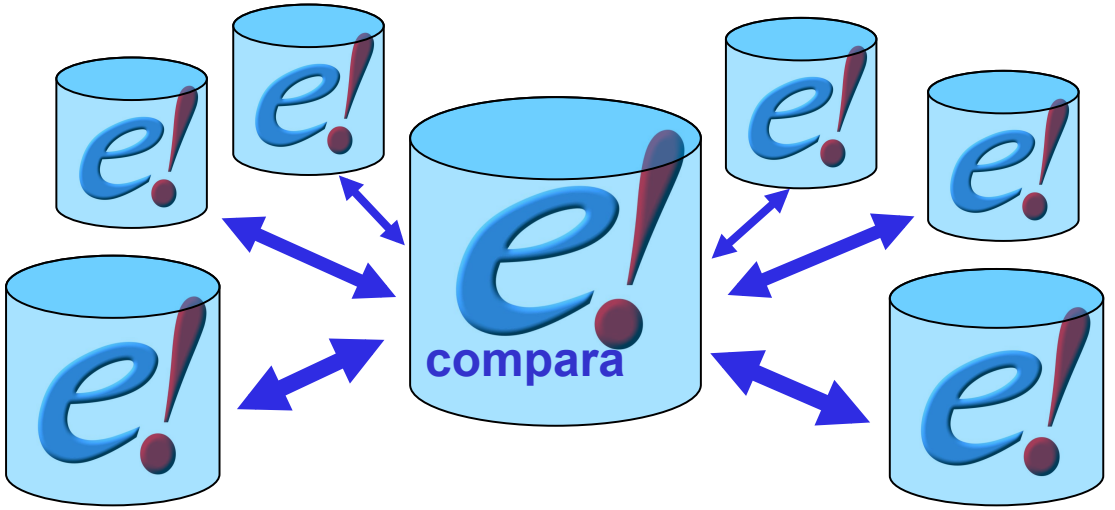
Ensembl Compara Perl API



EMBL-EBI

wellcome trust sanger institute

What is Ensembl Compara?

A single database which contains precalculated comparative genomics data and which is linked to all the Ensembl Species databases.

Access via perl API and mysql

A production system for generating that database

(not in this presentation)

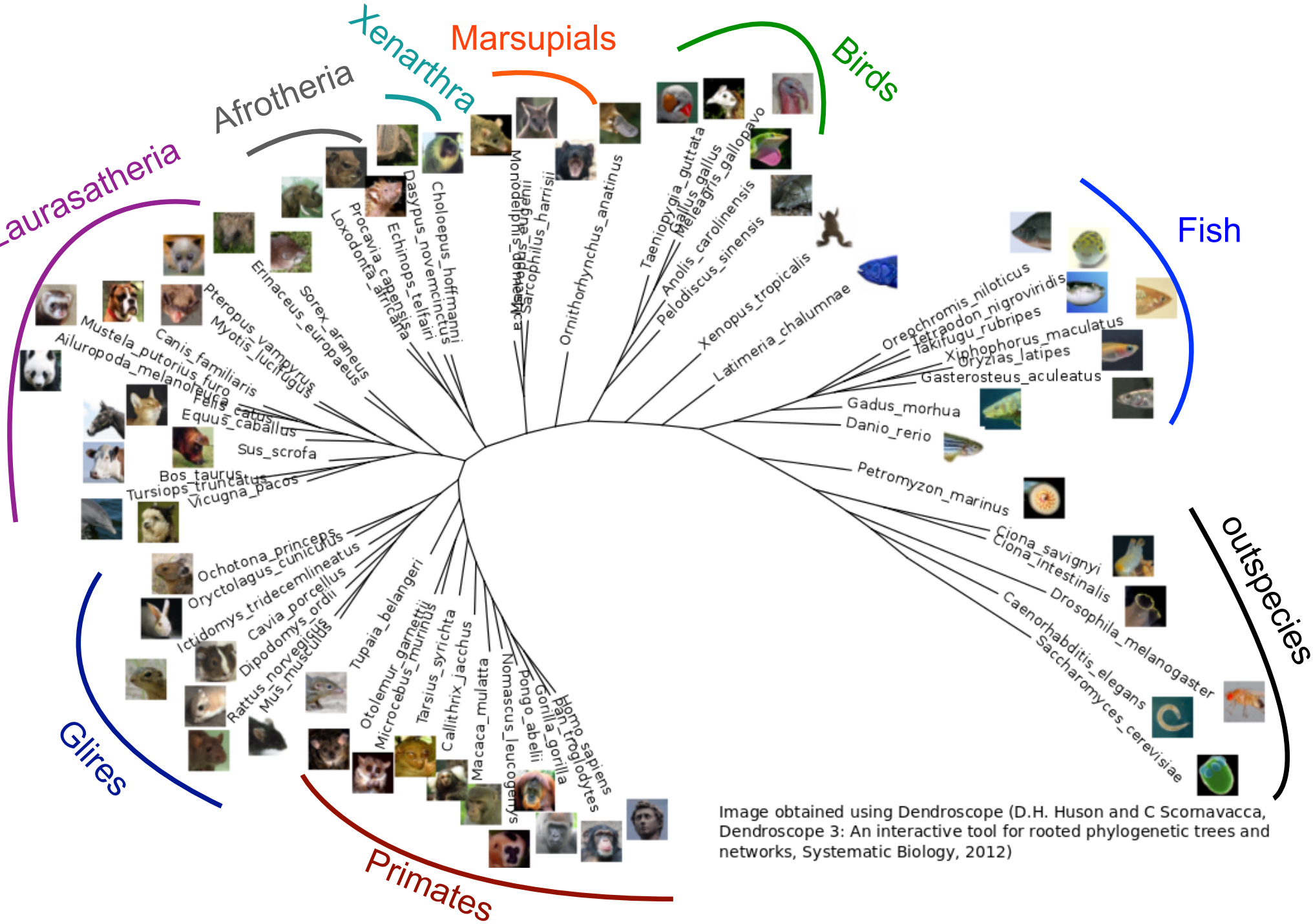
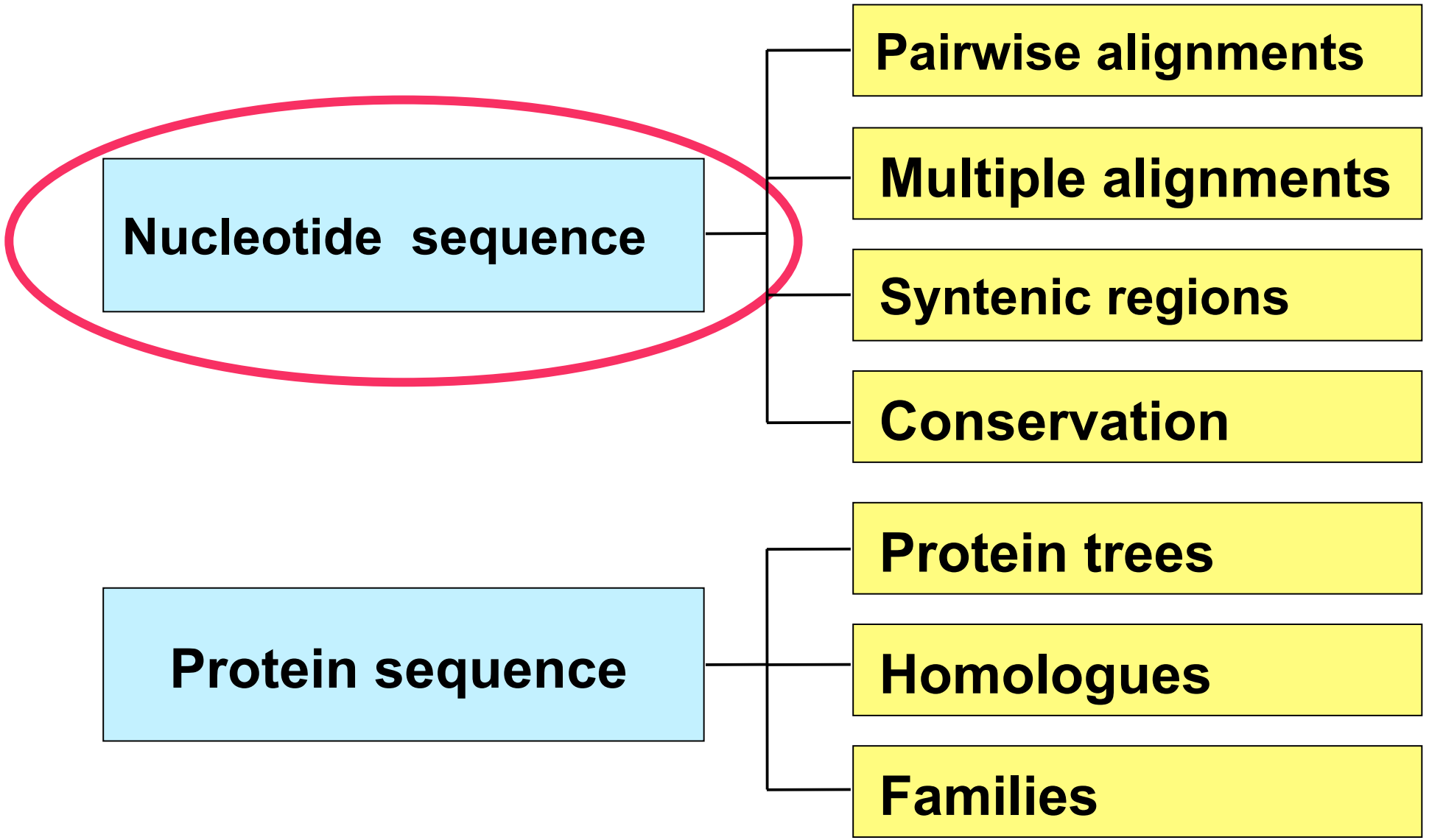


Image obtained using Dendroscope (D.H. Huson and C Scornavacca, Dendroscope 3: An interactive tool for rooted phylogenetic trees and networks, Systematic Biology, 2012)

Sequence types and outputs



Nucleotide sequence analyses

Pairwise Alignments

- BLASTZ-net
- LASTZ-net
- t-BLAT-net

Syntenic regions

- Only for species with chromosomal mappings

Multiple alignments

- Mercator-Pecan
- Enredo-Pecan-Ortheus

Conservation

- GERP Cons. Scores
- GERP Constr. Elements

Nucleotide sequence analyses

Pairwise Alignments

- BLASTZ-net
- LASTZ-net
- t-BLAT-net

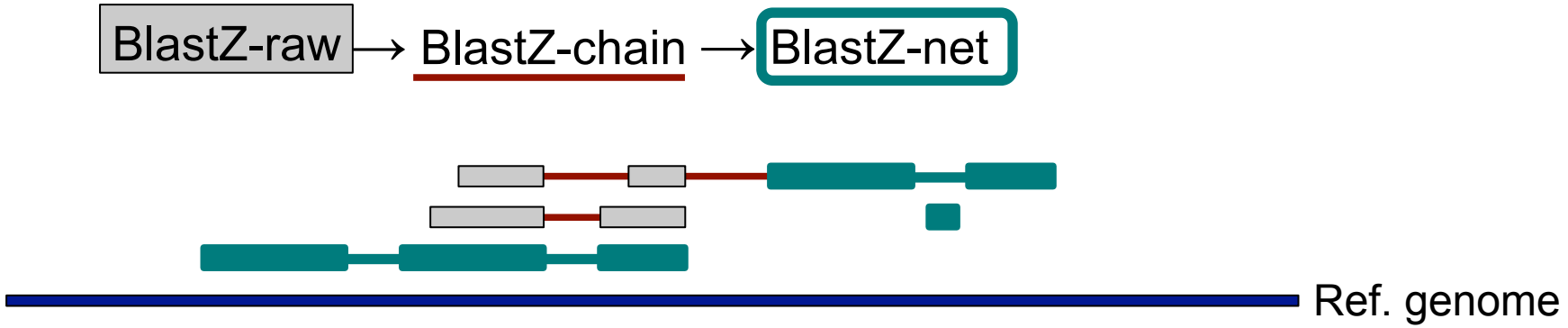
BLASTz-net / LASTz-net

- Closely related species
- LASTz is a replacement for BLASTz

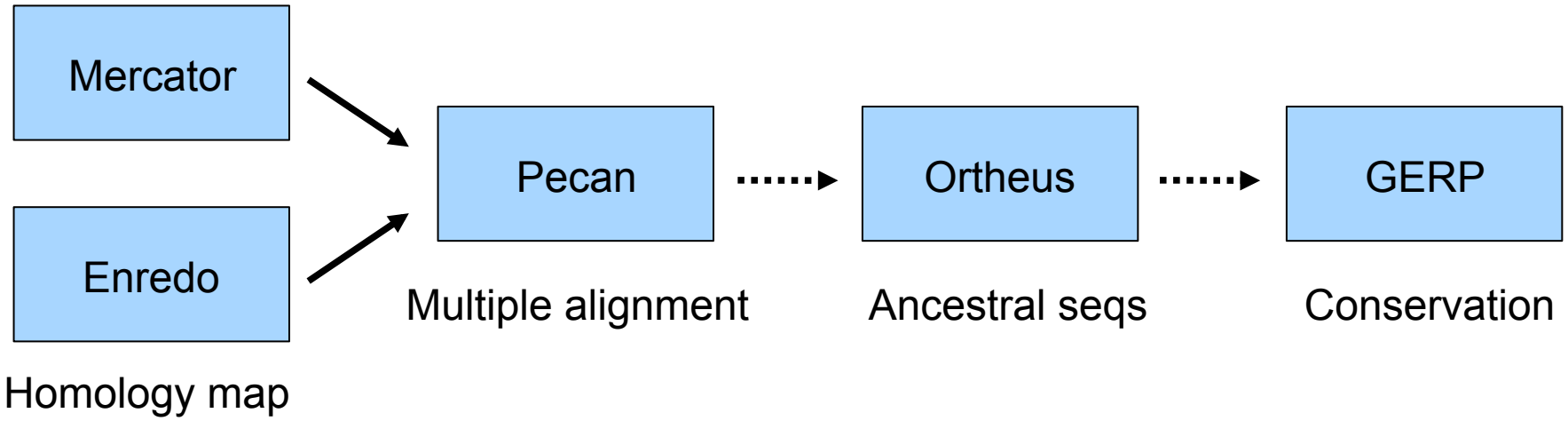
T-BLAT-net

- Distantly related species
- Coding + highly conserved

Chaining/Netting



Nucleotide sequence analyses



Multiple alignments

Mercator-Pecan

Enredo-Pecan-Ortheus

Conservation

GERP Cons. Scores

GERP Constr. Elements

Compara database is coupled to Ensembl core databases

Compara stores relationships between the genomes by loading references or ‘handles’ to external data.

Since there is minimal primary data inside Compara, to gain full access to the data these external links must be re-established

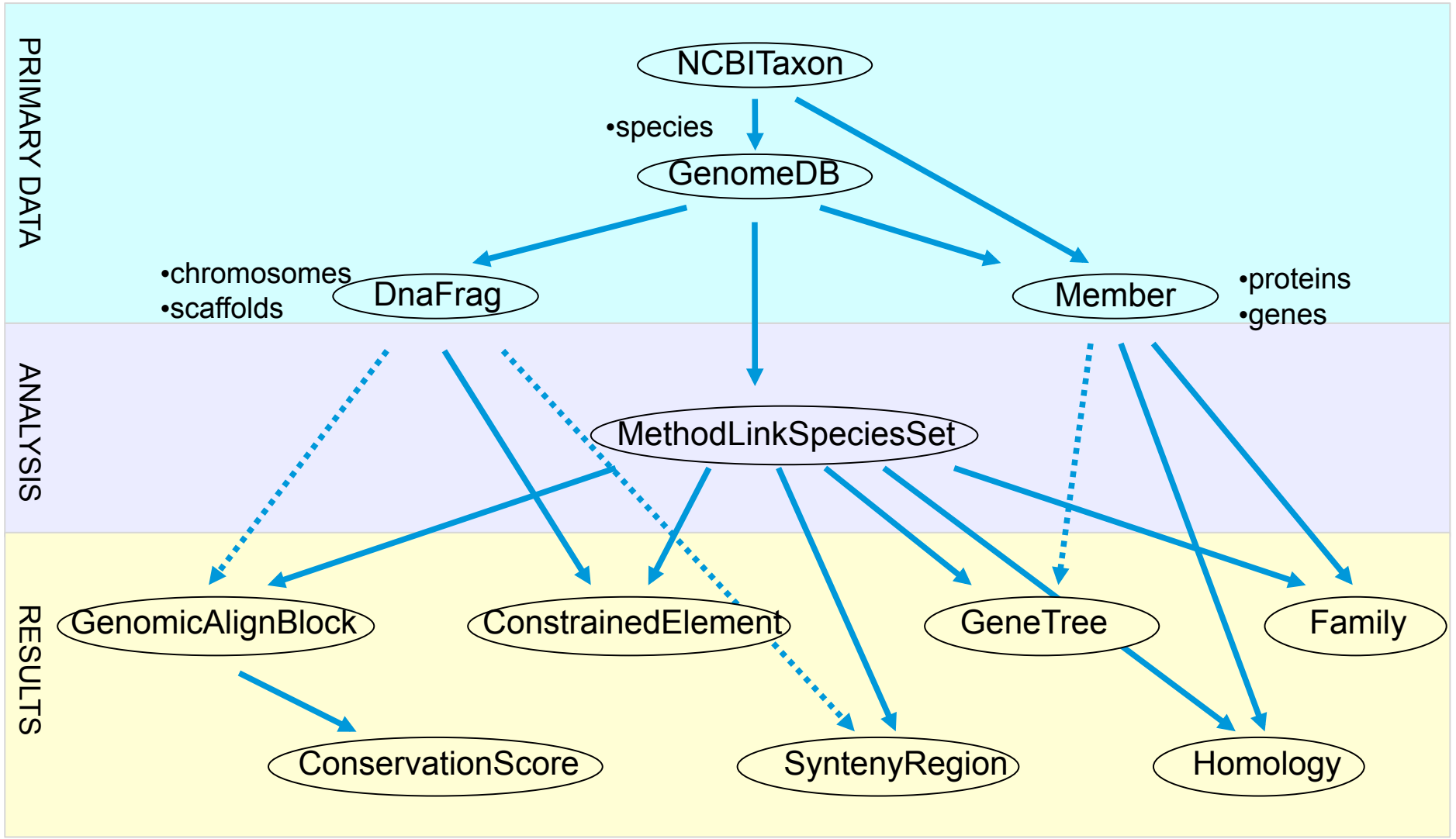
Example: compara_73 must be linked with the Ensembl core_73 databases

Proper REGISTRY configuration is critical (auto-loading is OK)

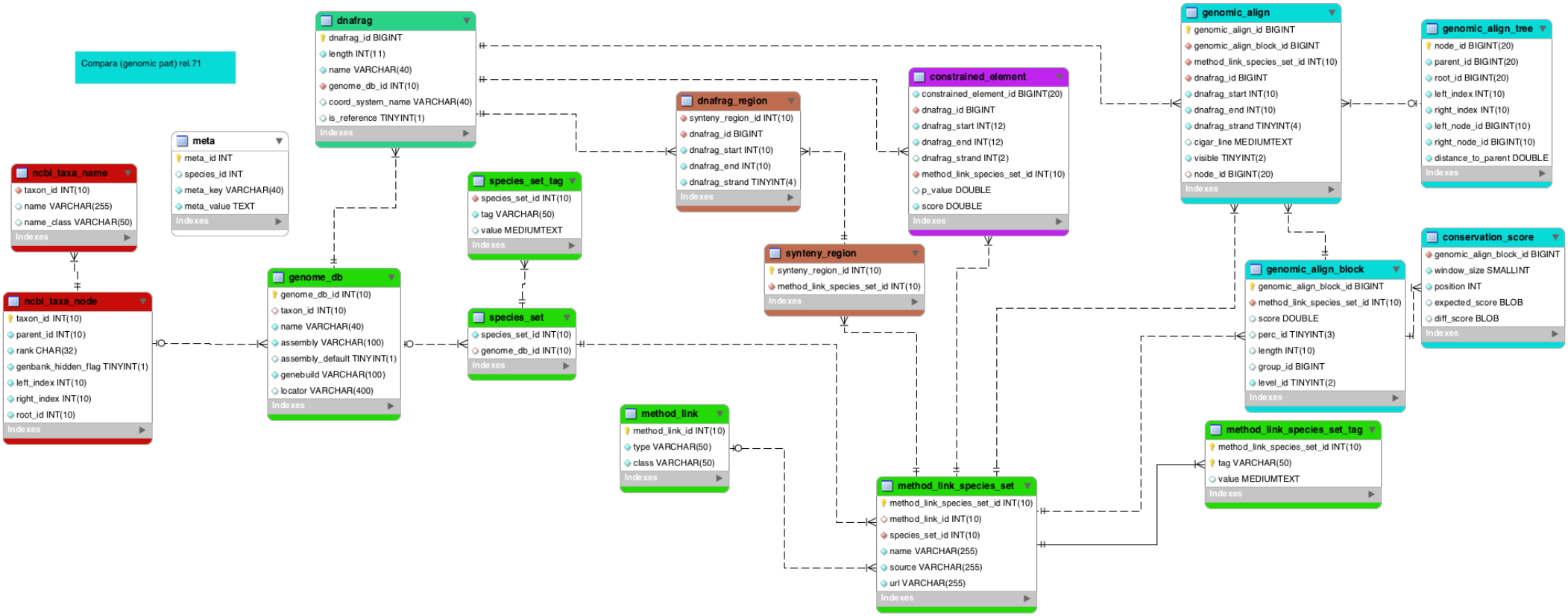
The Compara Perl API

- Written in Object-Oriented Perl
- Used to retrieve data from and store data into ensembl-compara database (only the production pipeline generates the alignments, trees, etc)
- Links species together for Ensembl website
- Generalized to extend to non-ensembl genomic data (Uniprot)
- Follows same ‘Data Object’, ‘Object Adaptor’ and 'DBAdaptor' design as the other Ensembl APIs

Compara object model overview



Database schema (genomic part)



ensembl-compara/docs/schema/diagrams/genomics_schema.png

Primary data

Conventions in these slides:

```
Methods returning values()
Methods returning objects()
Object Adaptor fetching method()
```

NCBITaxon: list of all species

- `taxon_id(), classification(), name()`

GenomeDB: relates to a particular Ensembl core DB

- `name(), assembly(), genebuild(), taxon()`
- `fetch_by_name_assembly(), fetch_by_registry_name(), fetch_by_Slice(), fetch_all()`

DnaFrag: relates to all "top level" SeqRegions

- `name(), length(), genome_db(), slice(), coord_system_name()`
- `fetch_by_Slice(), fetch_all_by_GenomeDB_region, fetch_by_GenomeDB_and_name()`

Perl allows you to concatenate the calls:

```
$dnafrag->genome_db->taxon->classification()
```

GenomeDB example code

```
use strict;
use Bio::EnsEMBL::Registry;
my $reg = "Bio::EnsEMBL::Registry";

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

my $genome_db_adaptor = $reg->get_adaptor("Multi", "compara", "GenomeDB");

my $genome_db = $genome_db_adaptor->fetch_by_registry_name("human");

print "Name: ", $genome_db->name, "\n";
print "Assembly: ", $genome_db->assembly, "\n";
print "GeneBuild: ", $genome_db->genebuild, "\n";
```

DnaFrag example code

```
use strict;
use Bio::EnsEMBL::Registry;
my $reg = "Bio::EnsEMBL::Registry";

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

my $genome_db_adaptor = $reg->get_adaptor("Multi", "compara", "GenomeDB");

my $genome_db = $genome_db_adaptor->fetch_by_registry_name("human");

my $dnafrag_adaptor = $reg->get_adaptor("Multi", "compara", "DnaFrag");

my $dnafrag = $dnafrag_adaptor->fetch_by_GenomeDB_and_name(
       $genome_db, "13");


print "Name: ", $dnafrag->name, "\n";
print "Length: ", $dnafrag->length, "\n";
print "CoordSystem: ", $dnafrag->coord_system_name, "\n";
```

API documentation & Help

- perldoc – Viewer for inline API documentation.
  - `shell> perldoc Bio::EnsEMBL::Compara::GenomeDB`
  - `shell> perldoc Bio::EnsEMBL::Compara::DBSQL::MemberAdaptor`
  - online at: http://www.ensembl.org/info/software/Pdoc/

- Tutorial document:

  cvs: ensembl-compara/docs/ComparaTutorial.pdf

- ensembl-dev mailing list:

  <dev@ensembl.org>

Exercises – GenomeDB & DnaFrag

GenomeDB:

- Print the name, assembly version and genebuild version for the pig genome.
- Do the same for all the GenomeDBs in the compara DB

DnaFrag

- Print the name and length of the pig chromosome 15
- Print the name and length of all the DnaFrags for chimp

Analysis

Conventions in these slides:

`Methods returning values()`
`Methods returning objects()`
`Object Adaptor fetching method()`

Method: type of analysis

- `type()`
- Possible values for the type are: BLASTZ_NET, LASTZ_NET, TRANSLATED_BLAT_NET, PECAN, EPO, EPO_LOW_COVERAGE, SYNTENY, FAMILY, ENSEMBL_ORTHOLOGUES, ENSEMBL_PARALOGUES, PROTEIN_TREES, etc.

SpeciesSet: group of species/genomes involved in an analysis

- **`genome_dbs()`**

MethodLinkSpeciesSet: one particular analysis set

- **`method()`**, **`species_set_obj()`**, `name()`, `source()`, `url()`
- `fetch_all()`, `fetch_by_method_link_type_species_set_name()`, `fetch_by_method_link_type_registry_aliases`, `fetch_all_by_method_link_type`, `etc.`

MethodLinkSpeciesSet example code

```
use strict;
use Bio::EnsEMBL::Registry;
my $reg = "Bio::EnsEMBL::Registry";

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

my $mlssa = $reg->get_adaptor("Multi", "compara", "MethodLinkSpeciesSet");

my $mlss = $mlssa->fetch_by_method_link_type_registry_aliases(
      "LASTZ_NET", ["human", "mouse"]);

print $mlss->name, "\n";

print "type: ", $mlss->method->type, "\n";

my $species_set = $mlss->species_set_obj();

foreach my $this_genome_db (@{$species_set->genome_dbs}) {
    print $this_genome_db->name(), "\n";
}
```

Exercises – MethodLinkSpeciesSet

- Print the name of the MethodLinkSpeciesSet for the pig-cow LASTZ-NET alignments.

- Print the list of all MethodLinkSpeciesSet entries stored in the database

- Print a list of the species and their internal IDs (dbIDs) for the 12 eutherian mammal EPO alignments

  HINT: the species_set_name for the eutherian mammals is "mammals".

GenomicAlignBlock

Conventions in these slides:

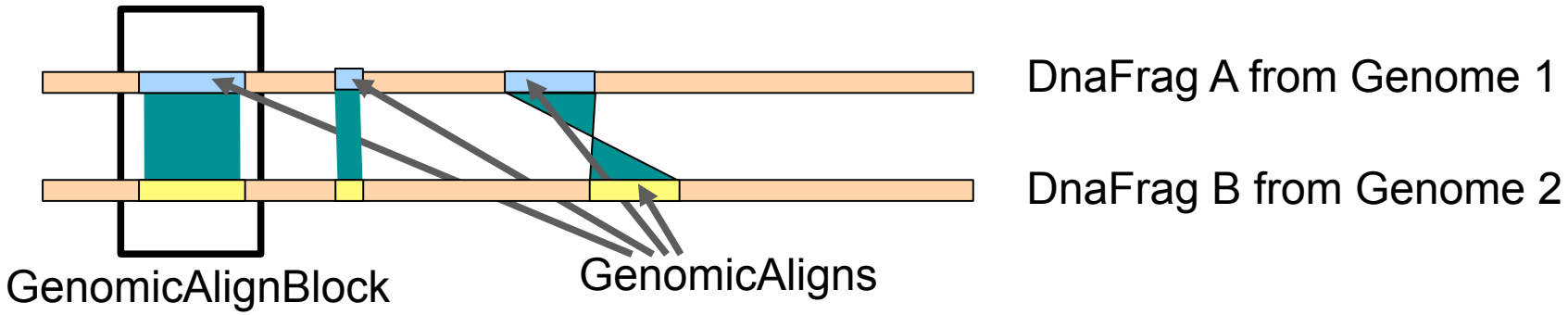
```
Methods returning values()
Methods returning objects()
Object Adaptor fetching method()
```

GenomicAlignBlock

- represents a genomic alignment
- contains 1 GenomicAlign per sequence
- **method_link_species_set()**, score(), length(), perc_id(), **get_all_GenomicAligns()**, **get_SimpleAlign()**
- fetch_all_by_MethodLinkSpeciesSet_Slice()

GenomicAlign

- **dnafrag()**, **genome_db()**, **get_Slice()**, dnafrag_start, dnafrag_end(), dnafrag_strand(), aligned_sequence()



Alignments are stored in the genomic_align and genomic_align_block tables

For example:

```
gorilla_gorilla/MT/935-953    gacat-ttaactaaaac-ccc
macaca_mulatta/MT/1469-1488   aacatcttaactaaacg-ccc
pan_troglodytes/MT/934-953    gatac-ttaacttaaaccccc
pongo_pygmaeus/MT/940-958     actac-ctaactaaaac-ccc
homo_sapiens/MT/1516-1534     gacat-ttaactaaaac-ccc
                                 *   ***** **   ***
```

```
GACATTTAACTAAAACCCC      5MD11MD3M
AACATCTTAACTAAACGCCC     17MD3M
GATACTTAACTTAAACCCCC     5MD15M
ACTACCTAACTAAAACCCC      5MD11MD3M
GACATTTAACTAAAACCCC      5MD11MD3M
```

5 genomic_align entries
1 genomic_align_block

Sequences from core

cigar lines

Multiple sequence alignments

Mercator-Pecan

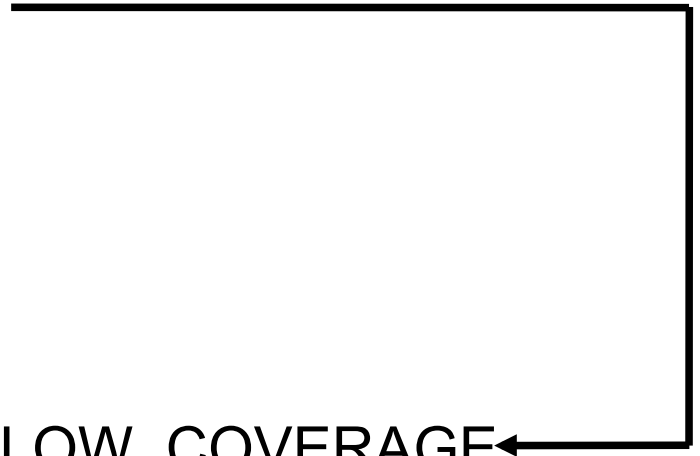
- 19-way amniota vertebrates Pecan

EPO

- 6 primates EPO
- 12 eutherian mammals EPO
- 3 neognath birds EPO
- 5 teleost fish EPO

EPO-2X (EPO_LOW_COVERAGE)

- 35 eutherian mammals EPO_LOW_COVERAGE



Adding low-coverage (2X) genomes

Low coverage genomes cannot be fully assembled

Resulting assembly is too scattered to be used with Enredo

Run EPO on high-coverage genomes only

Map 2X genomes using pairwise alignments

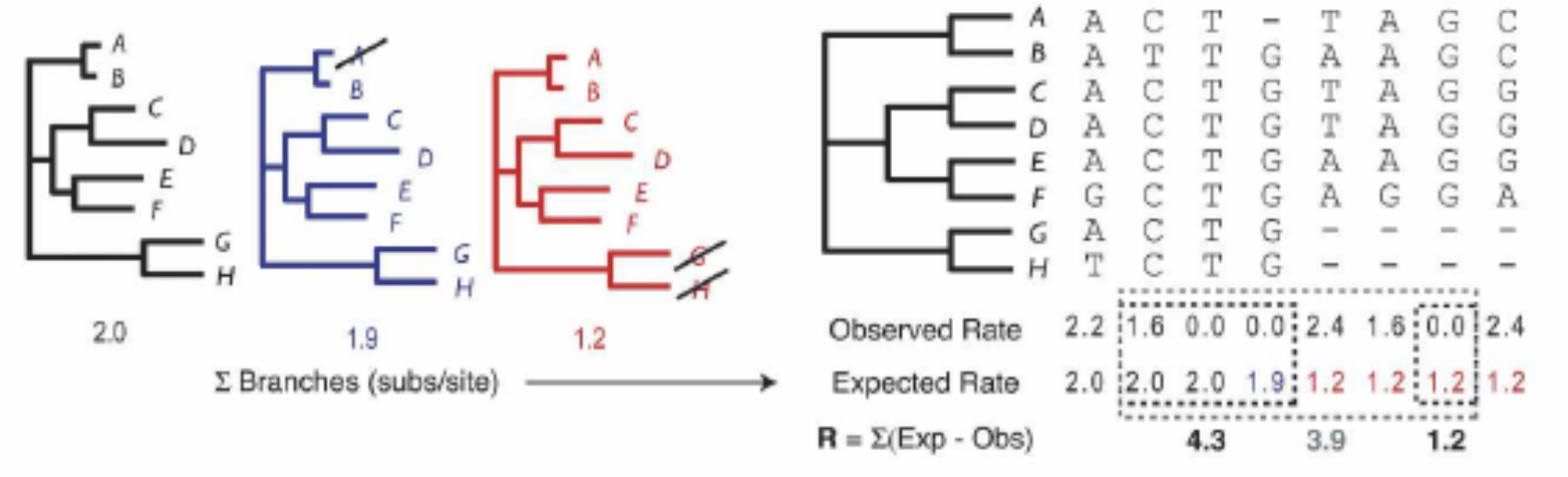
Exercises – GenomicAlignBlock

- Print the LASTZ_NET alignments for pig chromosome 15 with cow
  Use pig coordinates 15 : 89151597 - 89157190

- Change the above example so that it prints the alignments for the 12 eutherian mammals EPO

Gerp Constrained Elements

Stretches of the alignment with a high conservation



Cooper et al. Genome Research, 2005

Constrained elements and coding exons

74% of coding exons are associated with constr. elem.

22% of constr. elem. are associated with coding exons

Constrained elements

Conventions in these slides:

`Methods returning values()`
`Methods returning objects()`
`Object Adaptor fetching method()`

ConstrainedElement: a constrained element

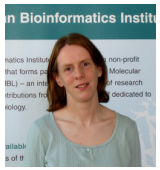
- `slice, start, end, strand, seq_region_start, seq_region_end`
- **`get_SimpleAlign()`:** this method gets the alignment from the corresponding GenomicAlignBlock and returns a Bio::SimpleAlign object.
- `fetch_all_by_MethodLinkSpeciesSet_Slice`

Exercises – ConstrainedElements

- Print the constrained element alignments from the previous pig locus (use the Constrained elements generated from the EPO_LOW_COVERGAGE mammals alignments)

Acknowledgements

Compara Team


Kathryn


Daniel


Leo


Stephen


Miguel


Matthieu

Nucleic Acids Research Advance Access published December 6, 2013

Nucleic Acids Research, 2013, 1–7
doi:10.1093/nar/gkt1196

Ensembl 2014

Paul Flicek[1,2,*], M. Ridwan Amode[2], Daniel Barrell[2], Kathryn Beal[1], Konstantinos Billis[2], Simon Brent[2], Denise Carvalho-Silva[1], Peter Clapham[2], Guy Coates[2], Stephen Fitzgerald[1], Laurent Gil[1], Carlos García Girón[2], Leo Gordon[1], Thibaut Hourlier[2], Sarah Hunt[1], Nathan Johnson[1], Thomas Juettemann[1], Andreas K. Kähäri[2], Stephen Keenan[1], Eugene Kulesha[1], Fergal J. Martin[2], Thomas Maurel[1], William M. McLaren[1], Daniel N. Murphy[2], Rishi Nag[2], Bert Overduin[1], Miguel Pignatelli[1], Bethan Pritchard[2], Emily Pritchard[1], Harpreet S. Riat[2], Magali Ruffier[1], Daniel Sheppard[2], Kieron Taylor[1], Anja Thormann[1], Stephen J. Trevanion[2], Alessandro Vullo[1], Steven P. Wilder[1], Mark Wilson[2], Amonida Zadissa[1], Bronwen L. Aken[2], Ewan Birney[1], Fiona Cunningham[1], Jennifer Harrow[2], Javier Herrero[1], Tim J.P. Hubbard[2], Rhoda Kinsella[1], Matthieu Muffato[1], Anne Parker[2], Giulietta Spudich[1], Andy Yates[1], Daniel R. Zerbino[1] and Stephen M.J. Searle[2]

[1]European Molecular Biology Laboratory, European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, CB10 1SD and [2]Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, CB10 1SA, UK

wellcome trust

EMBL

National Human Genome Research Institute

BBSRC bioscience for the future

European Commission
Framework Programme 7

SEVENTH FRAMEWORK PROGRAMME

GEN2PHEN

BLUEPRINT epigenome

Quantomics
From Sequence to Consequence :
Tools for the Exploitation of Livestock Genomes