing_event](#)
- [splicing_event_feature](#)
- [splicing_transcript_pair](#)
- [supporting_feature](#)
- [transcript](#)
- [transcript_attrib](#)
- [transcript_supporting_feature](#)
- [translation](#)
- [translation_attrib](#)

Ensembl Core DB Documentation (3)

Click on the ‘show columns’ link to the right to expand a list of gene table columns, their types, descriptions and indices over the columns.

gene		- Hide columns [Back to top]	
Column	Type	Default value	Description
gene_id	INT(10)		Primary key, internal identifier.
biotype	VARCHAR(40)		Biotype, e.g. protein_coding.
analysis_id	SMALLINT		Foreign key references to the analysis table.
seq_region_id	INT(10)		Foreign key references to the seq_region table.
seq_region_start	INT(10)		Sequence start position.
seq_region_end	INT(10)		Sequence end position.
seq_region_strand	TINYINT(2)		Sequence region strand: 1 - forward; -1 - reverse.
display_xref_id	INT(10)		External reference for Ensembl web site. Foreign key re
source	VARCHAR(20)		e.g ensembl, havana etc.
status	ENUM('KNOWN', 'NOVEL', 'PUTATIVE', 'PREDICTED', 'KNOWN_BY_PROJECTION', 'UNKNOWN', 'ANNOTATED')		Status, e.g.'KNOWN', 'NOVEL', 'PUTATIVE', 'PREDICTED', 'KNOWN_BY_PROJECTION', 'UNKNOWN'.
description	TEXT		Gene description

Ensembl Core DB Documentation (4)



Exercise 1

- a) Find documentation for the Exon class in the Ensembl core code base. Which method would you use to retrieve the DNA sequence for an exon? What is the return type for this method?
- b) Can you find a table which stores stable ids for transcripts? Which table stores DNA sequence? How many columns does this table have?

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The Registry

We know how to use Data Objects and Object Adaptors.

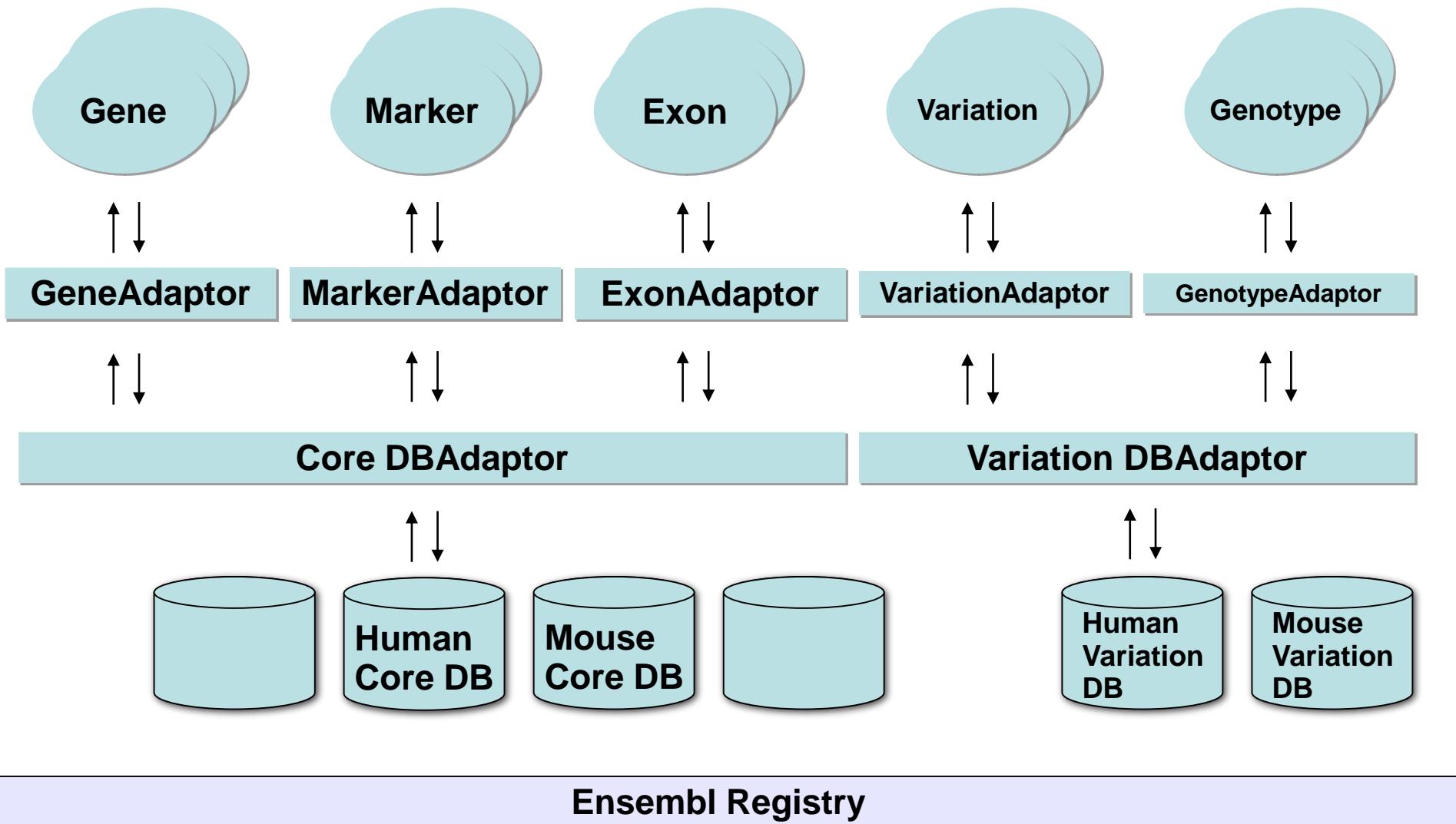
How do we make sure we get those from the right database?

This is what we use the Registry for.

The Registry:

- loads all databases of the same version as the API
- lazy loads so no connections are made until requested

Ensembl API Architecture



Review: The basic Ensembl script

```
use strict;
use warnings;
use Bio::EnsEMBL::Registry;

my $reg = 'Bio::EnsEMBL::Registry';

$reg->load_registry_from_db(
    -host => 'ensembldb.ensembl.org',
    -user => 'anonymous'
);

my $ga = $reg->get_adaptor('human', 'core', 'gene');

...
my $gene= $ga->fetch_by_stable_id('ENSG00000139618');
```

Exercise 2

Create a script which uses the method `load_registry_from_db` to load all databases into the Registry and prints the names of the databases loaded.

Hint: Have a look at the Doxygen documentation for the Registry object and method `load_registry_from_db` (<http://www.ensembl.org/info/docs/Doxygen/index.html>).

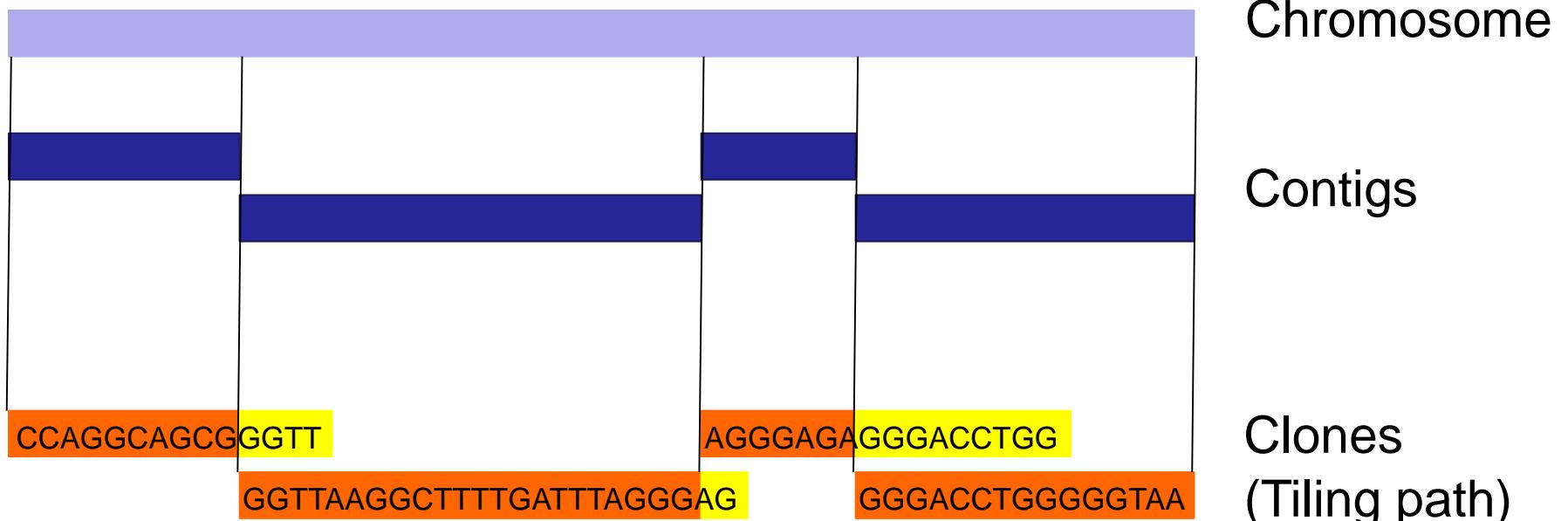
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Coordinate Systems (1)

Ensembl stores features and DNA sequence in a number of coordinate systems.

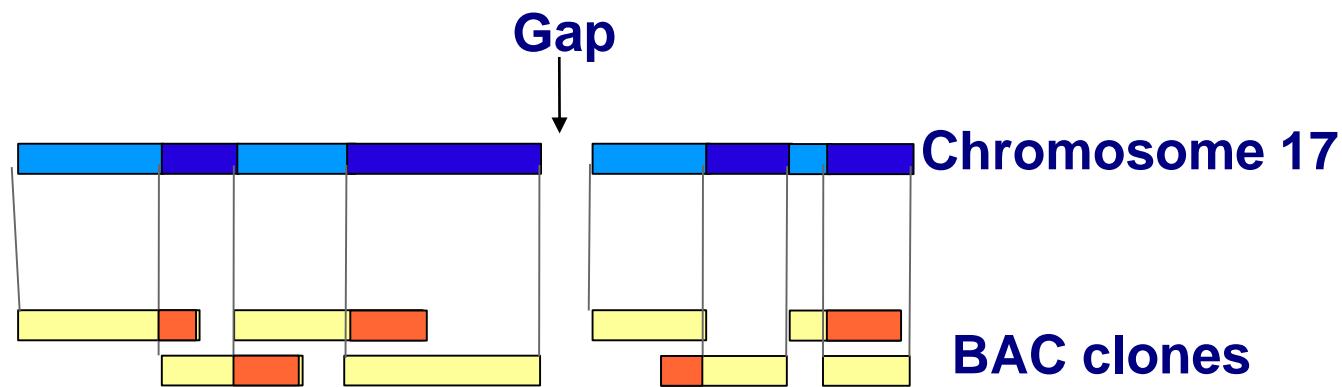
Top level coordinate system



Sequence level coordinate system

Coordinate Systems (2)

Regions in one coordinate system may be constructed from a tiling path of regions from another coordinate system.



Coordinate Systems - Code Example

```
# Obtain all coordinate systems for human

use Bio::EnsEMBL::Registry;
my $registry = 'Bio::EnsEMBL::Registry';

$registry->load_registry_from_db(
    -host => 'ensembldb.ensembl.org',
    -user => 'anonymous'
);
my $coordsystem_adaptor = $registry->get_adaptor( 'Human', 'Core', 'CoordSystem' );

my $coordsystems = $coordsystem_adaptor->fetch_all;

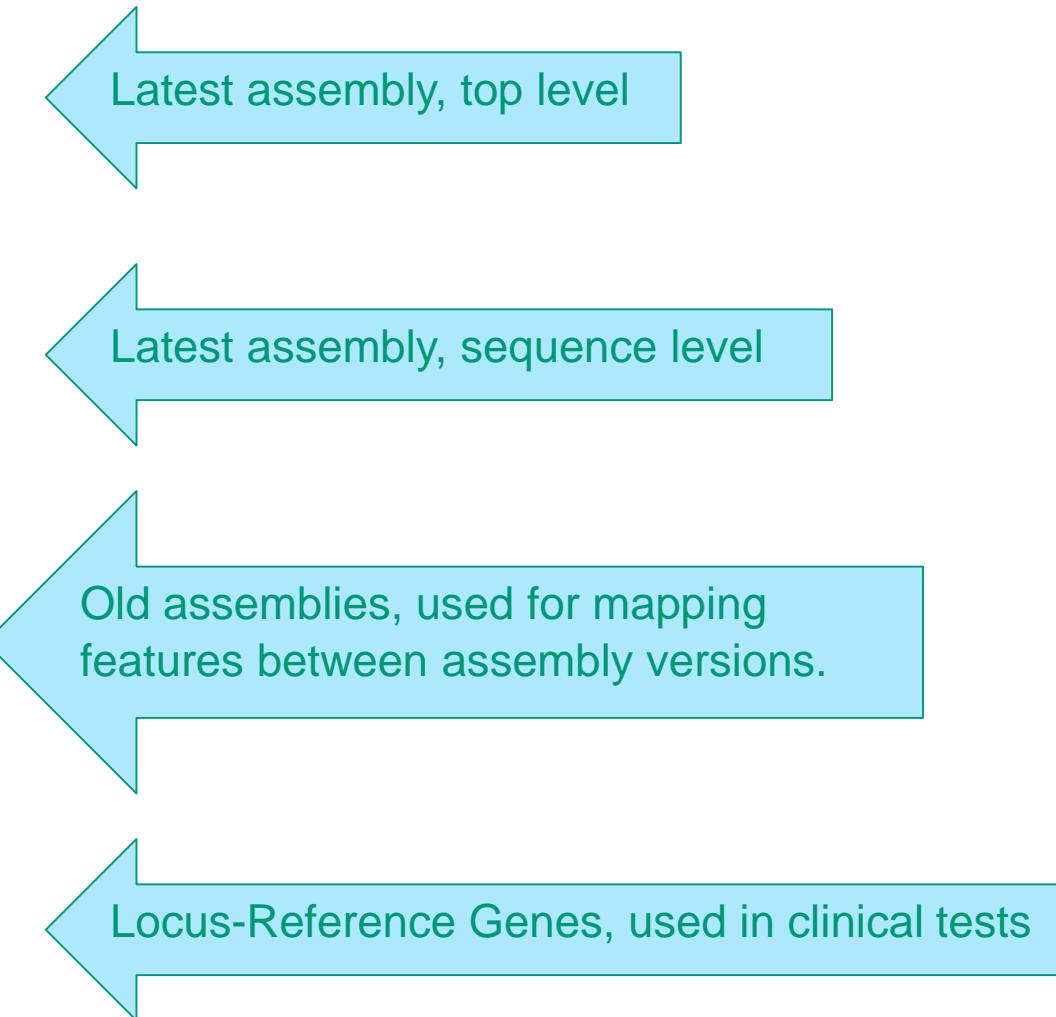
while ( my $coordsystem = shift @{$coordsystems} ) {
    print $coordsystem->name, "\t",
        $coordsystem->version, "\t",
        $coordsystem->rank ,"\n";
}
```

Note use of 'while' and 'shift' instead of 'foreach' – more memory efficient way for large datasets

Coordinate Systems – Code Output

OUTPUT:

name	version	rank
chromosome	GRCh38	1
scaffold	GRCh38	2
clone		3
contig		4
chromosome	GRCh37	5
chromosome	NCBI36	6
chromosome	NCBI35	7
chromosome	NCBI34	7
lrg		8

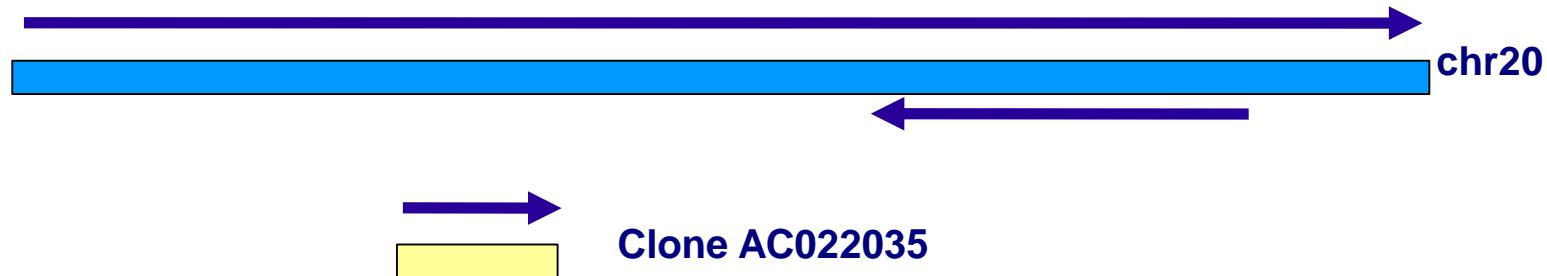


Slices

A *Slice Data Object* represents an arbitrary region of a genome, a slice of a Sequence Region.

Slices are not directly stored in the database.

A *Slice* is used to request sequence or features from a specific region in a specific coordinate system.



Slices - Code Example (1)

```
# get a slice covering the entire human Y chromosome

my $slice_adaptor = $registry->get_adaptor( 'Human', 'Core', 'Slice' );
my $slice = $slice_adaptor->fetch_by_region( 'chromosome', 'Y' );
print "Coord system:\t", $slice->coord_system_name, "\n",
      "Seq region:\t", $slice->seq_region_name, "\n",
      "Start:\t\t", $slice->start, "\n",
      "End:\t\t", $slice->end, "\n",
      "Strand:\t\t", $slice->strand, "\n",
      "Slice:\t\t", $slice->name, "\n";
```

OUTPUT:

Coord system: chromosome
Seq region: Y
Start: 1
End: 57227415
Strand: 1
Slice: chromosome:GRCh38:Y:1:57227415:1

Slices - Code Example (2)

```
# get the slice adaptor
my $slice_adaptor = $registry->get_adaptor('human', 'core', 'slice');

# fetch a slice on a region of chromosome 12
my $slice = $slice_adaptor->fetch_by_region('chromosome', '12',
                                              1e6, 2e6);

# print out the sequence from this region
print $slice->seq, "\n";

# get all clones in the database and print out their names
my @slices = @{ $slice_adaptor->fetch_all('clone') };
while ( my $slice = shift @{$slices} ) {
    print $slice->seq_region_name, "\n";
}
```

Exercise 3

- (a) Fetch all chromosomes for human. Determine their number and print the name and length for each of them. *The number of chromosomes is probably not what you would expect! Why is this?*
- (b) Use the gene stable id 'ENSG00000101266' to fetch a slice surrounding this gene with 2kb of flanking sequence.
(a) hint: use the Ensembl API documentation to find an appropriate method in SliceAdaptor class which retrieves a slice given a gene stable id (pay attention to the method's arguments)
- (c) Fetch the sequence of the first 10MB of chromosome 20 and write it to a file in FASTA format. Print the number of genes in this region.
- ✓ hint: Slice objects inherit from Bio::Seq so can be written to file easily using Bio::SeqIO, e.g.:

```
my $output = Bio::SeqIO->new( -file=>>'filename.fasta',
    -format=>'Fasta');
$output->write_seq($slice);
```

Outline

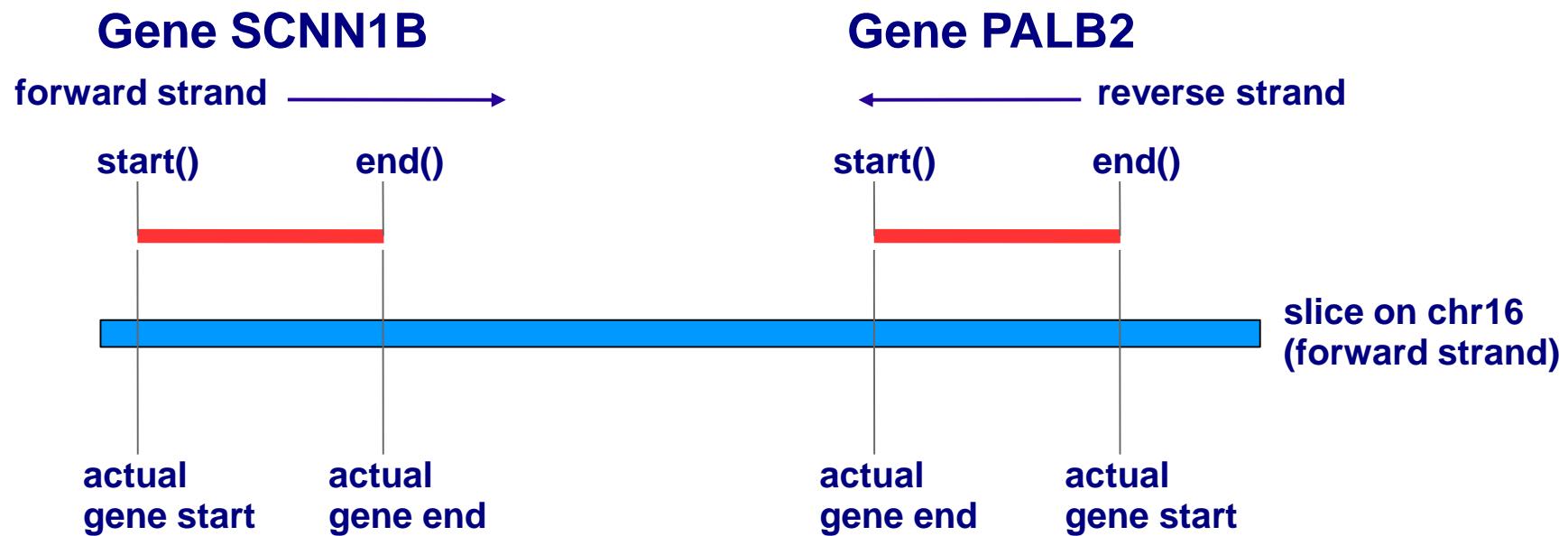
- a. Introduction
- b. Data objects & object adaptors
- c. Ensembl documentation
- d. The Registry & Ensembl API script design
- e. Coordinate systems & slices
- f. **Features**
- g. Genes, transcripts, exons & translations
- h. External references

Features (1)

Features have a defined location on the genome and are stored in a single coordinate system

All *Features* have a *start*, *end*, *strand* and *slice*

Start and *end* are plotted onto the forward strand: $\text{start} < \text{end}$

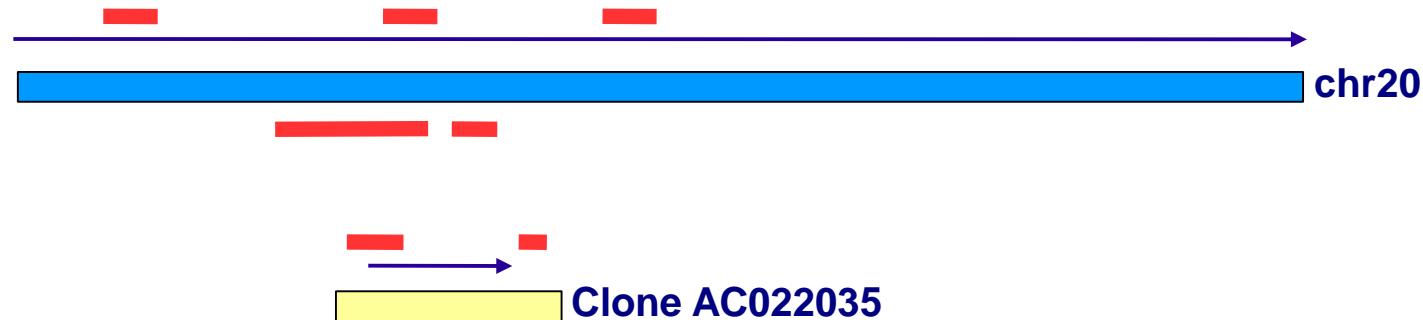


Features (2)

slice() method returns the *Slice* object with which the *Feature* is associated

feature_Slice() method returns the *Slice* object which covers only the *Feature* (will start at 1 and end with *Feature* length)

Features are retrieved from Object Adaptors using identifiers or regions (slices).



Features Objects – Biological Correspondence

Object	Biological entity
Gene, Transcript, Exon	Ensembl gene models
PredictionTranscript, PredictionExon	Genscan gene models
DNAAlignFeature, ProteinAlignFeature	cDNAs, proteins
RepeatFeature	repeats
MarkerFeature	markers
OligoFeature	microarray probes
KaryotypeBandFeature	cytogenetic bands
SimpleFeature	results of cpg, Eponine, FirstEF and tRNAscan
MiscFeature	clones, ENCODE regions

Align features

A sequence (mRNA or protein) is aligned against the *genome*

The result is stored in an *align_feature* table
(*dna_align_feature* or *protein_align_feature*)

A row represents the alignment between the genome sequence (a slice) and the target sequence (a hit)

seq_region_id	INT(10)		Foreign key references to the seq_region table.
seq_region_start	INT(10)		Sequence start position.
seq_region_end	INT(10)		Sequence end position.
seq_region_strand	TINYINT(1)	'1'	Sequence region strand: 1 - forward; -1 - reverse.
hit_start	INT(10)		Alignment hit start position.
hit_end	INT(10)		Alignment hit end position.
hit_name	VARCHAR(40)		Alignment hit name.

Exercise 4

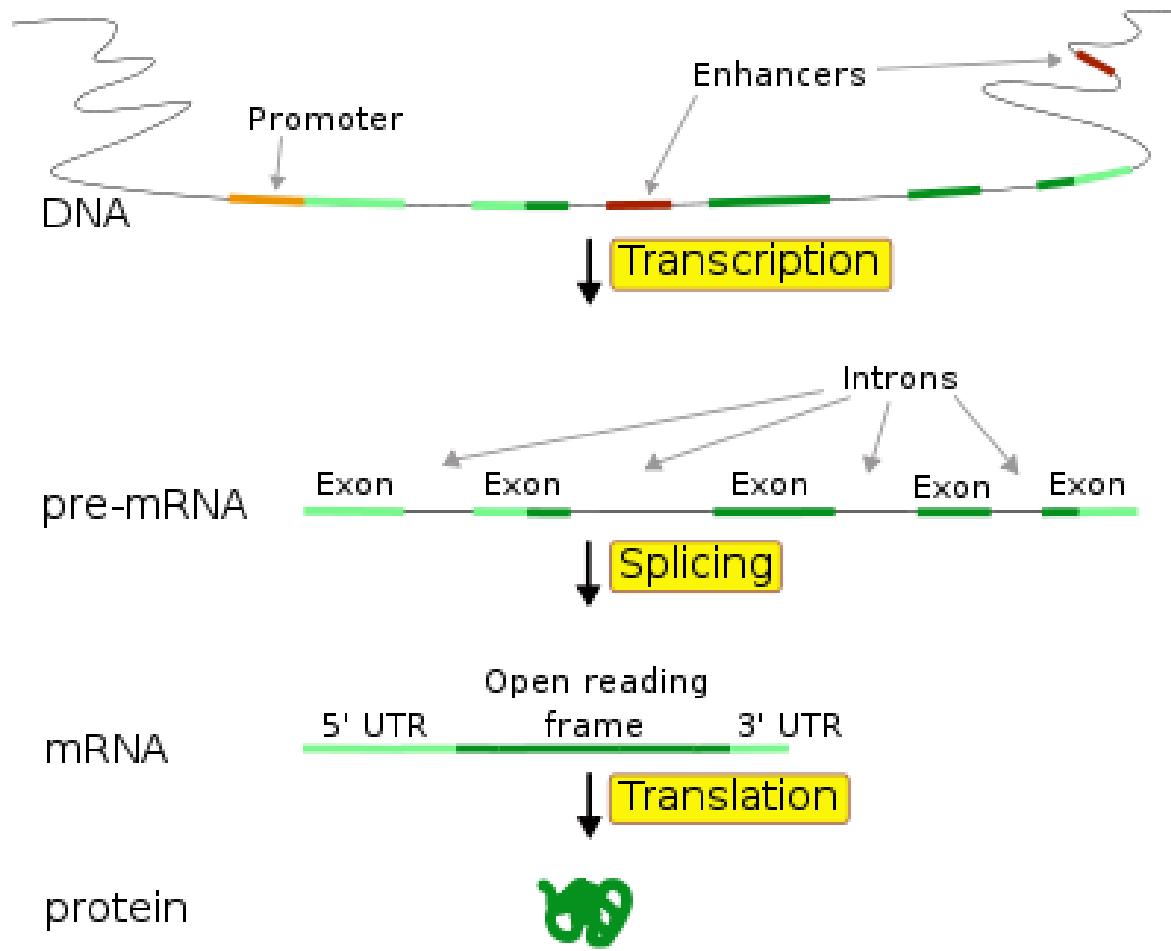
- (a) Get all the repeat features from chromosome 20:1-500k. Print out the name and position of each on the chromosome and the total number.
 - hint: create a slice, retrieve repeat features on this slice
- (b) Find which genomic region the RefSeq dna entry NM_000059.3 was mapped to. Print the name of the region and coordinates of the alignment on the genome as well as the name of the region and coordinates of the alignment on the RefSeq dna entry. Print the score and percentage identity for the alignment.
 - ✓ hint: use DnaAlignFeatureAdaptor; use the core schema documentation as a guide to appropriate methods which correspond to columns in dna_align_feature table

A list of useful Feature methods is in the Appendix at the end of the presentation slides

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- g. Genes, transcripts, exons & translations**
- h. External references

Genes, transcripts, exons & translations



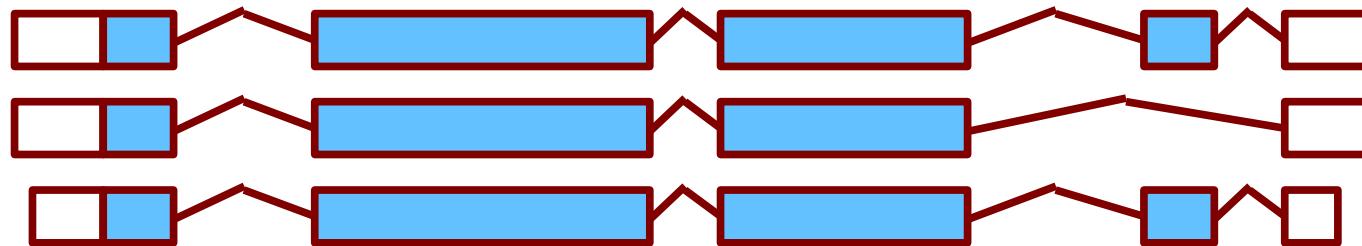
Genes, Transcripts and Exons

Genes, Transcript and Exons are objects that can be used just like any other Feature object

A Gene is a set of alternatively spliced Transcripts

A Transcript is a set of Exons

Introns are not explicitly defined in the database



Genes, Transcripts, Exons – Code Output

```
# helper function: returns location and stable_id string for a feature
sub get_string {
    my $feature = shift;
    my $stable_id = $feature->stable_id;
    my $seq_region = $feature->slice->seq_region_name;
    my $start = $feature->start;
    my $end = $feature->end;
    my $strand = $feature->strand;
    return "$stable_id $seq_region:$start-$end($strand)";
}

# fetch a gene by its stable identifier
my $gene = $gene_adaptor->fetch_by_stable_id('ENSG00000123427');

# print out the gene, its transcripts, and its exons
print "Gene: ", get_string($gene), "\n";
while ( my $transcript = shift @{$gene->get_all_Transcripts} ) {
    print " Transcript: ", get_string($transcript), "\n";
    while ( my $exon = shift @{$transcript->get_all_Exons} ) {
        print "     Exon: ", get_string($exon), "\n";
    }
}
```

Genes, Transcripts, Exons – Code Output

OUTPUT:

Gene: ENSG00000123427 12:57771492-57782541(1)

Transcript: ENST00000548256 12:57771492-57780430(1)

Exon: ENSE00002360002 12:57771492-57771625(1)

Exon: ENSE00003631087 12:57773017-57773128(1)

Exon: ENSE00003530124 12:57774629-57774767(1)

Exon: ENSE00002406112 12:57780255-57780430(1)

Transcript: ENST00000551420 12:57772200-57780780(1)

Exon: ENSE00002355737 12:57772200-57772397(1)

Exon: ENSE00003506271 12:57773017-57773128(1)

Exon: ENSE00002376752 12:57780255-57780780(1)

Transcript: ENST00000300209 12:57772600-57782403(1)

Exon: ENSE00002301479 12:57772600-57772901(1)

Exon: ENSE00003631087 12:57773017-57773128(1)

Exon: ENSE00002393444 12:57780255-57782403(1)

etc.

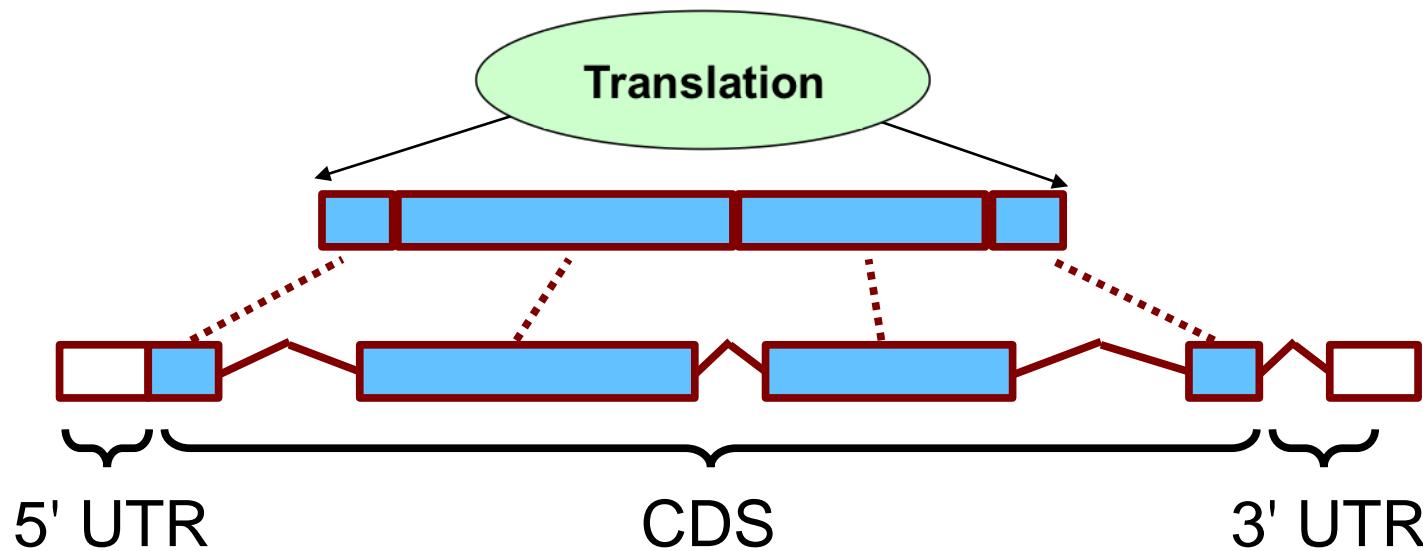
Translations

Translations are not Features.

A Translation object defines the UTR and CDS of a Transcript.

Peptides are not stored in the database, they are computed on the fly using Transcript objects.

Not all transcripts have a translation (e.g. ncRNAs)



Translations – Code Example

```
my $transcript_adaptor = $registry->get_adaptor( 'Homo sapiens', 'Core',
    'Transcript' );
# fetch a transcript from the database
my $transcript =
    $transcript_adaptor->fetch_by_stable_id('ENST00000333012');

# obtain the translation of the transcript
my $translation = $transcript->translation;

# print out the translation info
print "Translation: ", $translation->stable_id, "\n";
print "Start Exon: ", $translation->start_Exon->stable_id, "\n";
print "End Exon:    ", $translation->end_Exon->stable_id, "\n";

# cDNA start and end (spliced sequence with UTR)
print "Start : ", $translation->cdna_start, "\n";
print "End   : ", $translation->cdna_end, "\n";

# print the peptide which is the product of the translation
print "Peptide : ", $transcript->translate->seq, "\n";
```

Translations – Code Output

OUTPUT:

Translation: ENSP00000327425

Start Exon: ENSE00002340145

End Exon: ENSE00002428887

Start : 48

End : 497

Peptide :

MADPGPDPESESESVPREVGLFADSYSEKSQFCFCGHVLTITQNFGSRLGVAARVWDAALSLCNYFESQNVDFR
GKKVIELGAGTGIVGILAALQGAYGLVRETEDDVIEQELWRGMRGACGHALSMSTMTPWESIKGSSVRGGCYHH

Exercise 5

- (a) Fetch gene 'CSNK2A1' and print the number of its transcripts and exons.
- ✓ hint: use GeneAdaptor method `fetch_by_display_label`; remember that not all transcripts have a translation

Gene: CSNK2A1 ENSG00000101266

Description casein kinase 2, alpha 1 polypeptide [Source:HGNC Symbol;Acc:HGNC:2457]
Location Chromosome 20: 473,591-543,821 reverse strand.
INSDC coordinates chromosome:GRCh38:CM000682.2:473591:543821::1
Transcripts This gene has 11 transcripts (splice variants) [Hide transcript table](#)

Show All entries Show/hide columns (2 hidden) Filter

Name	Transcript ID	Length	Protein	Biotype	CCDS	Flags
CSNK2A1-002	ENST00000217244	4416 bp	391 aa (view)	Protein coding	CCDS13003	GENCODE basic
CSNK2A1-001	ENST00000349736	4299 bp	391 aa (view)	Protein coding	CCDS13003	GENCODE basic
CSNK2A1-003	ENST00000400217	1451 bp	255 aa (view)	Protein coding	CCDS13004	GENCODE basic
CSNK2A1-201	ENST00000619188	2606 bp	397 aa (view)	Protein coding	-	GENCODE basic
CSNK2A1-009	ENST00000400227	1499 bp	385 aa (view)	Protein coding	-	GENCODE basic

- (b) For the above gene, get all the transcripts and list the number of exons for each. Also show any translations associated with the transcripts.
- (c) Why do the exon numbers not match?

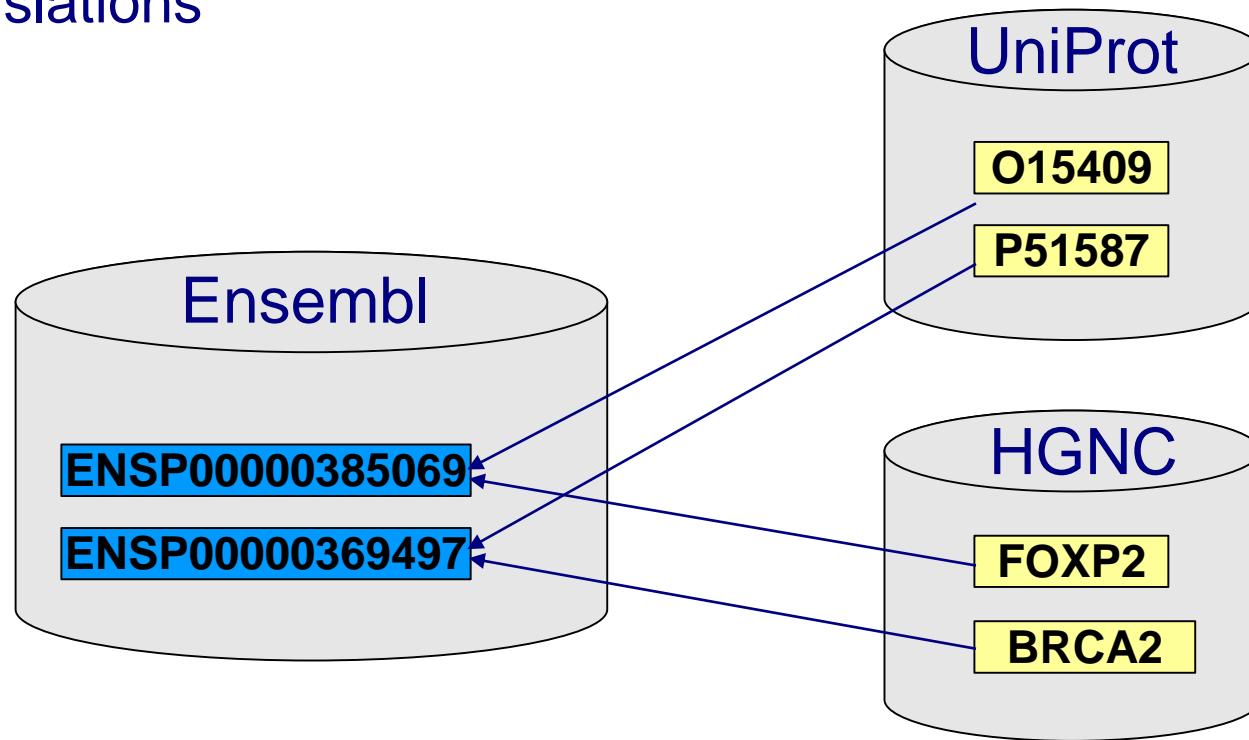
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External References

Ensembl cross references its Gene models with identifiers from other databases, such as HGNC, WikiGenes, UniProtKB/Swiss-Prot, RefSeq, MIM etc.

External References (Xrefs) can be linked to genes, transcripts or translations



Xrefs - Code Example (1)

```
# Obtain external references for Ensembl gene ENSG00000139618
```

```
my $gene = $gene_adaptor->fetch_by_stable_id( 'ENSG00000139618' );
```

this method will only return xrefs linked to the object it's called on (e.g. gene)

```
my $gene_xrefs = $gene->get_all_DBEntries;
```

```
print "Xrefs on gene level: \n\n";
```

```
while ( my $gene_xref = shift @{$gene_xrefs} ) {
```

```
    print $gene_xref->dbname, ":", $gene_xref->display_id, "\n";
```

```
}
```

```
my $all_xrefs = $gene->get_all_DBLinks;
```

this method will return xrefs on all levels (gene, transcript and translation)

```
print "\nXrefs on gene, transcript and protein level: \n\n";
```

```
while ( my $all_xref = shift @{$all_xrefs} ) {
```

```
    print $all_xref->dbname, ":", $all_xref->display_id, "\n";
```

```
}
```

Xrefs – Code Output (1)

OUTPUT:

Xrefs on gene level:

Vega_gene:OTTHUMG00000017411
Vega_gene:BRCA2
PUBMED:15057823
PUBMED:7581463
PUBMED:8091231
RefSeq_dna:NM_000059
OTTG:OTTHUMG00000017411
ENS_LRG_gene:LRG_293
ArrayExpress:ENSG00000139618
DBASS3:BRCA2
DBASS5:BRCA2
EntrezGene:BRCA2
HGNC:BRCA2
MIM_GENE: BRCA2 GENE [*600185]
MIM_MORBID: BREAST CANCER [#114480]
MIM_MORBID: GLIOMA SUSCEPTIBILITY 3 [#613029]
MIM_MORBID: PANCREATIC CANCER, SUSCEPTIBILITY [#613347]
UniGene:Hs.34012
UniGene:Hs.686439

Uniprot_gn:BRCA2

WikiGene:BRCA2

Xrefs on gene, transcript and translation level:
(same as on gene level + transcript and translation level)

Vega_gene:OTTHUMG00000017411
Vega_gene:BRCA2
PUBMED:15057823
PUBMED:7581463
PUBMED:8091231
RefSeq_dna:NM_000059
OTTG:OTTHUMG00000017411
ENS_LRG_gene:LRG_293
ArrayExpress:ENSG00000139618
DBASS3:BRCA2
DBASS5:BRCA2
EntrezGene:BRCA2
HGNC:BRCA2
Uniprot/SPTREMBL:E9PIQ1
Uniprot/SPTREMBL:K4JTT2

etc.

Xrefs - Code Example (2)

```
# Retrieve Ensembl IDs for a list of UniProt protein IDs

my $translation_adaptor
= $registry->get_adaptor(
  'Human', 'Core', 'Translation');

my @uniprot_ids = qw(P51587 P15056 B8A597 B8A595 B7ZW72);

while ( my $uniprot_id = shift @{$uniprot_ids} ) {
  my @trans =
    $translation_adaptor->fetch_all_by_external_name($uniprot_id, 'Uniprot%');
}

while ( my $translation = shift @{$trans} ) {
  print $translation->stable_id."\t".$uniprot_id."\n";
}
```

Proteins map to Ensembl Translation objects so we will use a TranslationAdaptor

Xrefs – Code Output (2)

OUTPUT :

ENSP00000439902	P51587
ENSP00000369497	P51587
ENSP00000288602	P15056
ENSP00000387217	B8A597
ENSP00000386781	B8A595
ENSP00000307640	B7ZW72

Cross references can map to more than one Ensembl identifier

Exercise 6

Retrieve a list of GO term IDs and term names linked to the gene with stable id ‘ENSG00000139618’

- ✓ Use `get_all_DBLinks` with an external database name argument to restrict the number of xrefs returned
- ✓ Ontology term data such as term name and definition are stored outside of the core database. Create an `OntologyTerm` Adaptor with the help of the Registry method `get_adaptor` using arguments: ‘Multi’ (species), ‘Ontology’ (database type), ‘`OntologyTerm`’ (adaptor type)
- ✓ For all xrefs returned by `get_all_DBLinks` use the `OntologyTerm` Adaptor to fetch the relevant term and print its accession and name (xref display_id is the same as term accession)

Recap - Ensembl API script design

Always:

- Load the registry

Which features (genes, repeats, SNPs, etc.) are in my particular region of interest?

- Get the SliceAdaptor
- Fetch the Slice for your region of interest
- Get the features from your Slice

What do we know about a particular gene (or any other feature)?

- Get the GeneAdaptor
- Fetch your Gene of interest
- Get more details about the gene:
 - Gene structure (transcripts, exons, translations)
 - Annotations: GO xrefs, HGNC symbols, etc.
 - Features in the same region -> get the Slice for the Gene!

Documentation & Help

- Installation instructions, web-browsable version of the POD (Perldoc), database schema and tutorial:
<http://www.ensembl.org/info/docs/api/index.html>
- Inline Perl POD (Plain Old Documentation)
- dev@ensembl.org mailing list:
<http://www.ensembl.org/info/about/contact/mailing.html>
searchable mailing list archive:
<http://blog.gmane.org/gmane.science.biology.ensembl.devel>
- Ensembl helpdesk:
helpdesk@ensembl.org

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Ensembl 2014

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Appendix – Adaptors

The screenshot shows the Ensembl API & Software documentation. The top navigation bar includes links for BLAST/BLAT, BioMart, Tools, Downloads, Help & Documentation, Blog, and Mirrors. Below this, a breadcrumb trail shows the current location: Help & Documentation > API & Software > Doxygen Perl documentation. The main menu has tabs for Overview, Classes, Namespaces (which is highlighted in blue), and Files. A sidebar on the left contains sections for Ensembl (Related Pages, Full Class List, Class Index, Class Hierarchy) and Namespace List. The main content area displays a 'Namespace List' table with a header 'A list of all the namespaces used in these packages'. The table lists various namespaces, with 'Bio::EnsEMBL' and 'Bio::EnsEMBL::DBSQL' being specifically highlighted by red arrows pointing from the text below.

Namespace List	
A list of all the namespaces used in these packages	
Bio	
Bio::EnsEMBL	
Bio::EnsEMBL::Analysis	
Bio::EnsEMBL::DB	
Bio::EnsEMBL::DBFile	
Bio::EnsEMBL::DBSQL	
Bio::EnsEMBL::DBSQL::Driver	
Bio::EnsEMBL::DBSQL::Support	
Bio::EnsEMBL::DensityPlot	
Bio::EnsEMBL::External	
Bio::EnsEMBL::IdMapping	
Bio::EnsEMBL::IdMapping::InternalIdMapper	
Bio::EnsEMBL::IdMapping::StableIdGenerator	
Bio::EnsEMBL::Map	
Bio::EnsEMBL::Map::DBSQL	
Bio::EnsEMBL::Mapper	
Bio::EnsEMBL::Utils	
Bio::EnsEMBL::Utils::Converter	
Bio::EnsEMBL::Utils::IO	

“What kinds of adaptors are there?”

The online API documentation lists them all under their respective namespaces.

Bio::EnsEMBL for Data Objects
Bio::EnsEMBL::DBSQL for Adaptors

Appendix – CoordSystem Methods

Attribute	Example value(s)	Method(s)
name	chromosome, scaffold, contig, clone	\$coordsystem->name
version	GRCh37, NCBI36, NCBIM37	\$coordsystem->version

Appendix – Feature Methods

Attribute	Example value(s)	Method(s)
name	AluSp, D1S2217	\$feature->display_id
coordinates		\$feature->seq_region_name \$feature->start \$feature->end \$feature->seq_region_start \$feature->seq_region_end \$feature->strand
sequence		\$feature->seq
length	399	\$feature->length
slice	returns Slice object with which feature is associated	\$feature->slice
feature slice	returns Slice object that covers feature	\$feature->feature_Slice

Appendix – Gene Methods

Attribute	Example value(s)	Method(s)
stable ID	ENSG00000139618	\$gene->stable_id
name	BRCA2	\$gene->external_name
description	breast cancer 2, early onset	\$gene->description
biotype	protein_coding, miRNA	\$gene->biotype
analysis	ensembl, havana, ensembl_havana_gene	\$gene->analysis->logic_name
status	KNOWN, NOVEL	\$gene->status
transcripts	returns listref of Transcript objects	\$gene->get_all_Transcripts
exons	returns listref of Exon objects	\$gene->get_all_Exons

Appendix - Transcript Methods

Attribute	Example value(s)	Method(s)
stable ID	ENST00000380152	\$transcript->stable_id
name	BRCA2-001	\$transcript->external_name
biotype	protein_coding, nonsense-mediated_decay	\$transcript->biotype
analysis	ensembl, havana, ensembl_havana_transcript	\$transcript->analysis-> logic_name
status	KNOWN, NOVEL	\$transcript->status
CDS (spliced sequence, no UTR)	ATGCCTATTGGATCCAAAGAGAGGC...	\$transcript->translateable_seq
UTRs	returns Seq object	\$transcript->five_prime_utr \$transcript->three_prime_utr
cDNA (spliced sequence + UTR)	GGGCTTGTGGCGCGAGCTTCTGAAA...	\$transcript->spliced_seq
translation	returns Translation object	\$transcript->translation



Appendix - Translation Methods

Attribute	Example value(s)	Method(s)
stable id	ENSP00000369497	\$translation->stable_id
length	3418	\$translation->length
sequence	MPIGSKERPTFFEIFKTRCNKADLG...	\$translation->seq