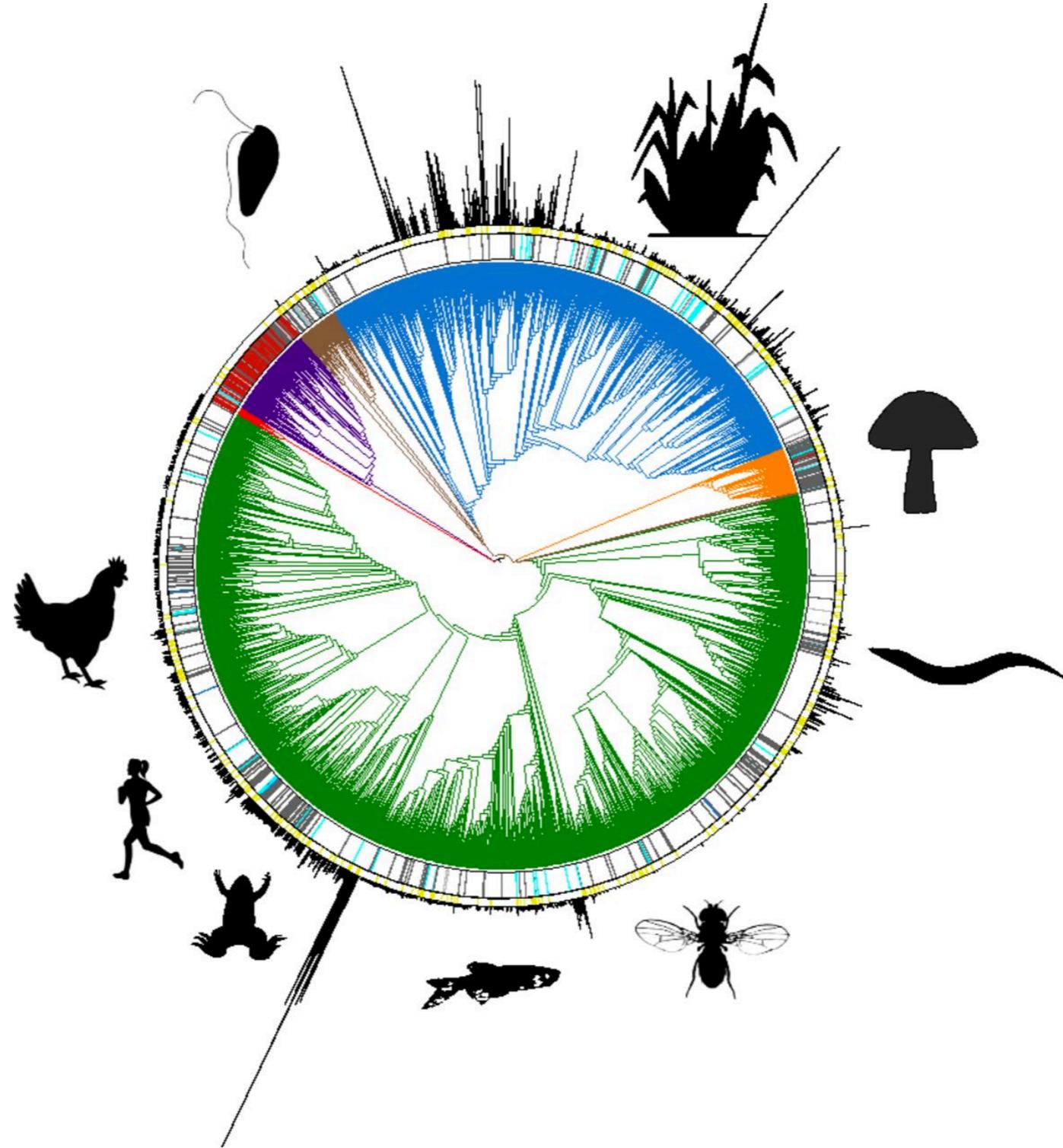


COMPARATIVE GENOMICS



CONTACTS



ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA



Andrea Luchetti

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Department of Biological, Geological, and Environmental Sciences

Academic discipline: BIO/05 Zoology

Short Bio

Evolutionary biologist and zoologist, my research activity focuses on molecular phylogeny and phylogeography, comparative genomics and the evolution of transposable elements in the animal genome. [Go to the Curriculum vitae](#)

Contacts

E-mail: andrea.luchetti@unibo.it

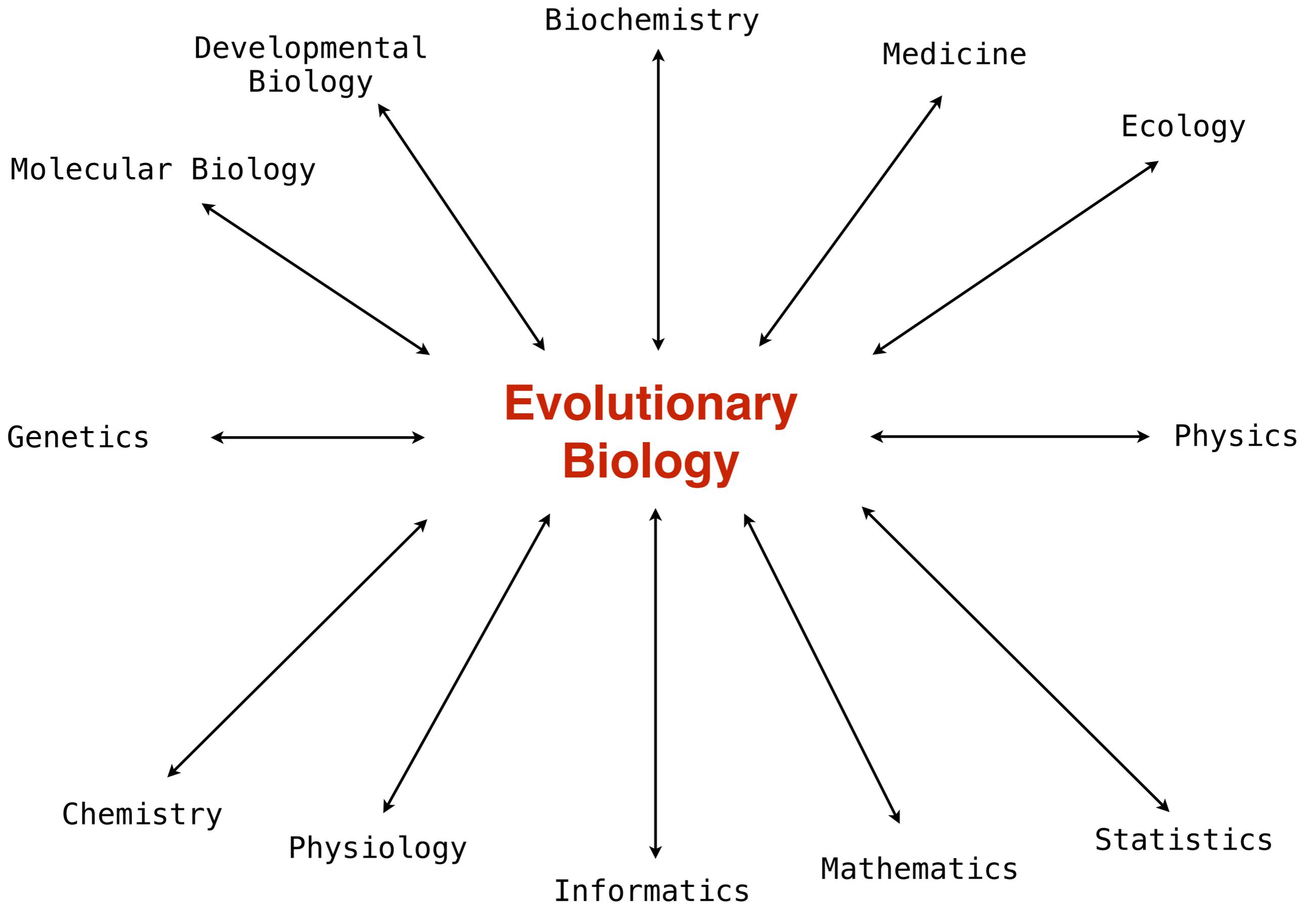
Tel: +39 051 20 9 4165

Aims of the Talk

A **VERY** short (and incomplete) introduction to:

- ▶ Sequencing technologies
- ▶ Sequencing approaches/strategies
- ▶ Technical/computational challenges
- ▶ Data analysis pipelines
- ▶ Genome anatomy
- ▶ Genome comparison

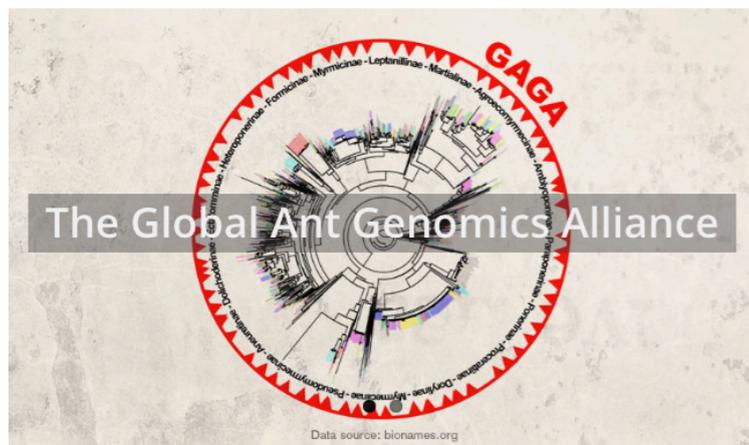
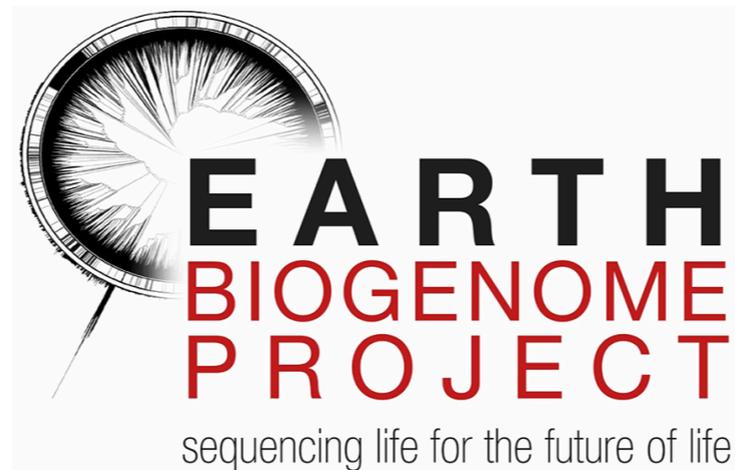
Evolutionary Biology



Genomics Timeline

- ▶ 1975 – Sanger sequencing
- ▶ 1995 – 1st genome sequenced: *Haemophilus influenzae*
- ▶ 1996 – 1st eukaryote sequenced: *Saccharomyces cerevisiae*
- ▶ 1996 – 1st archaeon sequenced: *Metanococcus janneschii* (sampled @ 2600m of depth in the Pacific Ocean)
- ▶ 1998 – 1st metazoan sequenced: *Caenorhabditis elegans*
- ▶ 1999 – *Drosophila melanogaster* genome sequenced
- ▶ 2000 – 1st draft of the human genome completed
- ▶ 2001 – Publication of the human genome
- ▶ 2002 – *Mus musculus* sequenced
- ▶ 2004 – *Rattus norvegicus* sequenced
- ▶ 2005 – Chimpanzee genome sequenced
- ▶ 2008 – 1KGP starts
- ▶ 2009 – Genome 10K project established
- ▶ 2011 – i5k Project established
- ▶ 2013 – 1st GIGA workshop
- ▶ 2017 – Vertebrate Genome Project started
- ▶ 2018 – Earth BioGenome project launched
- ▶ 2020 – ERGA consortium





Sequencing Technology Timeline

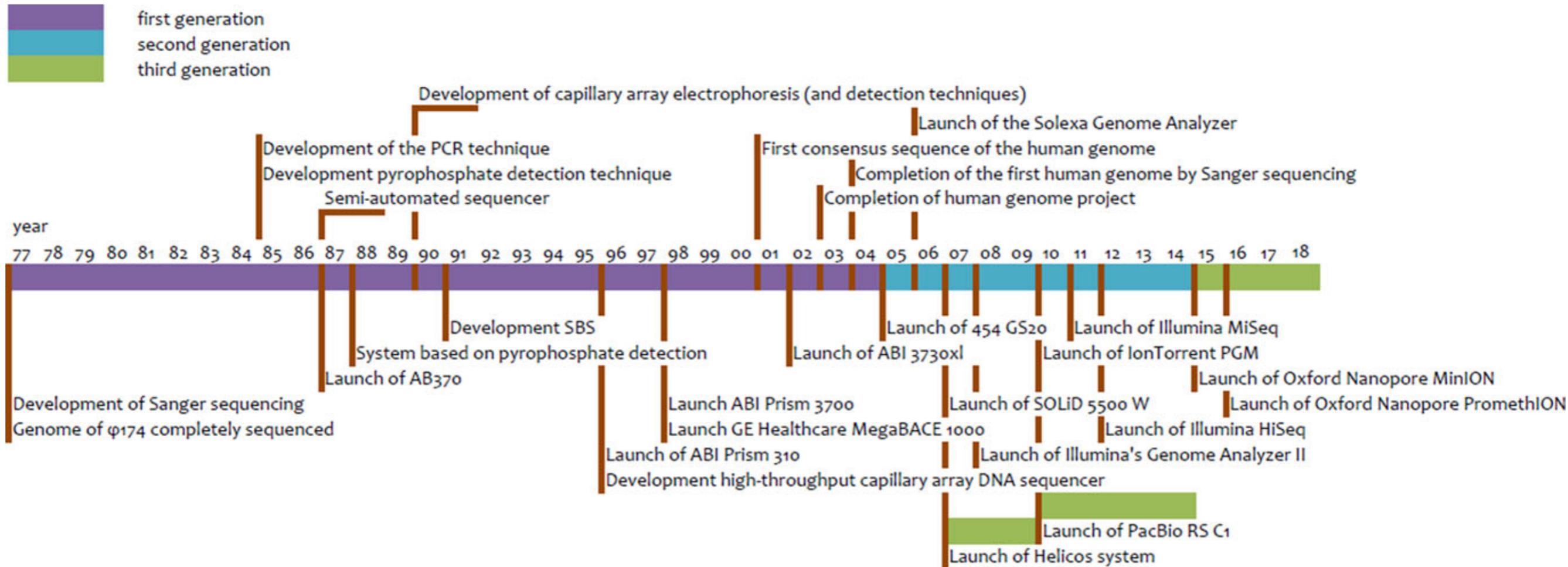
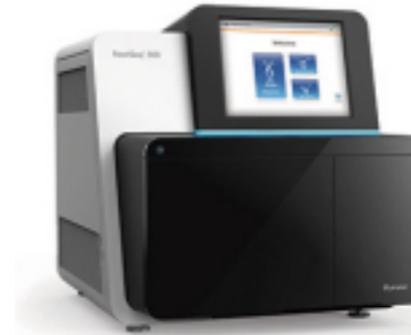
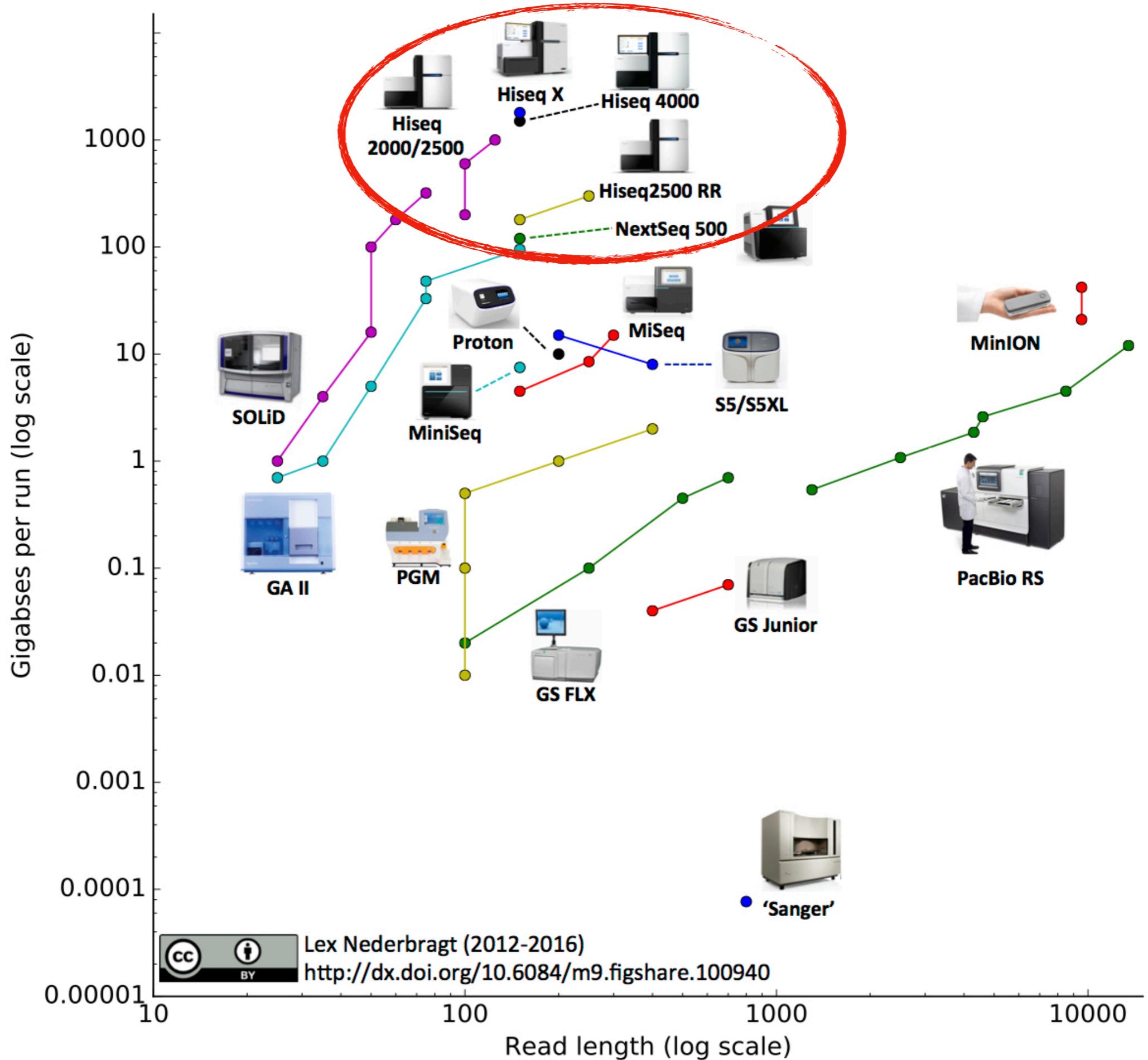


Table 1. Characteristics of the different sequencing techniques (first, second, and third generation). The read length range covers the read length at the introduction of the technique till the read length which can be obtained nowadays. Throughput and run time are for the machine that has currently the highest capacity. Throughput, reads and sequence data; AB, Applied BiosystemsTM; em-PCR; LT, Life Technologies; SBS, sequencing by synthesis [1, 3, 5, 7–9, 15–17]

Generation	Method	Launch	Technique	Read length (nt)	Throughput and run time	Comments
I	Sanger	1977	Cloning/chain termination	25–1200	96, 84 Kb, 2 h	First commercialized by AB (now LT)
II	454	2005	em-PCR/SBS/pyrosequencing	100–1000	1 million, 0.7 Gb, 24 h	Purchased by Roche in 2007
	Solexa/HiSeq [®] /MiSeq [®]	2006	Bridge PCR/SBS/reverse termination	36–300	6 billion, 1.8 Tb, several days	Solexa purchased by Illumina [®] in 2007
	SOLiD [®]	2007	em-PCR/ligation/probes	35–75	6 billion, 320 Gb, 1–2 weeks	Purchased by AB in 2006 (now LT)
	Ion Torrent TM	2010	em-PCR/ion-sensitive SBS/pH change	200–400	60–80 million, 50 Gb, 2 h	Purchased by LT in 2010
III	PacBio [®]	2010	SMRT [®] /ZMW wells	8000–20000	350000, 7Gb, 0.5–6 h	
	(Oxford) nanopore	2014	Ion current shift	9545–200000	100000, 2–4 Tb up to 48 h	

Sequencing Technologies: Overview



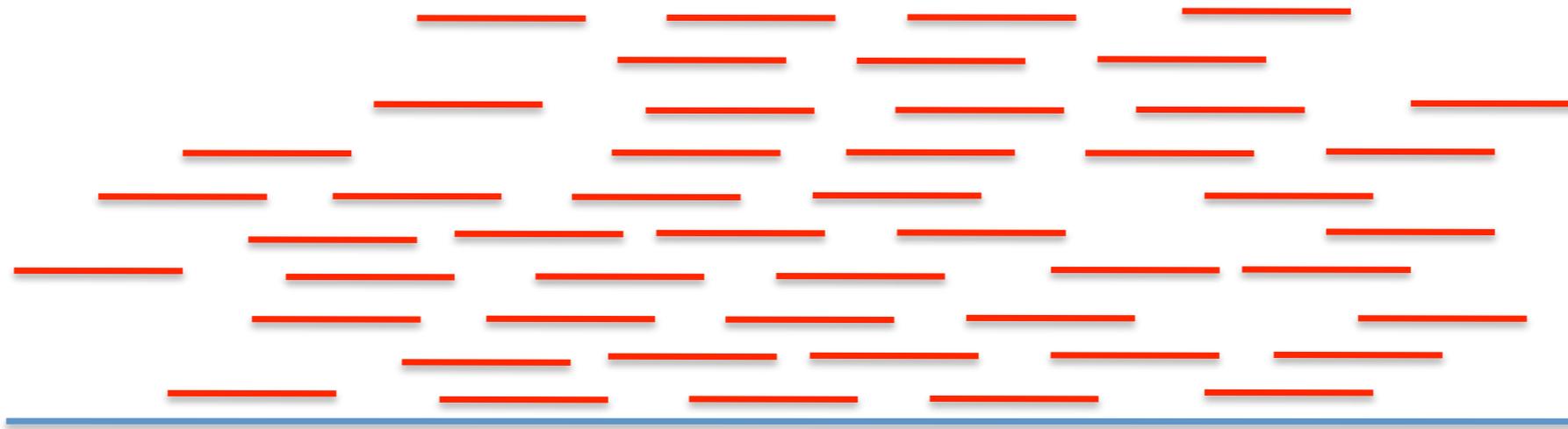



 Lex Nederbragt (2012-2016)
<http://dx.doi.org/10.6084/m9.figshare.100940>

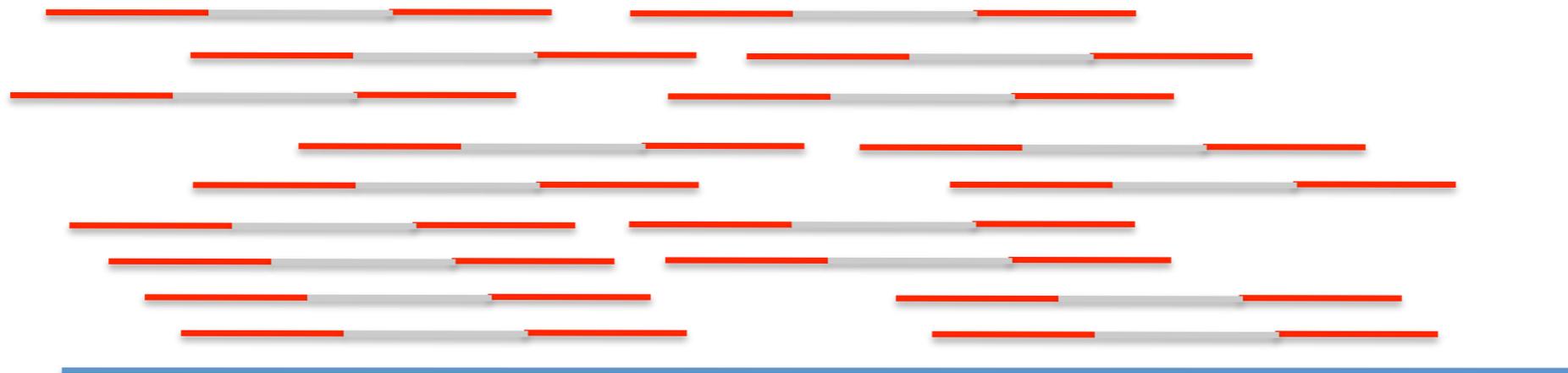
Sequencing Modes

Short reads

- Single-end sequencing



- Paired-end sequencing

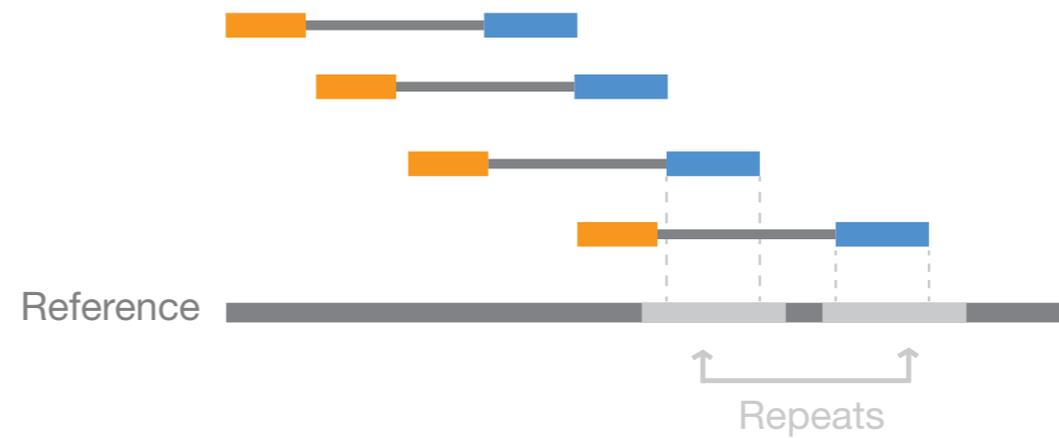


Paired-End Reads

Paired-End Reads

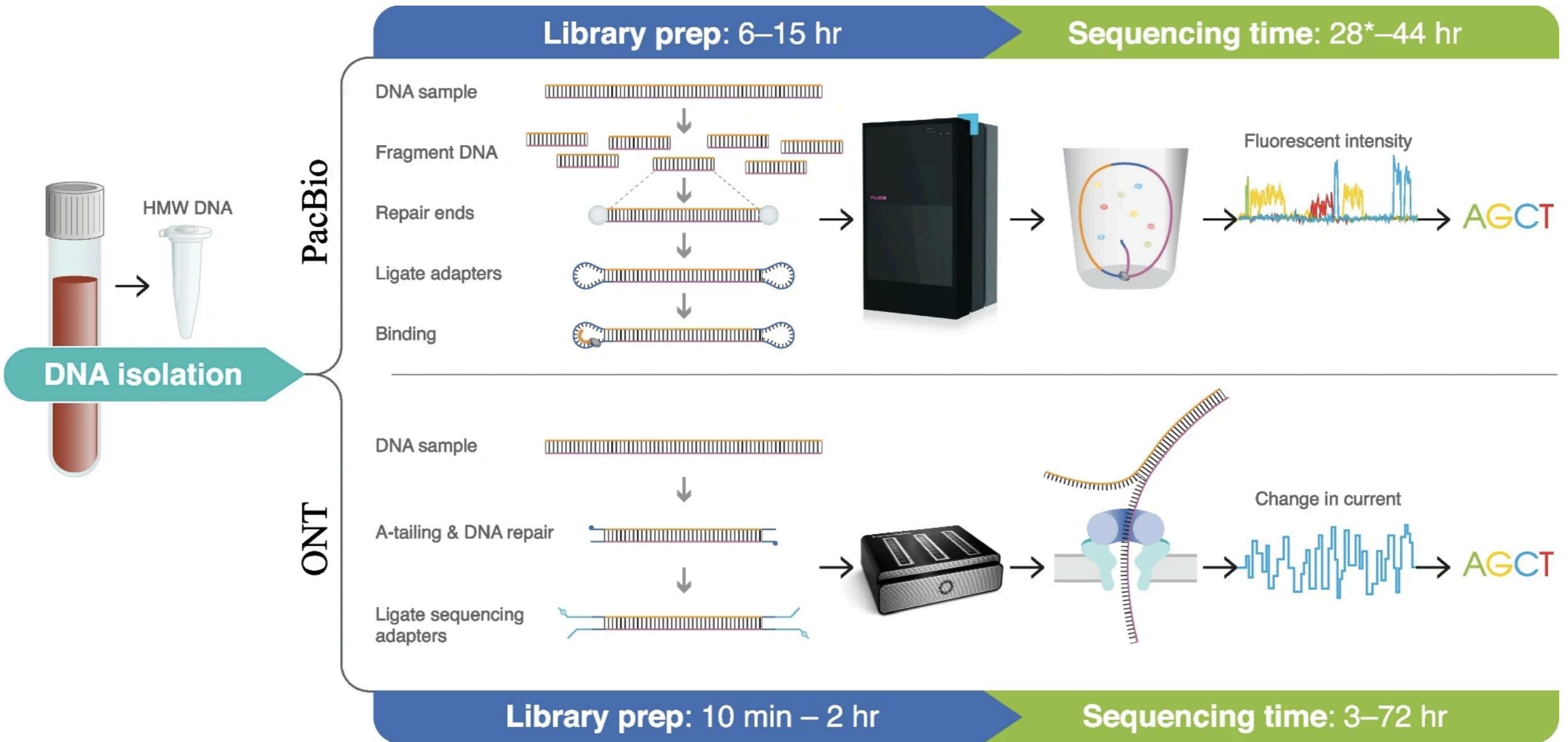


Alignment to the Reference Sequence

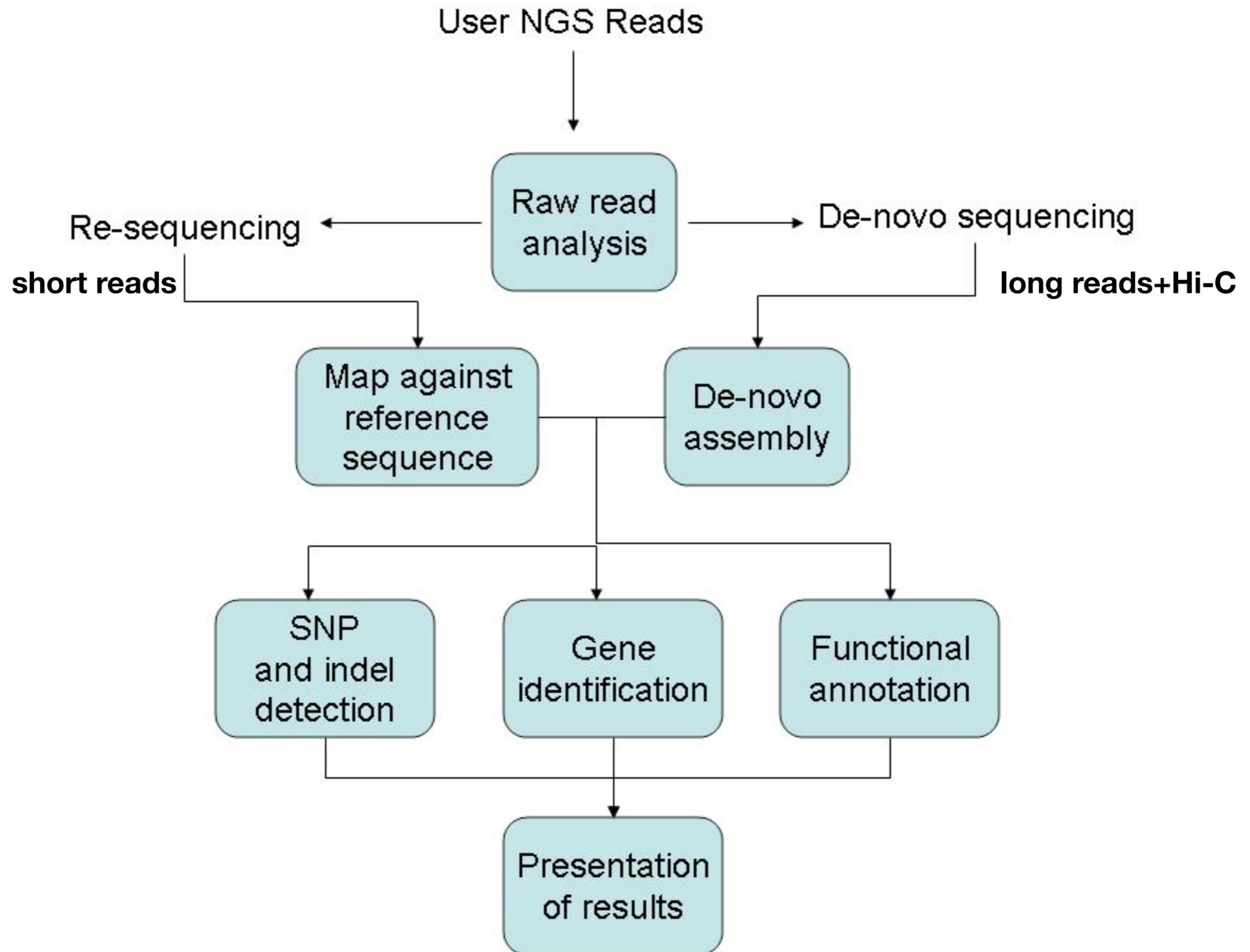


Paired-end sequencing enables both ends of the DNA fragment to be sequenced. Because the distance between each paired read is known, alignment algorithms can use this information to map the reads over repetitive regions more precisely. This results in much better alignment of the reads, especially across difficult-to-sequence, repetitive regions of the genome.

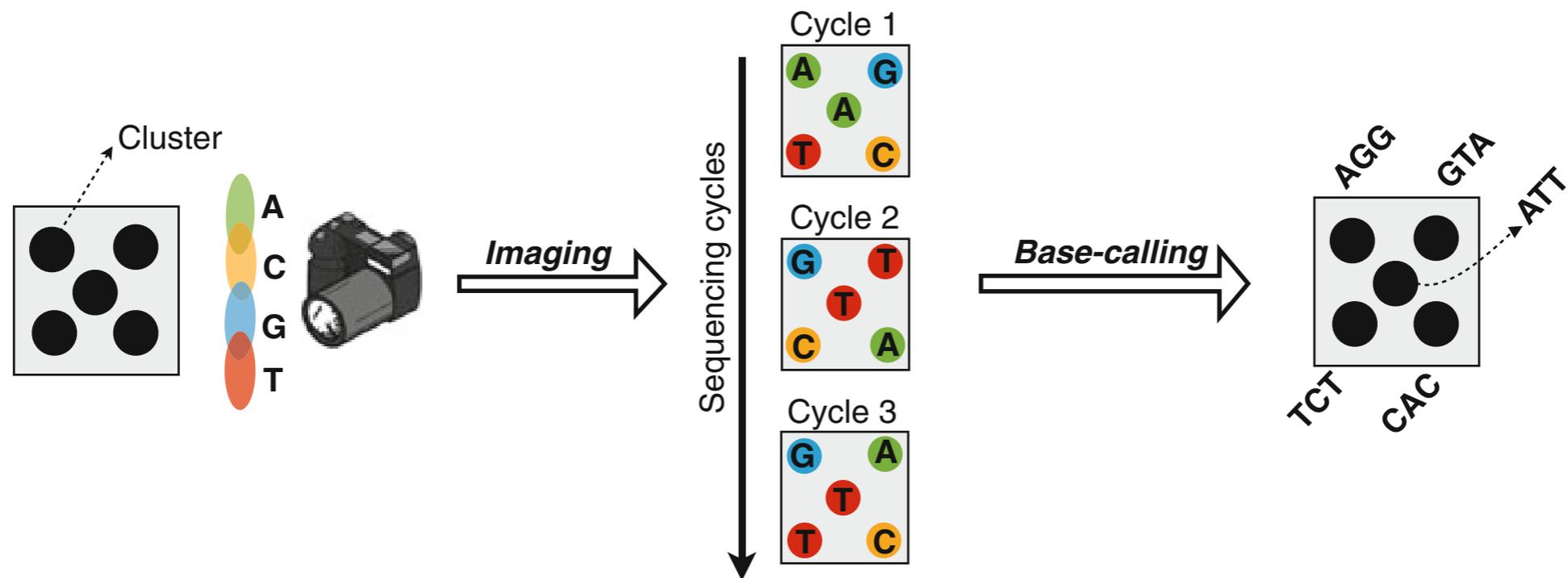
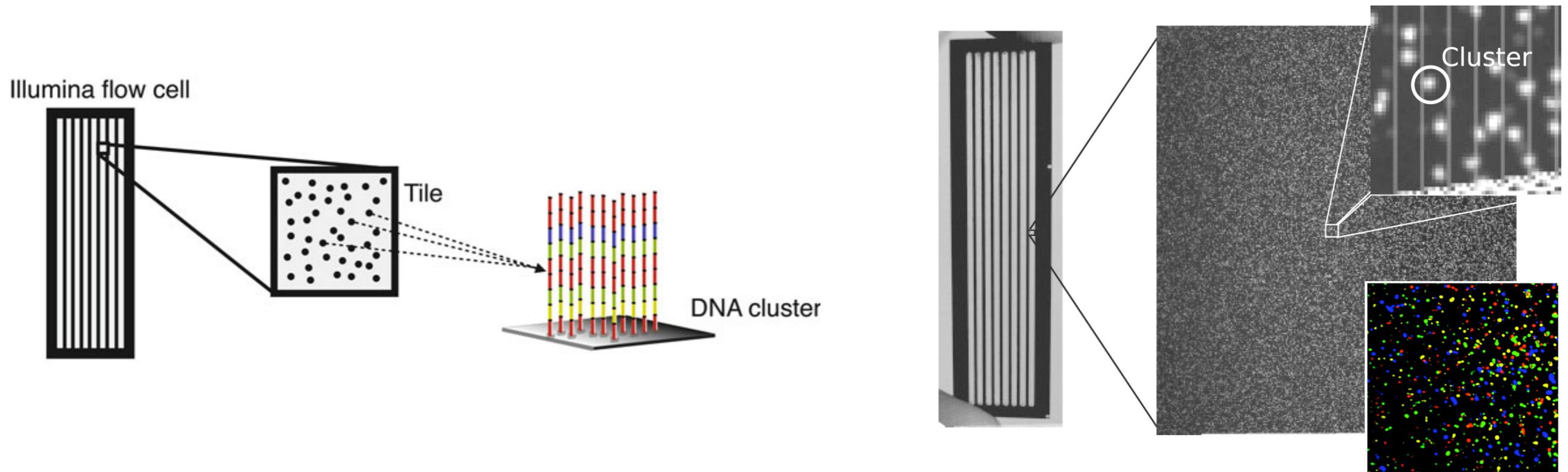
Long Reads



MPS Workflow



Output: Imaging/Base Calling



Output: Fastq Files

- fastq file:

```
@HWI-ST867_0034:2:1101:1250:2103#CGATGT/1
TGTCCGGCCGCACACATCTAGAGCATCCAGGTCAGCGATCAGCCCCGAGAGCACACAGGATAAGTGCCTGCAGGTCTCATTGTTGTTTCACACCCATCAGA
+HWI-ST867_0034:2:1101:1250:2103#CGATGT/1
ffffeffefcfaeffffefffffcffff_ffeffffff\deeUaedeedffffeffd_ce]dfbefeadd\ad`ded_effdffddcdffffdcd^dc
```

} 4 lines

- 1st line = header line
 - Contains information about the sequence

```
@HWI-ST867_0034:2:1101:1250:2103#CGATGT/1
```

@HWI-ST867_0034 ← Unique name of the Illumina instrument

2 ← Flowcell lane (1 to 8)

1101 ← Tile number

1250 ← X-coordinate within tile

2103 ← Y-coordinate within tile

#CGATGT ← Unique tag for multiplexing samples

/1 ← Member number of a pair (either 1 or 2)

- fastq file:

```
@HWI-ST867_0034:2:1101:1250:2103#CGATGT/1
TGTCGGCCGCACACATCTAGAGCATCCAGGTCAGCGATCAGCCCCGAGAGCACACAGGATAAGTGCCTGCAGGTCTCATTGTTGTTTCACACCCATCAGA
+HWI-ST867_0034:2:1101:1250:2103#CGATGT/1
ffffeffefcfaeffffefffffcffff_ffeffffff\deeUaedeedffffeffd_ce]dfbefehead\ad`ded_effdffddcdffffdcd^dc
```

} 4 lines

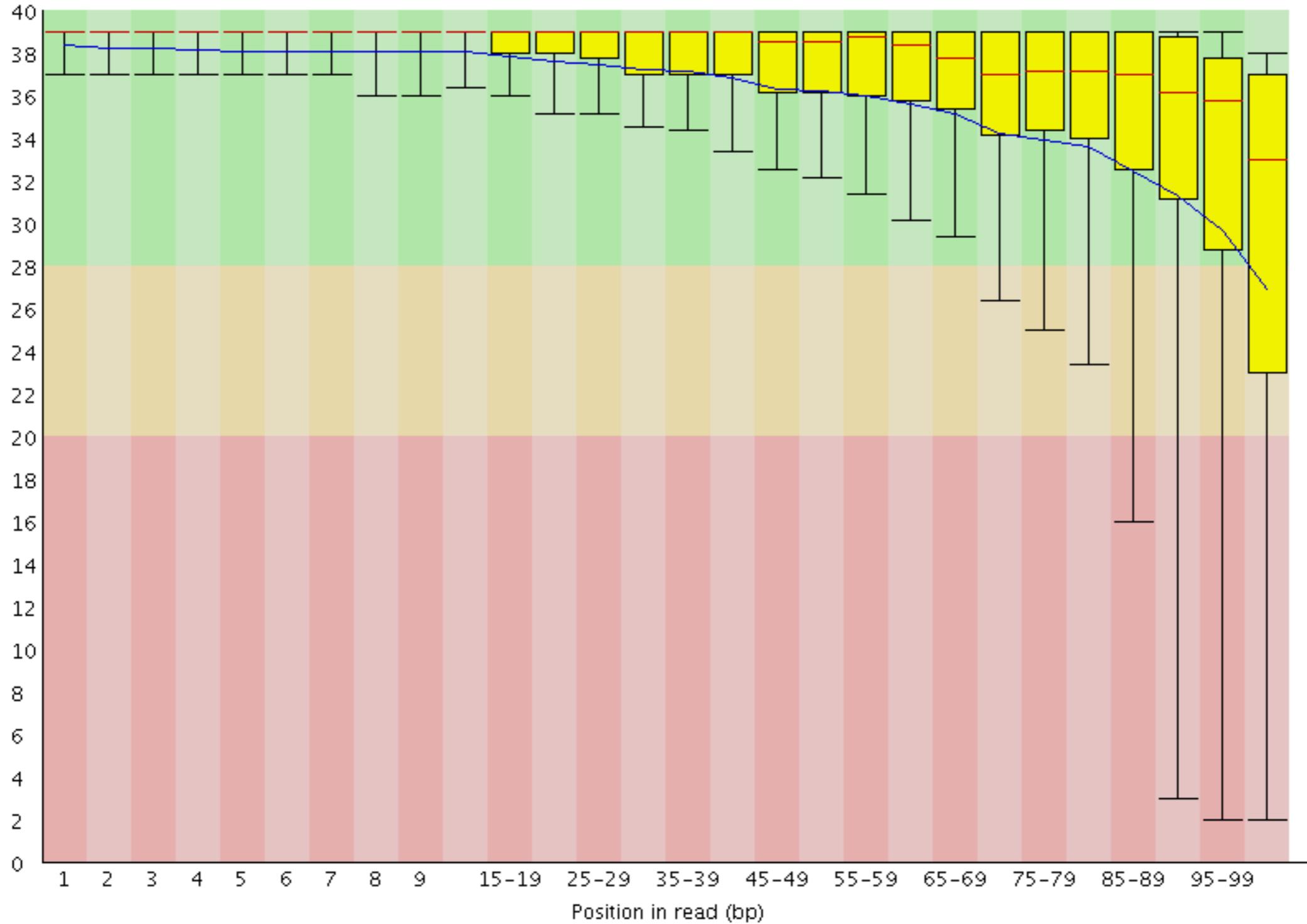
- 3rd line often equivalent to 1st line
 - Can otherwise contain more information

```
@HWI-ST867_0034:2:1101:1250:2103#CGATGT/1
```

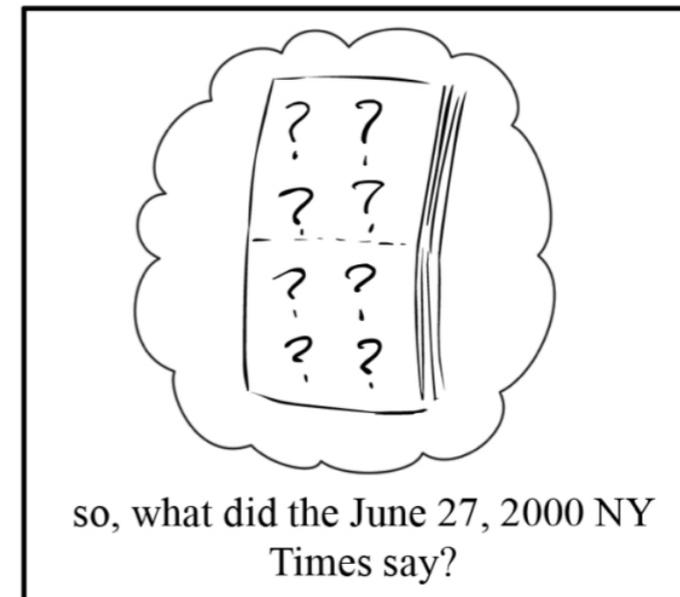
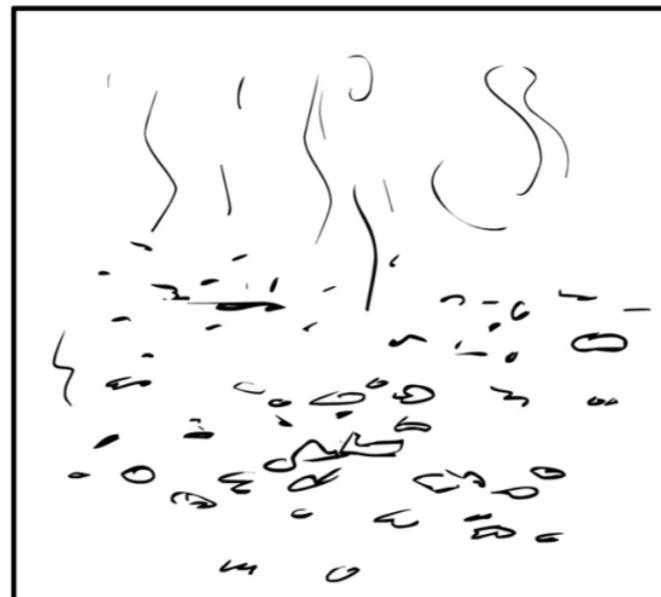
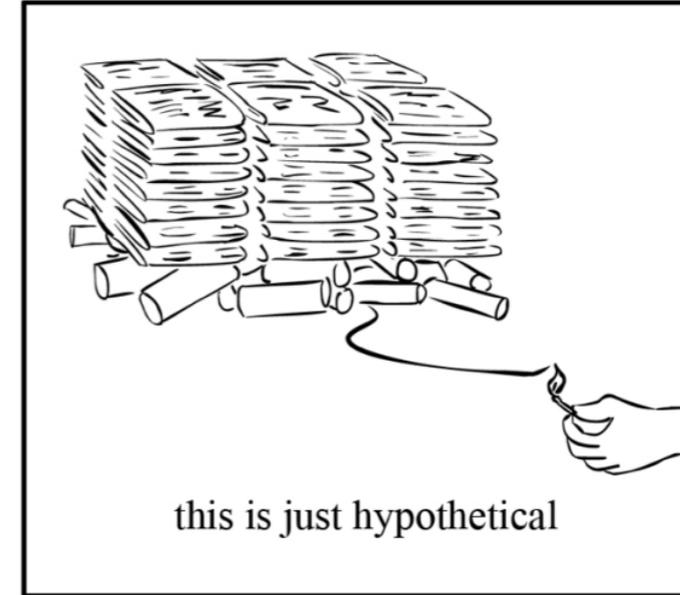
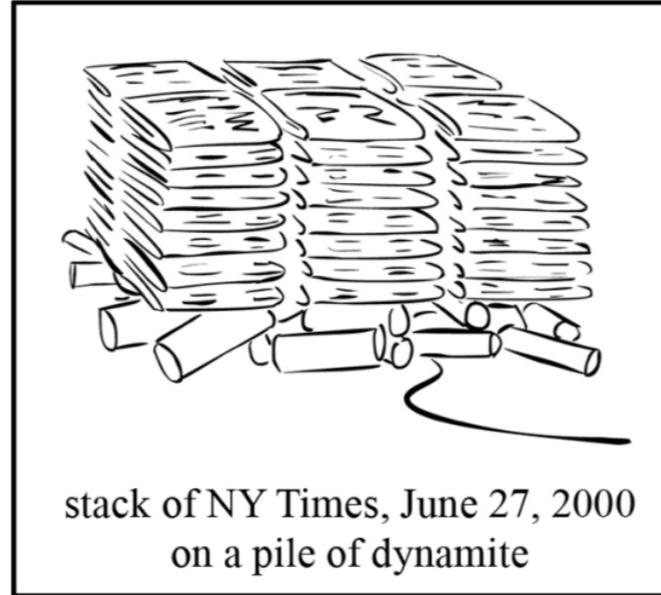
```
+HWI-ST867_0034:2:1101:1250:2103#CGATGT/1
```

- 2nd line contains actual sequence
 - String of A, C, G or T characters
- 4th line contains quality score for sequence
 - Identical in length to 2nd line
 - Each letter of “quality” corresponds to a letter of “sequence”
 - Quality score encoded in ASCII character “Phred” scores

✔ **Per base sequence quality**



De novo Assembly



De novo Assembly

Multiple (Unsequenced) Genome Copies



Read Generation

Reads



Fragment Assembly

Sequenced Genome



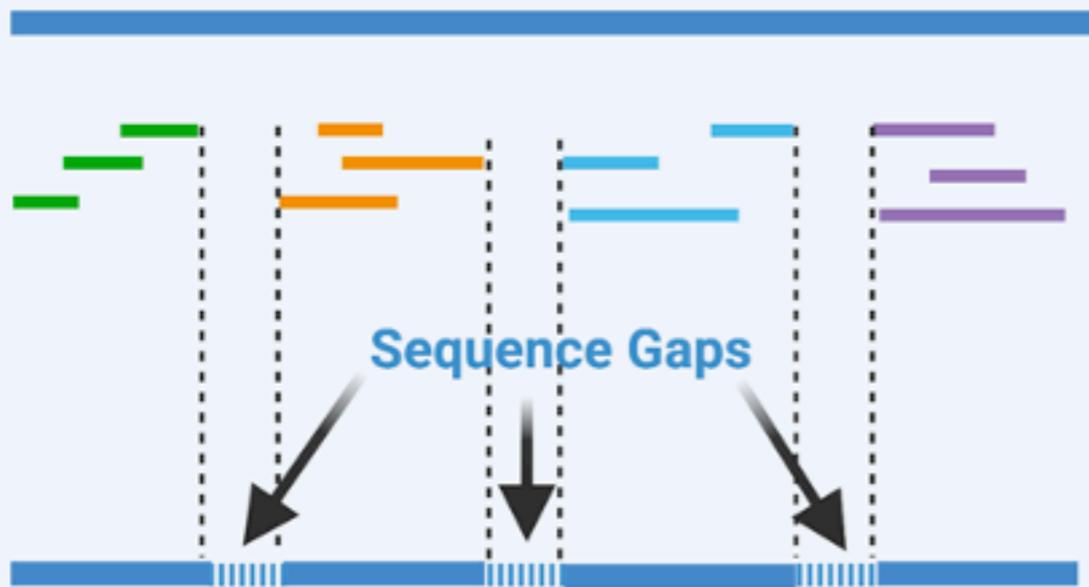
...GGCATGCGTCAGAACTATCATAGCTAGATCGTACGTAGCC...

De novo Assembly

① Short Reads



Reference Genome

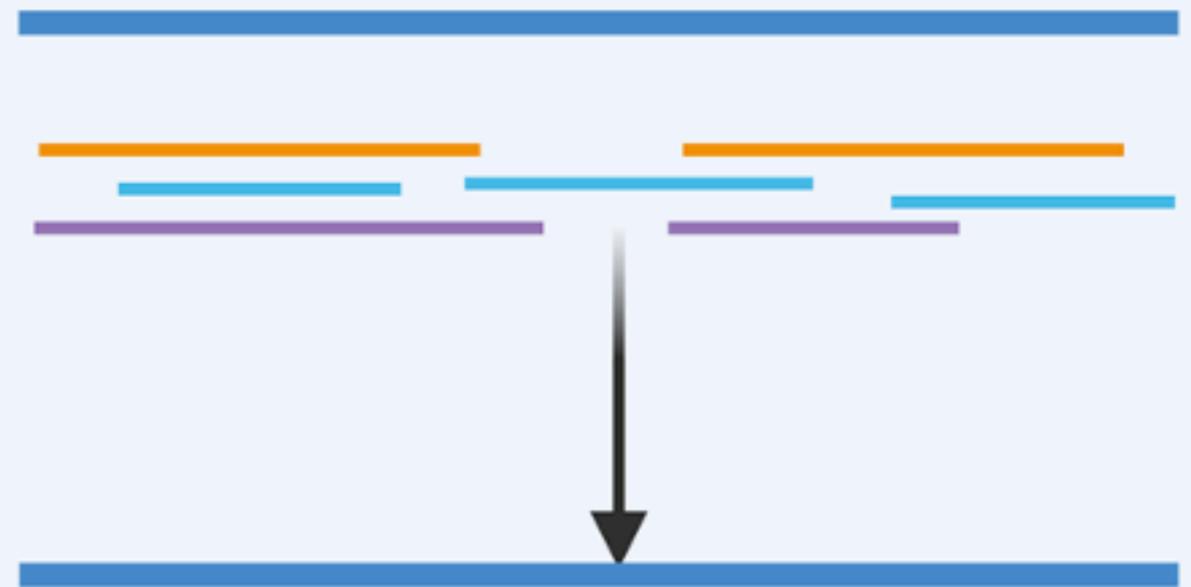


Missing sequence data leads to gaps in genome coverage and limits variant detection

② Long Reads



Reference Genome



Long reads map uniquely and span large variants providing comprehensive variant detection

De novo Assembly

Phase 1 (contig assembly)

(a) Sequence genome to produce short reads



(b) Find overlaps between reads

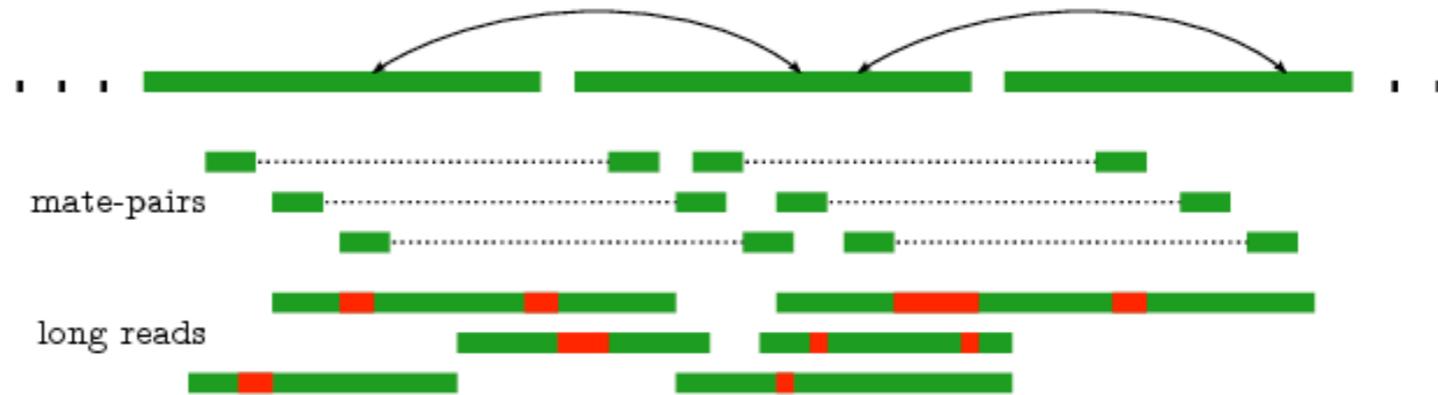
```
GATGGACAACCGAACGGTCA
      GAACGTCATATAGTCAAATGG
```

(c) Assemble unambiguous overlaps into contigs



Phase 2 (scaffolding)

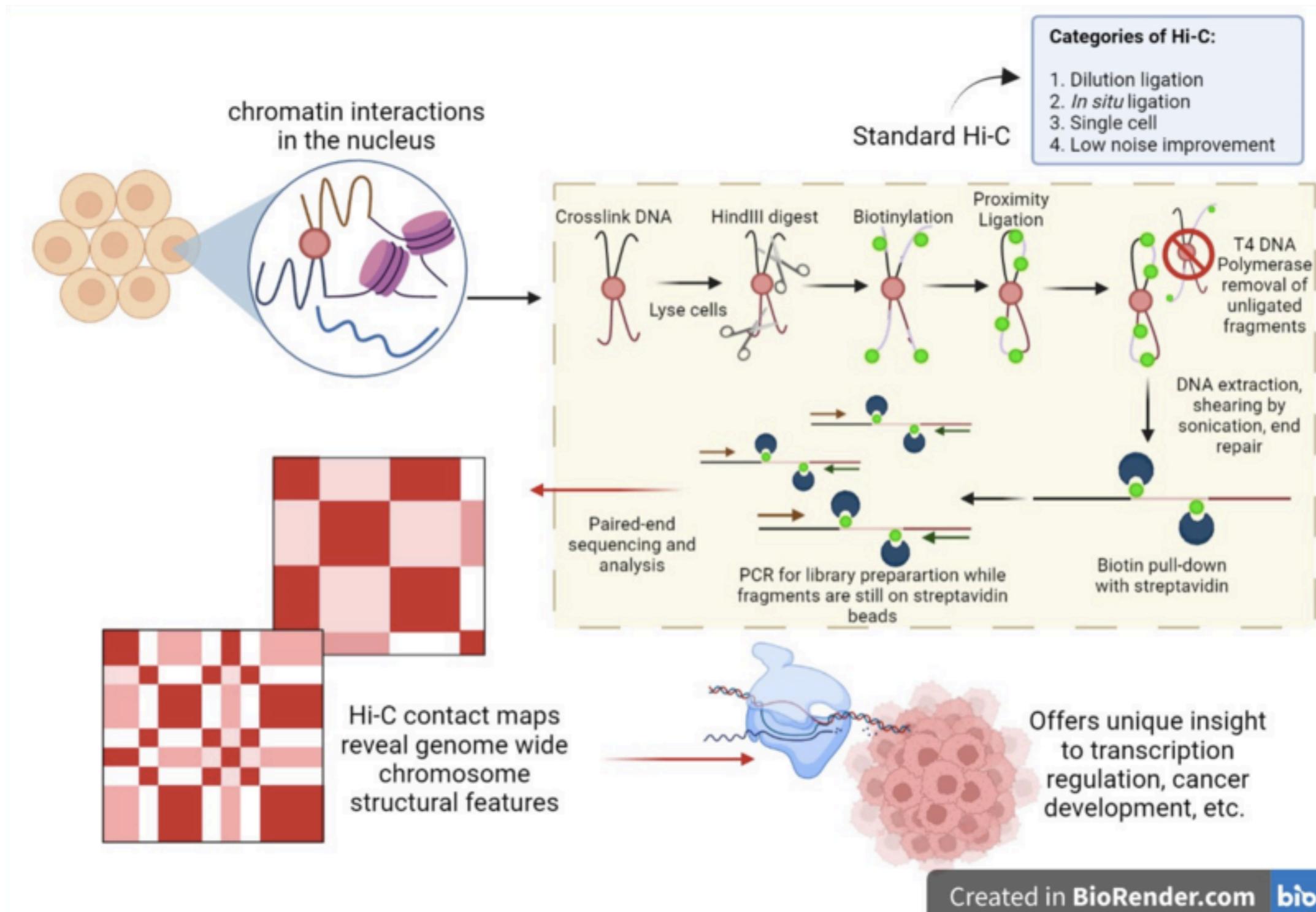
(d) Map mate-pairs or long reads to contigs and identify links



(e) Connect linked contigs into scaffolds



Hi-C (chromatin capture conformation)



Assembly Stats: N50, N90

- ▶ **N50** statistic defines assembly quality in terms of contiguity. Given a set of contigs, **the N50 is defined as the sequence length of the shortest contig at 50% of the total genome length.** It can be thought of as the point of half of the mass of the distribution.
- ▶ **N50** can be described as a **weighted median statistic such that 50% of the entire assembly is contained in contigs or scaffolds equal to or larger than this value.**
- ▶ The **N90** statistic is the length for which the collection of all contigs of that length or longer contains at least 90% of the sum of the lengths of all contigs, and for which the collection of all contigs of that length or shorter contains at least 10% of the sum of the lengths of all contigs.
- ▶ Example:

# Scaffolds	Gsize	N50	N50_scaffold#	N90	N90_scaffold#
301516	2021935850	12068	46019	2414	170482

- ▶ In this case, **50% of the assembly is represented by 46,019 scaffolds with length \geq 12068bp.** 90% of the assembly is represented by 170,482 scaffolds with length \geq 2414bp.

Assembly Stats: method comparison

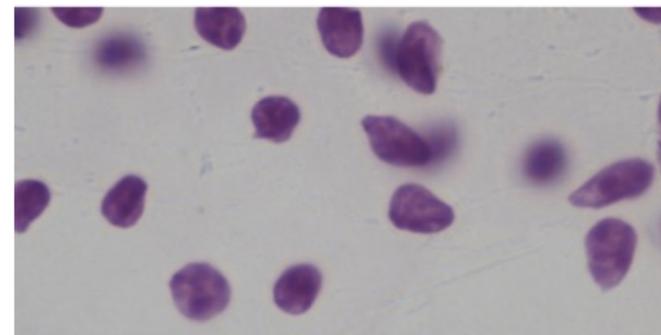
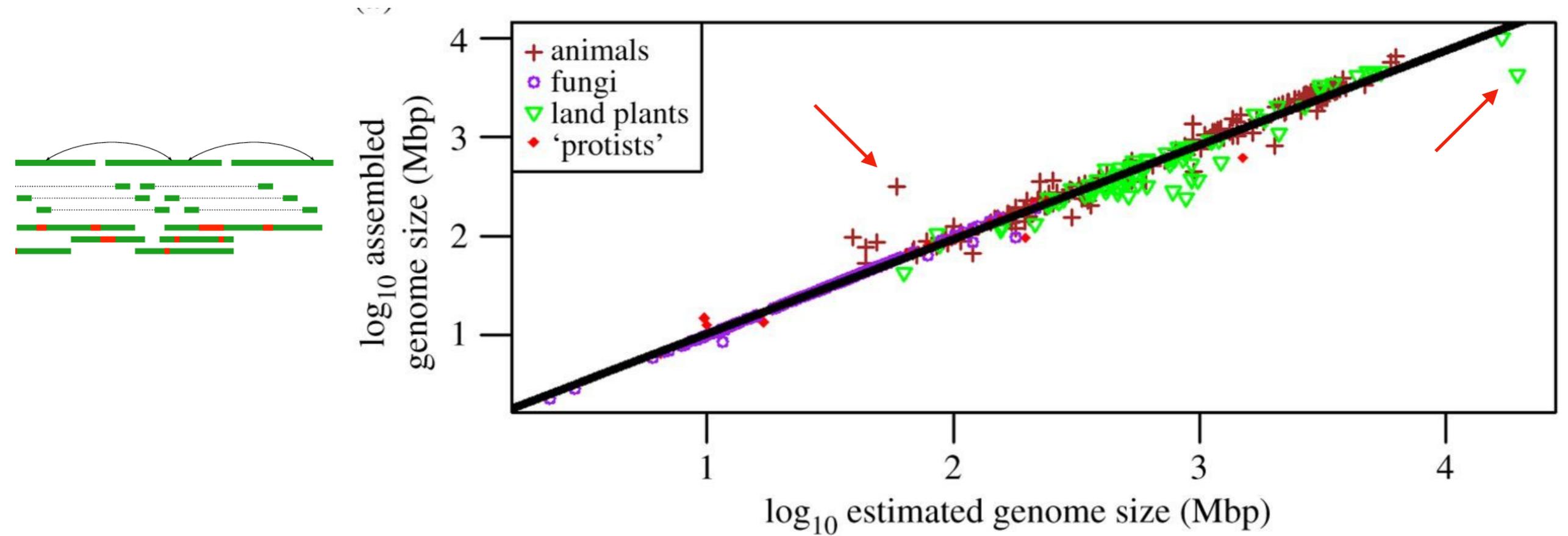
De Novo assembly stats of the
Japanese subterranean termite
Reticulitermes speratus



Method	Gsize	# Scaffolds	N50	Genome coverage
Illumina Hiseq	881 Mb	5817	37.4 kb	59.4x
PacBio Sequel	881 Mb	427	44.4 Mb	114.0x

Assembly Quality

Comparison of assembly size vs estimated genome size



Assembly Quality



UNIVERSITÉ
DE GENÈVE
FACULTÉ DE MÉDECINE

Zdobnov's Computational Evolutionary Genomics
group



CEGG Home | OrthoDB v9 | BUSCO v3

BUSCO v3

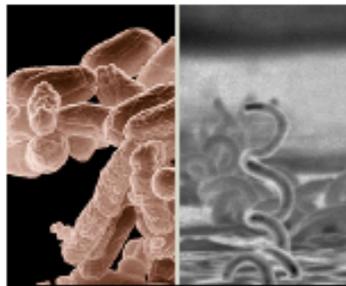
Assessing genome assembly and annotation completeness with
Benchmarking **U**niversal **S**ingle-**C**opy **O**rthologs

About BUSCO

BUSCO v3 provides quantitative measures for the assessment of genome assembly, gene set, and transcriptome completeness, based on evolutionarily-informed expectations of gene content from near-universal single-copy orthologs selected from [OrthoDB v9](#).

BUSCO assessments are implemented in open-source software, with a large selection of lineage-specific sets of Benchmarking Universal Single-Copy Orthologs. These conserved orthologs are ideal candidates for large-scale phylogenomics studies, and the annotated BUSCO gene models built during genome assessments provide a comprehensive gene predictor training set for use as part of genome annotation pipelines.

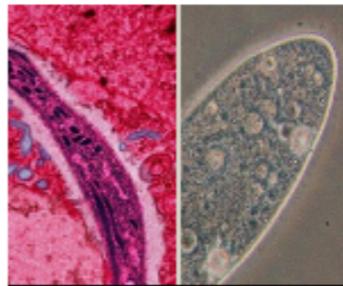
Datasets



Bacteria sets



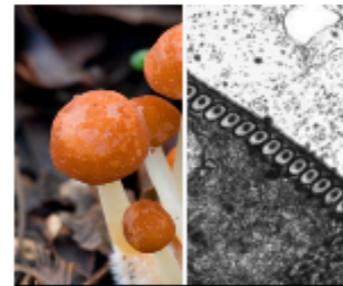
Eukaryota sets



Protists sets



Metazoa sets



Fungi sets



Plants set

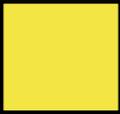
Assembly Quality

BUSCO results



 Complete

 Duplicated

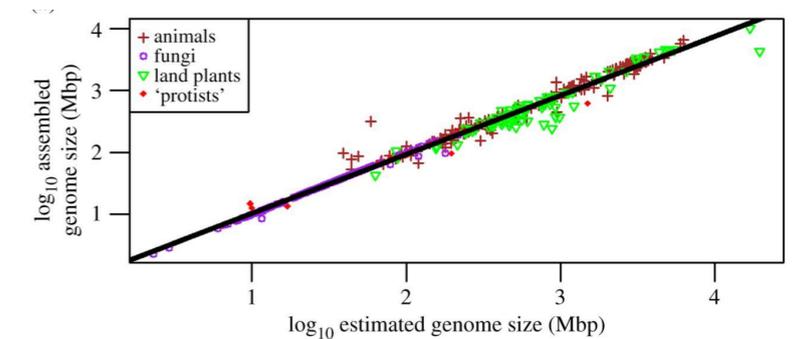
 Fragmented

 Missing

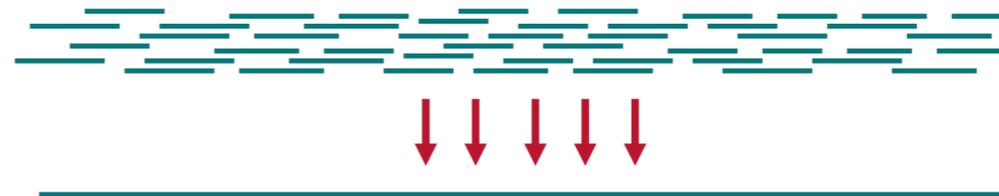
Assembly Quality

Summarizing, three questions:

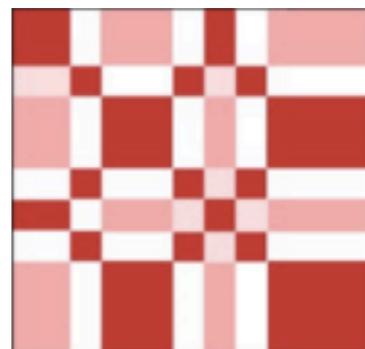
1) How much of the genome is really sequenced



2) How accurate is the sequencing



3) Genome contiguity



Annotation

1. Sequence Similarity:

- ▶ Nucleotide sequence (e.g. blastn)
- ▶ Amino acid sequence (e.g. blastp)
- ▶ HMM profile (es. hmmer)
- ▶ Signatures (es. InterProScan)

2. Assignment of **GO Terms**.

Gene ontology (GO) is a major bioinformatics initiative to unify the representation of gene and gene product attributes across all species.

The project aims to:

- 1) maintain and develop its controlled vocabulary of gene and gene product attributes;
- 2) annotate genes and gene products, and assimilate and disseminate annotation data;
- 3) provide tools for easy access to all aspects of the data provided by the project, and to enable functional interpretation of experimental data using the GO, for example via enrichment analysis.

In computer science and information science, **an ontology encompasses a representation, formal naming and definition of the categories, properties and relations between the concepts, data and entities that substantiate one, many or all domains.**

Annotation

The ontology covers three domains:

- **Cellular component**, the parts of a cell or its extracellular environment;
- **Molecular function**, the elemental activities of a gene product at the molecular level, such as binding or catalysis;
- **Biological process**, operations or sets of molecular events with a defined beginning and end, pertinent to the functioning of integrated living units: cells, tissues, organs, and organisms.

Each GO term within the ontology has a term name, which may be a word or string of words; a unique alphanumeric identifier; a definition with cited sources; and a namespace indicating the domain to which it belongs.

Terms may also have synonyms, which are classed as being exactly equivalent to the term name, broader, narrower, or related; references to equivalent concepts in other databases; and comments on term meaning or usage.

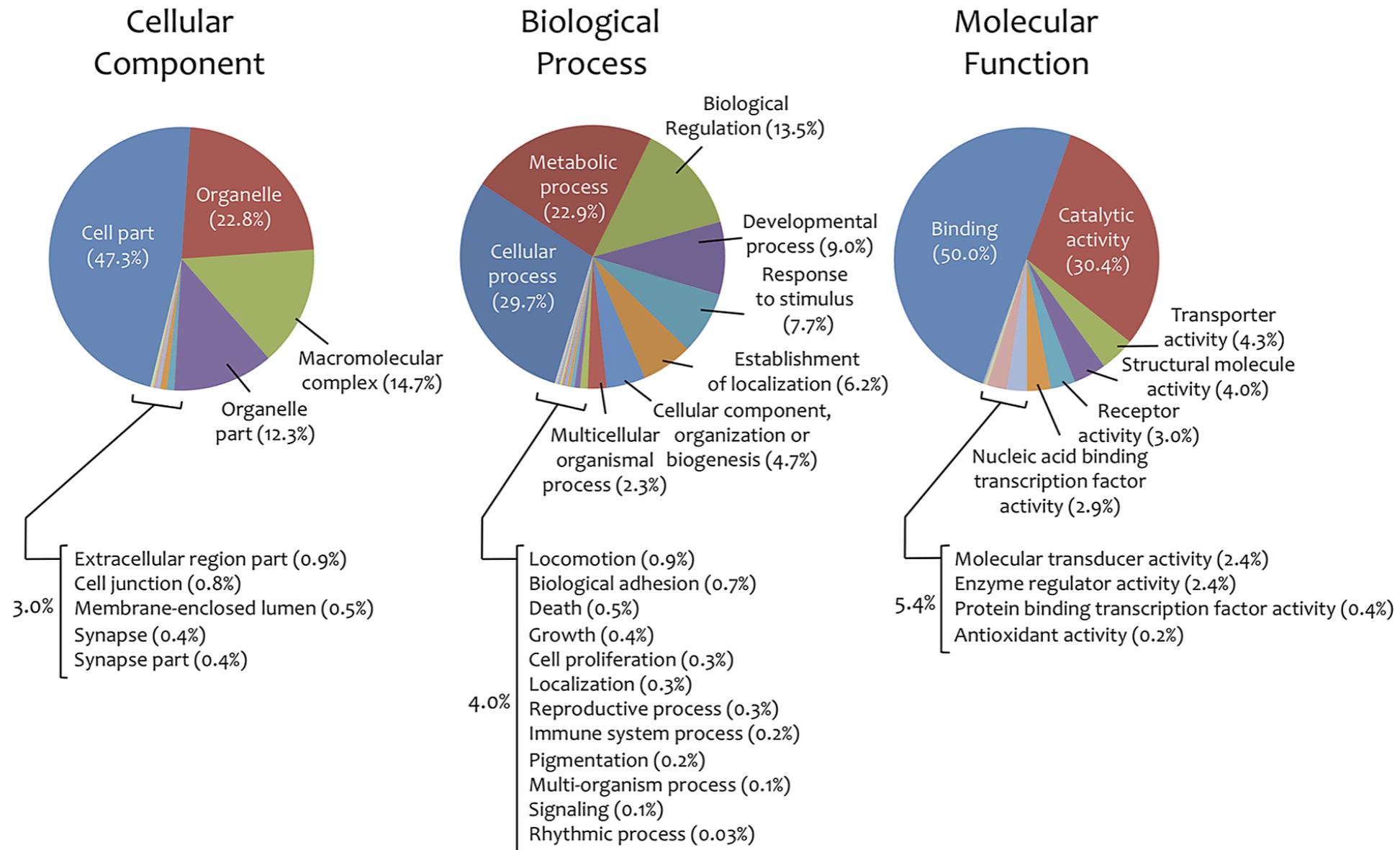
The GO ontology is structured as a directed acyclic graph, and each term has defined relationships to one or more other terms in the same domain, and sometimes to other domains.

The GO vocabulary is designed to be species-neutral, and includes terms applicable to prokaryotes and eukaryotes, single and multicellular organisms.

Annotation

```

id:          GO:0000016
name:        lactase activity
namespace:   molecular_function
def:         "Catalysis of the reaction: lactose + H2O = D-glucose + D-galactose." [EC:3.2.1.108]
synonym:     "lactase-phlorizin hydrolase activity" BROAD [EC:3.2.1.108]
synonym:     "lactose galactohydrolase activity" EXACT [EC:3.2.1.108]
xref:        EC:3.2.1.108
xref:        MetaCyc:LACTASE-RXN
xref:        Reactome:20536
is_a:        GO:0004553 ! hydrolase activity, hydrolyzing O-glycosyl compounds
    
```



Why Sequencing Genomes?

- ▶ Gain better understanding of biology
- ▶ Gain knowledge about genetic variation
- ▶ Allow the comparisons between taxa (understand evolution)
 - ▶ How much/How genes vary across taxa?
 - ▶ How much/How genome architecture changes?
 - ▶ How much/How gene content changes?
 - ▶ Reconstruct phylogenetic relationships and evolution of taxa
 - ▶ Reconstruct the evolutionary history of a species
- ▶ Biomedical/veterinary applications
- ▶ Forensic applications

Some MPS Applications

- ▶ **FUNCTIONAL GENOMICS**

Understanding the function of genes and other genetic elements in a genome

- ▶ **COMPARATIVE GENOMICS**

Comparing genomes of different organisms

- ▶ **POPULATION GENOMICS**

Large-scale comparison of DNA sequences in populations

- ▶ **METAGENOMICS**

Study of genetic material directly from environmental samples

- ▶ **CONSERVATION GENOMICS**

Application of genomic analysis to the preservation of the viability of populations and the biodiversity of living organisms

Functional Genomics

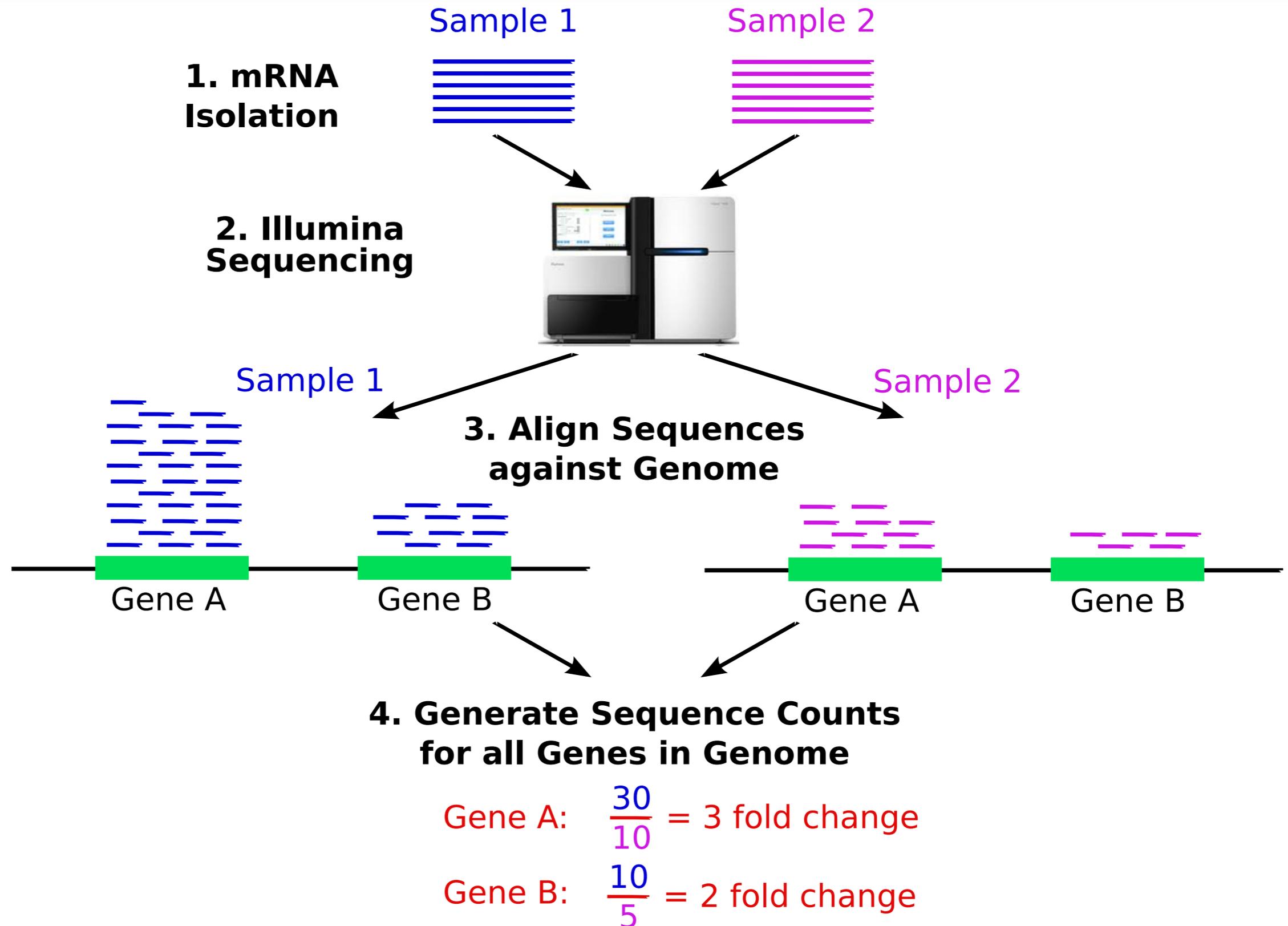
Use of the vast wealth of data given by **genomic** and **transcriptomic** projects to **describe gene functions and interactions**.

Focuses on the dynamic aspects such as gene **transcription, translation, regulation of gene expression, and protein–protein interactions**, as opposed to the static aspects of the genomic information such as DNA sequence or structures.

Attempts to answer questions about the **function of genetic elements at the levels of genes, RNA transcripts, and protein products**.

A key characteristic of functional genomics studies is their **genome-wide approach** to these questions, **generally involving high-throughput methods** rather than a more traditional “gene-by-gene” approach.

RNA-Seq Technology



De Novo Assembly of the Manila Clam *Ruditapes philippinarum* Transcriptome Provides New Insights into Expression Bias, Mitochondrial Doubly Uniparental Inheritance and Sex Determination

Fabrizio Ghiselli,^{1,*} Liliana Milani,¹ Peter L. Chang,² Dennis Hedgecock,³ Jonathan P. Davis,⁴ Sergey V. Nuzhdin,² and Marco Passamonti¹

¹Dipartimento di Biologia Evoluzionistica Sperimentale, Università di Bologna, Bologna, Italy

²Program in Molecular and Computational Biology, Department of Biological Sciences, University of Southern California

³Marine and Environmental Biology Section, Department of Biological Sciences, University of Southern California

⁴Taylor Shellfish Farms, Quilcene, Washington

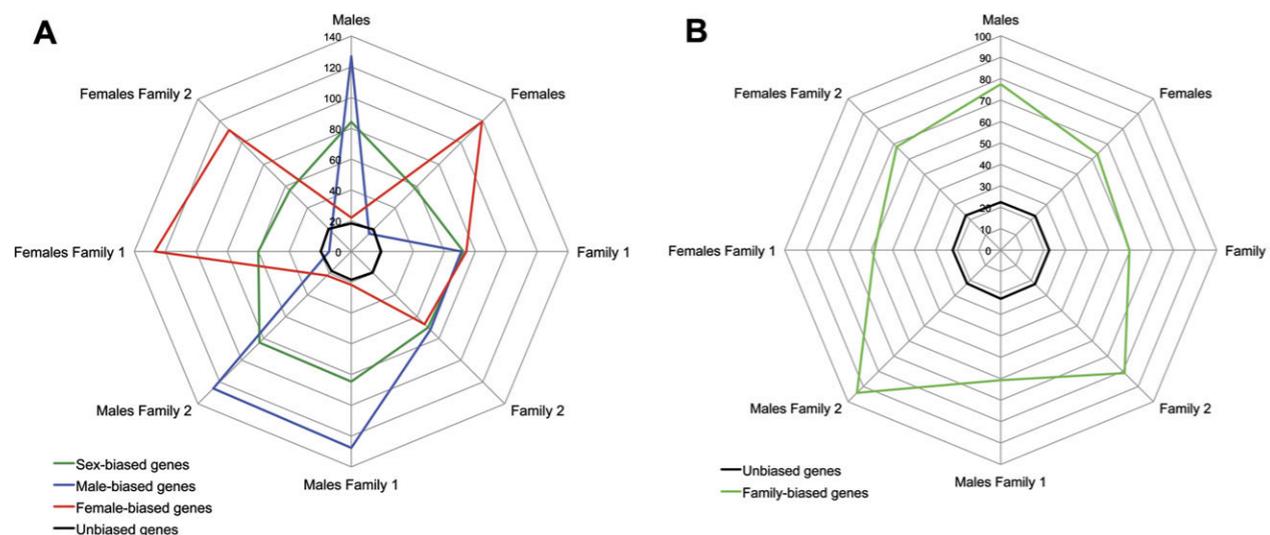
*Corresponding author: E-mail: fabrizio.ghiselli@unibo.it.

Associate editor: Richard Thomas

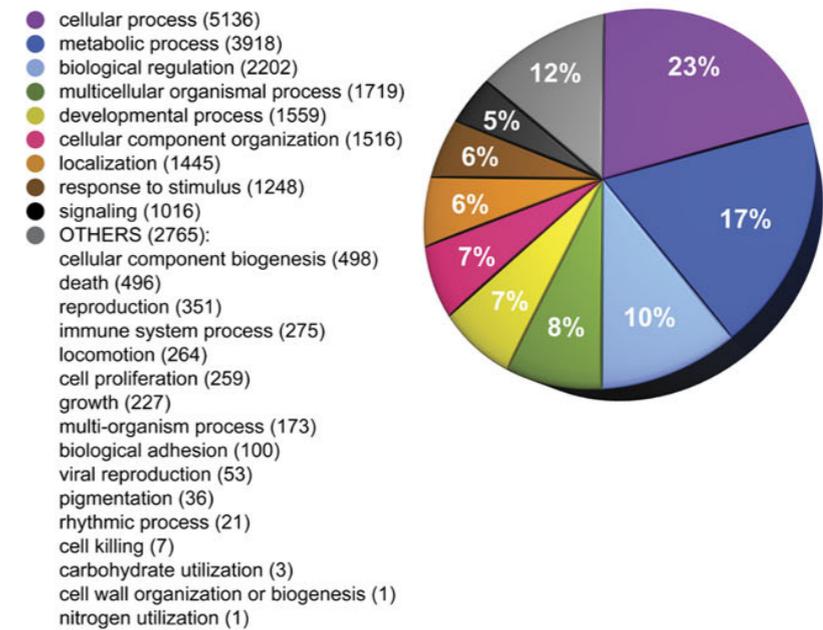
Abstract

Males and females share the same genome, thus, phenotypic divergence requires differential gene expression and sex-specific regulation. Accordingly, the analysis of expression patterns is pivotal to the understanding of sex determination mechanisms. Many bivalves are stable gonochoric species, but the mechanism of gonad sexualization and the genes involved are still unknown. Moreover, during the period of sexual rest, a gonad is not present and sex cannot be determined. A mechanism associated with germ line differentiation in some bivalves, including the Manila clam *Ruditapes philippinarum*, is the doubly uniparental inheritance (DUI) of mitochondria, a variation of strict maternal inheritance. Two mitochondrial lineages are present, one transmitted through eggs and the other through sperm, as well as a mother-dependent sex bias of the progeny. We produced a de novo annotation of 17,186 transcripts from *R. philippinarum* and compared the transcriptomes of males and females and identified 1,575 genes with strong sex-specific expression and 166 sex-specific single nucleotide polymorphisms, obtaining preliminary information about genes that could be involved in sex determination. Then we compared the transcriptomes between a family producing predominantly females and a family producing predominantly males to identify candidate genes involved in regulation of sex-specific aspects of DUI system, finding a relationship between sex bias and differential expression of several ubiquitination genes. In mammalian embryos, sperm mitochondria are degraded by ubiquitination. A modification of this mechanism is hypothesized to be responsible for the retention of sperm mitochondria in male embryos of DUI species. Ubiquitination can additionally regulate gene expression, playing a role in sex determination of several animals. These data enable us to develop a model that incorporates both the DUI literature and our new findings.

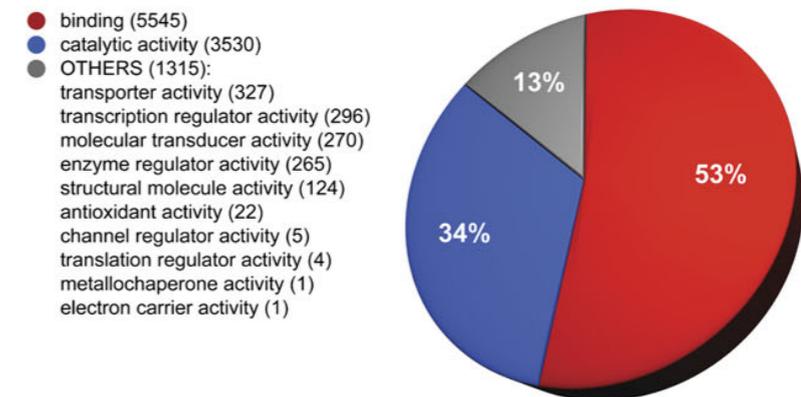
Key words: *Ruditapes philippinarum*, de novo, transcriptome, doubly uniparental inheritance, sex bias, sex determination.



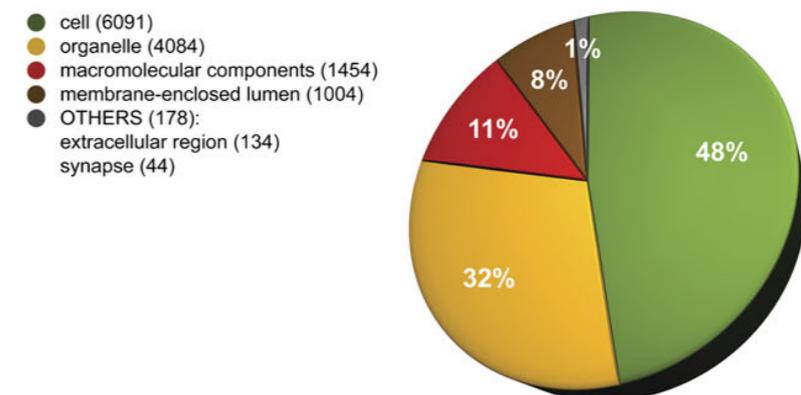
BIOLOGICAL PROCESS - GO ANNOTATION



MOLECULAR FUNCTION - GO ANNOTATION



CELLULAR COMPONENT - GO ANNOTATION



Comparative Transcriptomics in Two Bivalve Species Offers Different Perspectives on the Evolution of Sex-Biased Genes

Fabrizio Ghiselli^{1,*†}, Mariangela Iannello^{1,†}, Guglielmo Puccio¹, Peter L. Chang², Federico Plazzi¹, Sergey V. Nuzhdin^{2,†}, and Marco Passamonti^{1,†}

¹Department of Biological, Geological, and Environmental Sciences, University of Bologna, Italy

²Program in Molecular and Computational Biology, Department of Biological Sciences, University of Southern California, Los Angeles, USA

†These authors contributed equally to this work.

*Corresponding author: E-mail:fabrizio.ghiselli@unibo.it.

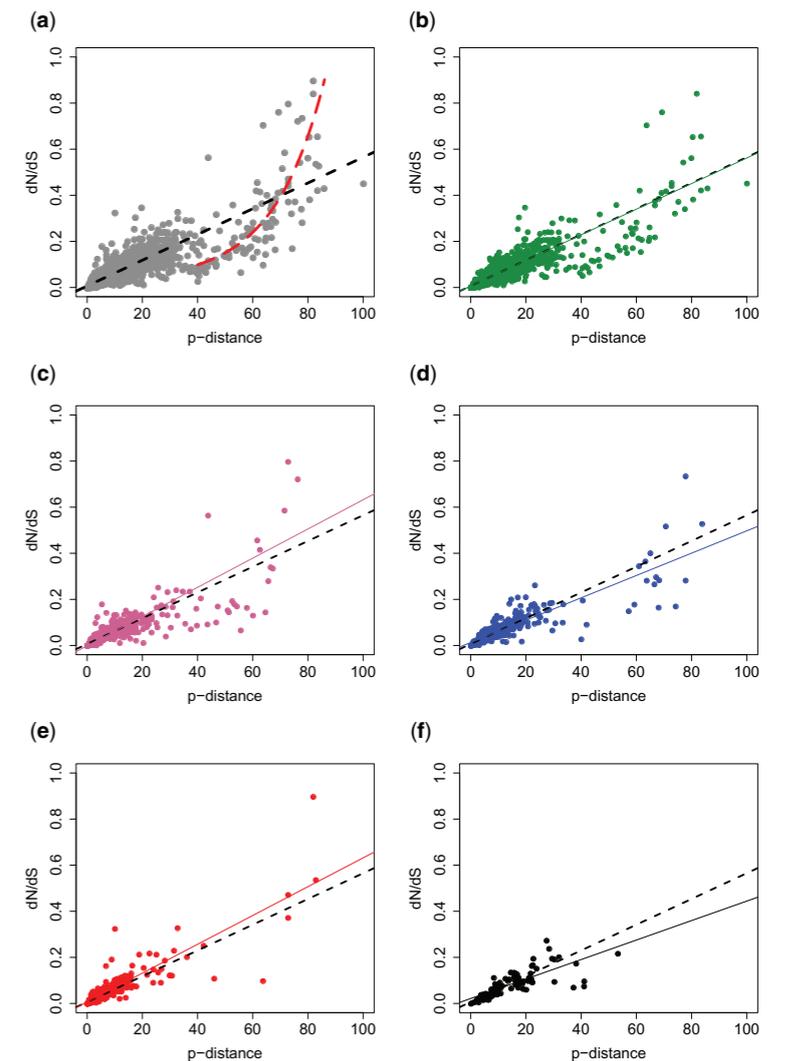
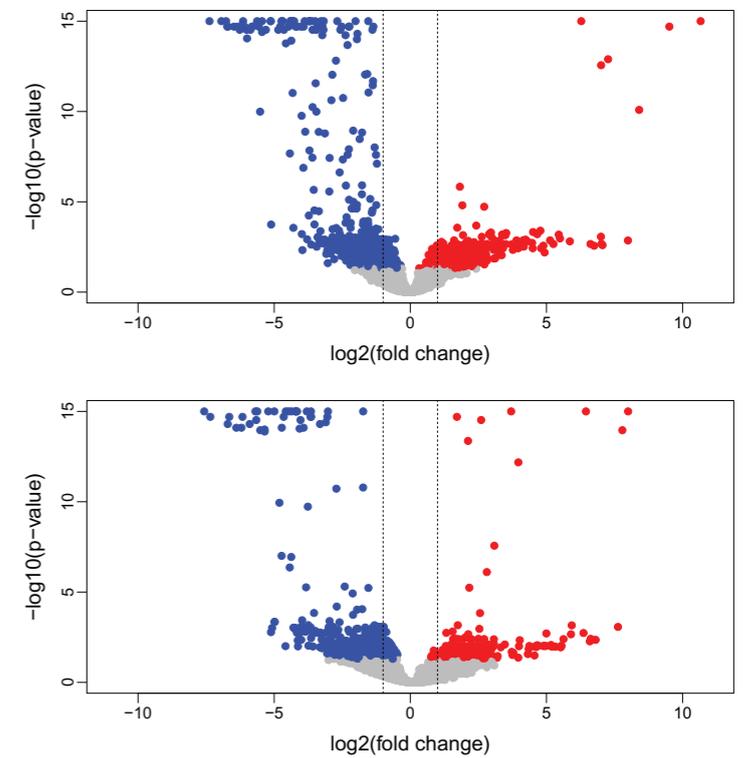
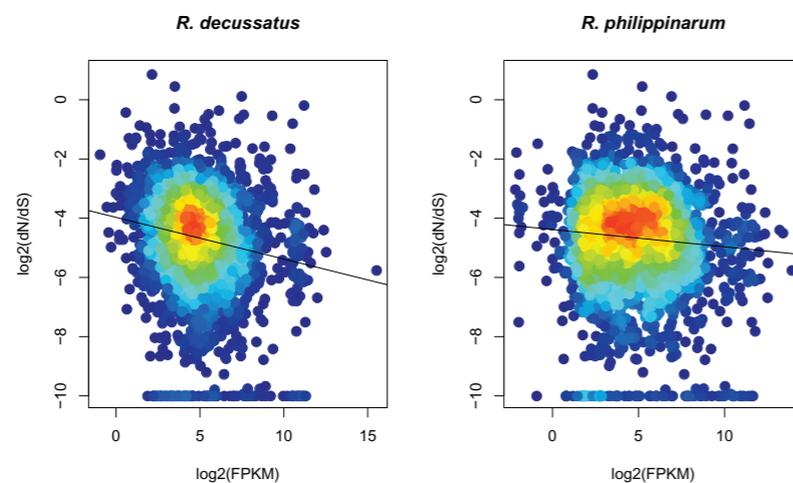
Accepted: April 19, 2018

Data deposition: This project has been deposited at NCBI BioProject under the accessions PRJNA170478 and PRJNA68513; and on figshare, at the link: <https://doi.org/10.6084/m9.figshare.5398618.v1>

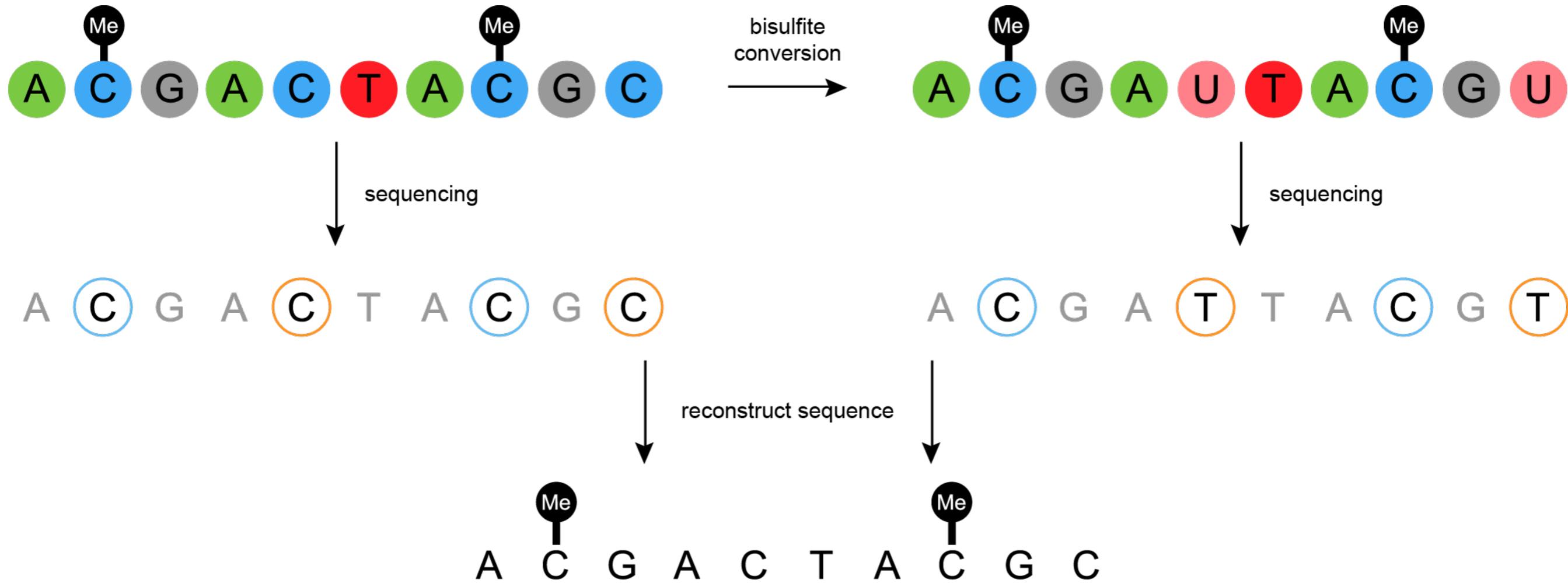
Abstract

Comparative genomics has become a central tool for evolutionary biology, and a better knowledge of understudied taxa represents the foundation for future work. In this study, we characterized the transcriptome of male and female mature gonads in the European clam *Ruditapes decussatus*, compared with that in the Manila clam *Ruditapes philippinarum* providing, for the first time in bivalves, information about transcription dynamics and sequence evolution of sex-biased genes. In both the species, we found a relatively low number of sex-biased genes (1,284, corresponding to 41.3% of the orthologous genes between the two species), probably due to the absence of sexual dimorphism, and the transcriptional bias is maintained in only 33% of the orthologs. The dN/dS is generally low, indicating purifying selection, with genes where the female-biased transcription is maintained between the two species showing a significantly higher dN/dS . Genes involved in embryo development, cell proliferation, and maintenance of genome stability show a faster sequence evolution. Finally, we report a lack of clear correlation between transcription level and evolutionary rate in these species, in contrast with studies that reported a negative correlation. We discuss such discrepancy and call into question some methodological approaches and rationales generally used in this type of comparative studies.

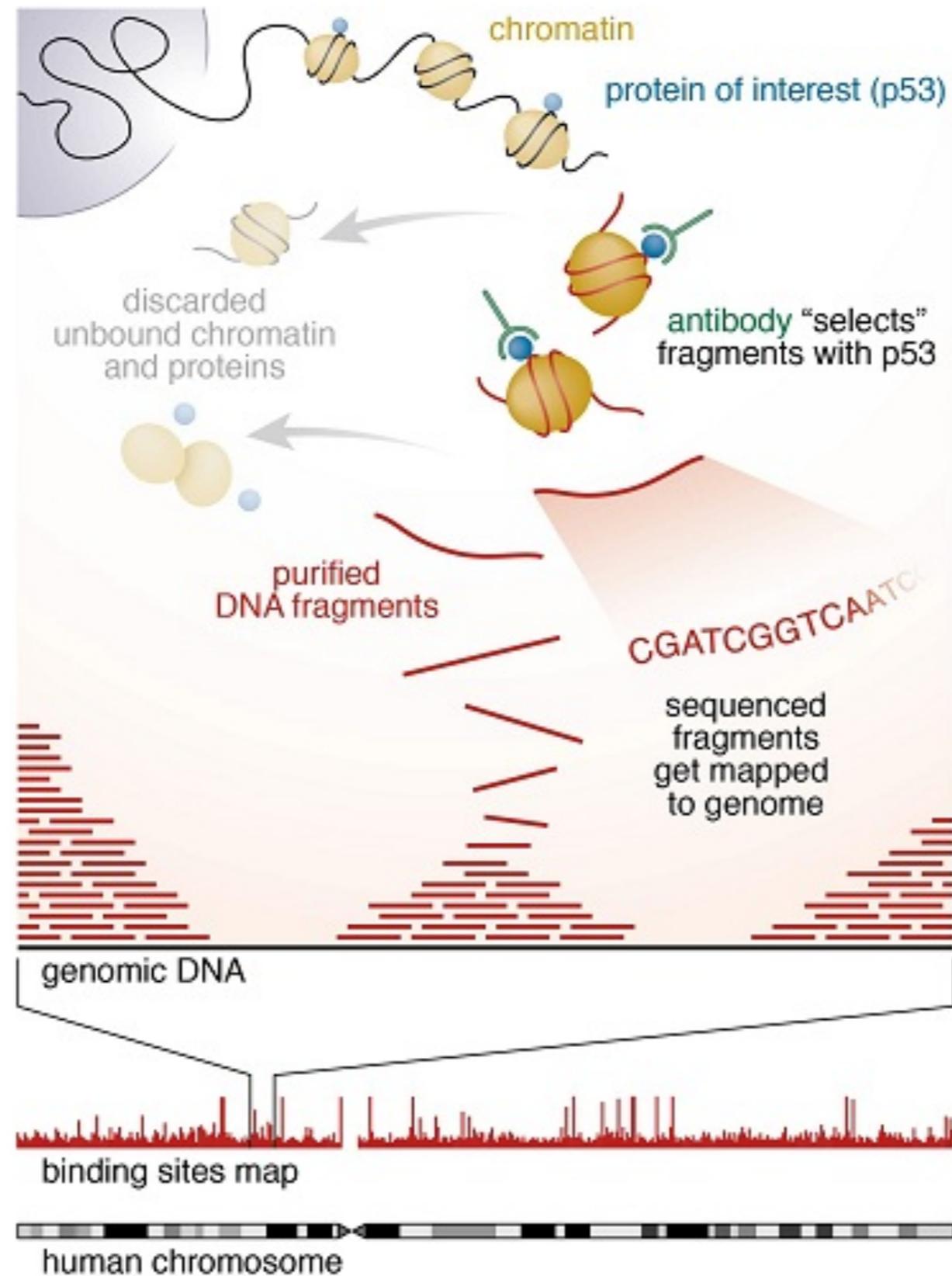
Key words: RNA-Seq, transcription level, evolutionary rate, gametogenesis, embryo development, E-R correlation.



Epigenomics: Bisulfite Sequencing



ChIP-Seq



Comparative Genomics

Compares the genomic features (DNA sequence, genes, gene order, regulatory sequences, and other genomic structural landmarks) of different organisms.

Whole or large parts of genomes resulting from genome projects are compared to study basic biological similarities and differences as well as evolutionary relationships between organisms.

The major principle of comparative genomics is that common features of two organisms will often be encoded within the DNA that is evolutionarily conserved between them.

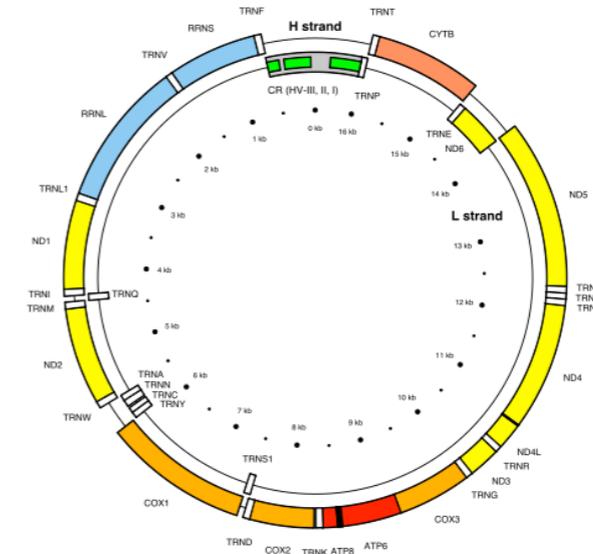
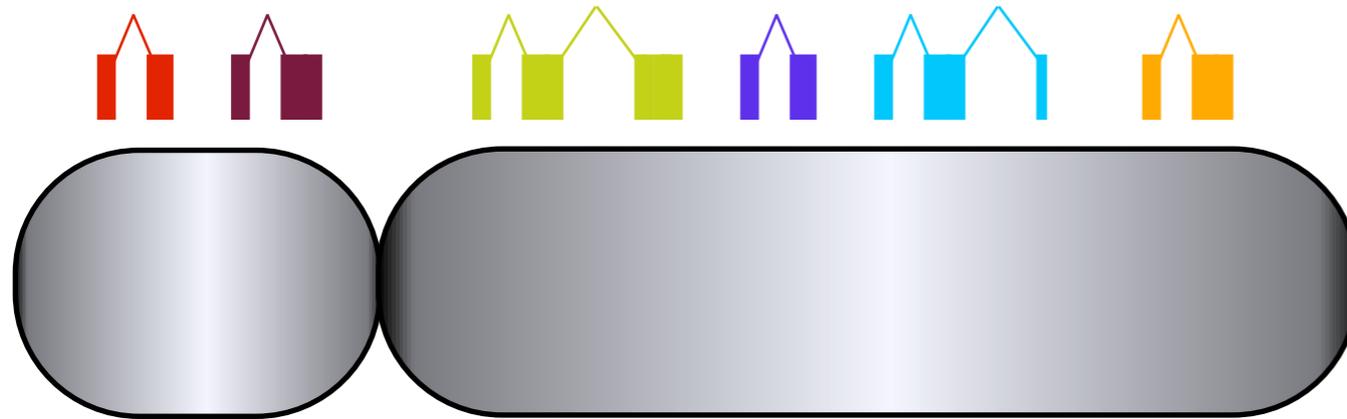
Comparative genomic approaches start with making some form of alignment of genome sequences and looking for orthologous sequences (sequences that share a common ancestry) in the aligned genomes and checking to what extent those sequences are conserved. Based on these, genome and molecular evolution are inferred and this may in turn be put in the context of, for example, phenotypic evolution or population genetics.

Genome anatomy

Genome

(from Wikipedia, the free encyclopedia)

In the fields of [molecular biology](#) and [genetics](#), a genome is all genetic information of an organism.^[1] It consists of nucleotide sequences of [DNA](#) (or [RNA](#) in [RNA viruses](#)). The genome includes both the [genes](#) (the [coding regions](#)) and the [noncoding DNA](#), as well as [mitochondrial DNA](#) and [chloroplast DNA](#).



therefore the genome is plenty of genes...

Genome anatomy

mtDNA

vs

nDNA

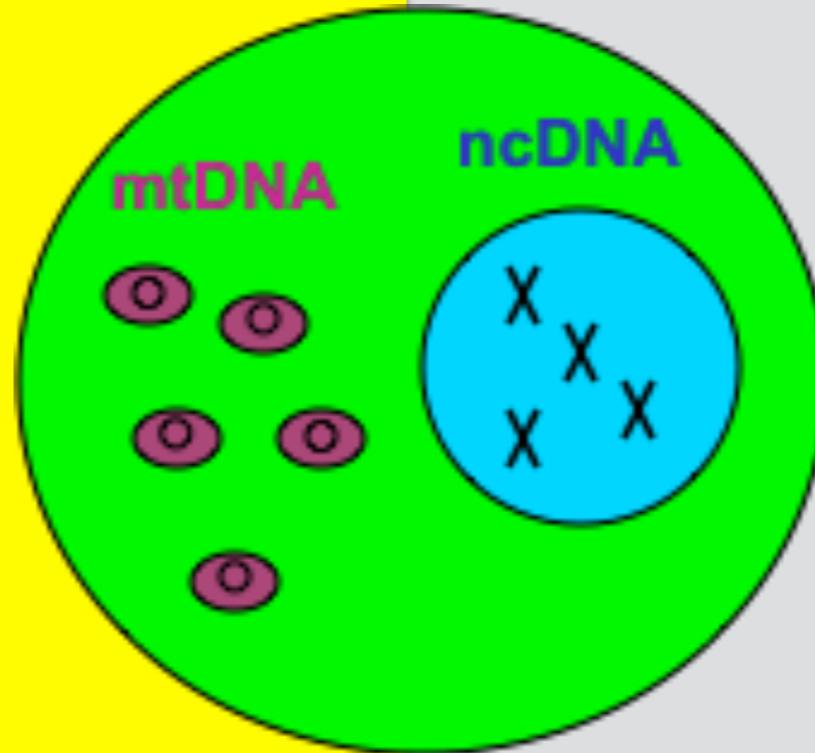
more variable

no recombination (?)

haploid

compact genome
(*obvious orthology*)

half of the story!!!



less variable

recombination

di(n)ploid

a mess!

Genome anatomy

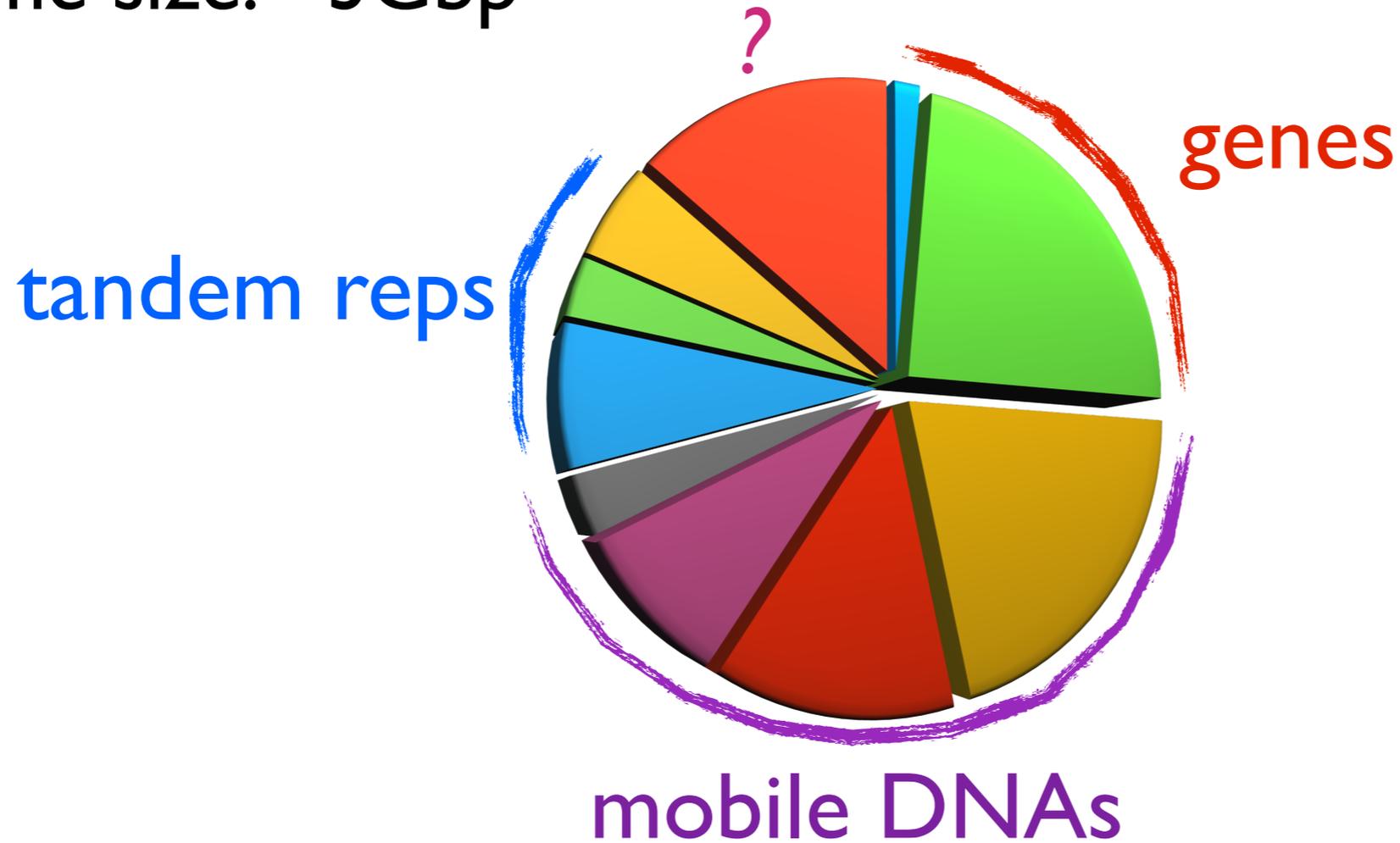
articles

Initial sequencing and analysis of the human genome

International Human Genome Sequencing Consortium*

NATURE | VOL 409 | 15 FEBRUARY 2001 |

genome size: ~3Gbp

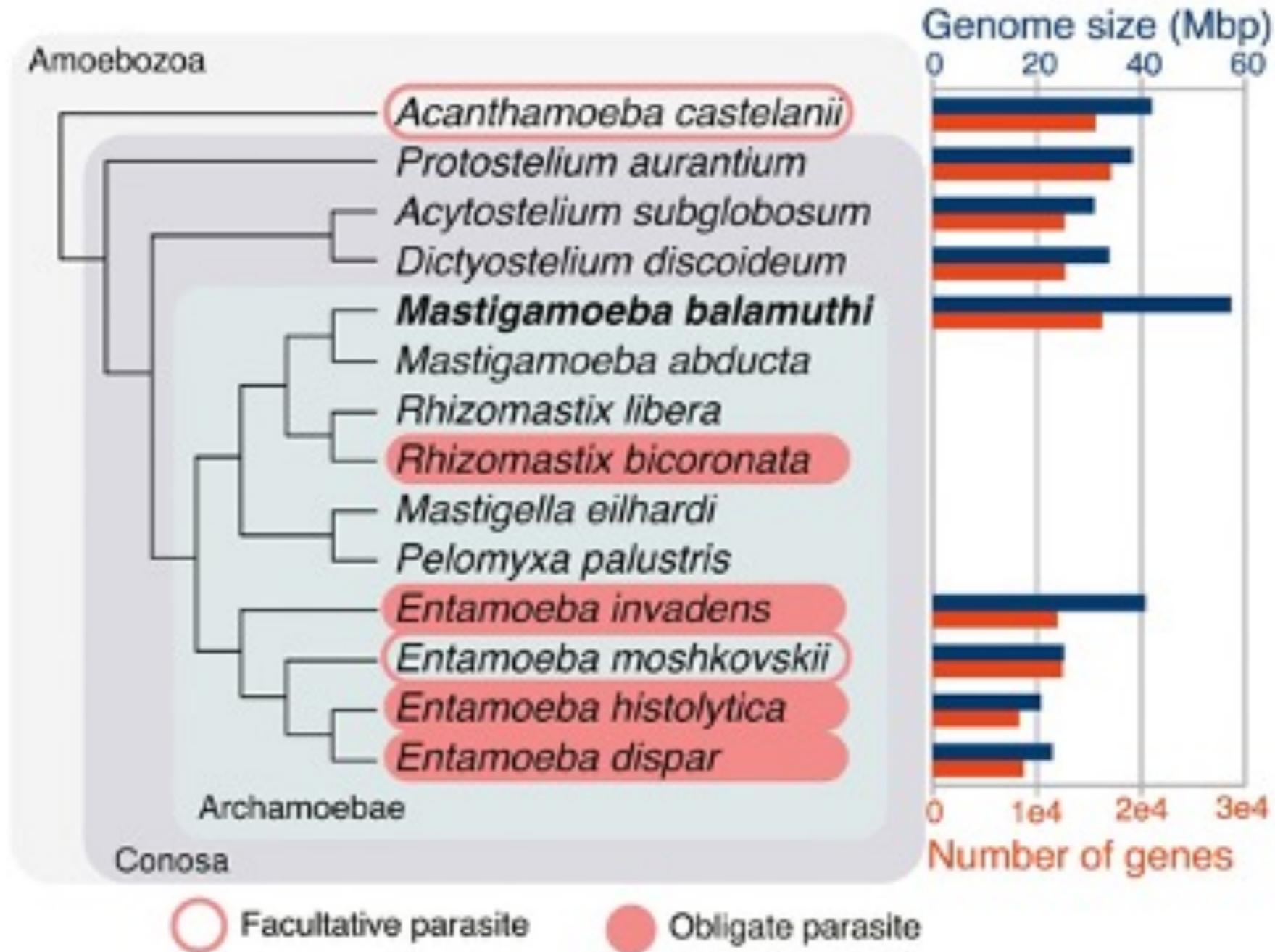


- exon
- reg region
- line
- sine
- LTR
- DNA
- sat
- msat
- segm dupl
- other

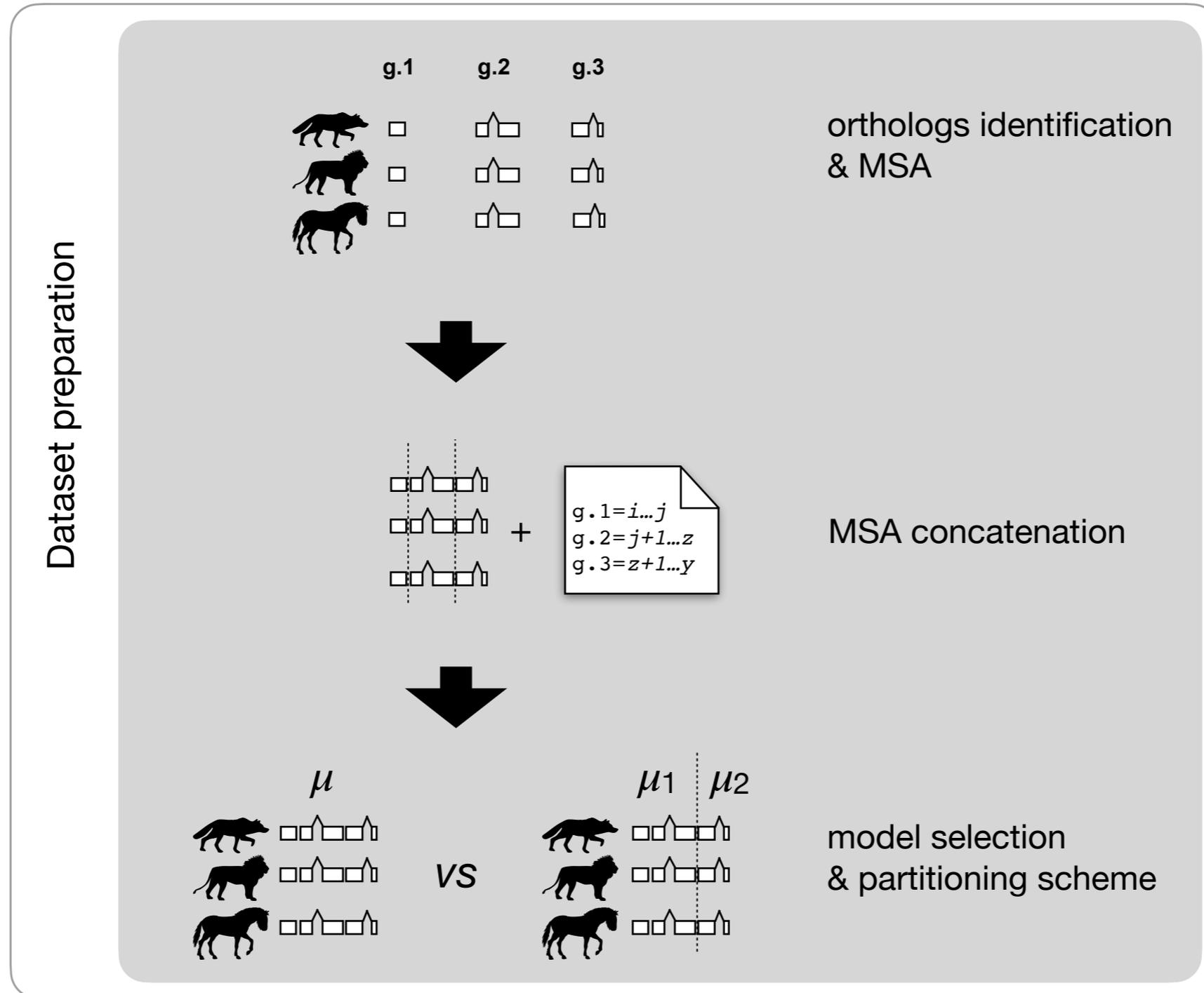
Genome anatomy

Assembly size	811,852,226 bp
Number of scaffold (N50)	63,275 (30,597 bp)
Number of contigs (N50)	135,150 (10,077 bp)
Mapping rate	98%
k-mer completeness	97%
G+C content	39.6%
BUSCO (N=1,013)	C:84.2%[S:83.1%,D:1.1%],F:12.9%,M:2.9%
N. of predicted genes	17.407
N. of highly supported genes (AED < 0.5)	16.535
Proportion of repeats coverage	44.53%
LINE	13.12%
SINE	9.96%
LTR	4.33%
DNA	12.67%
MITE	3.74%

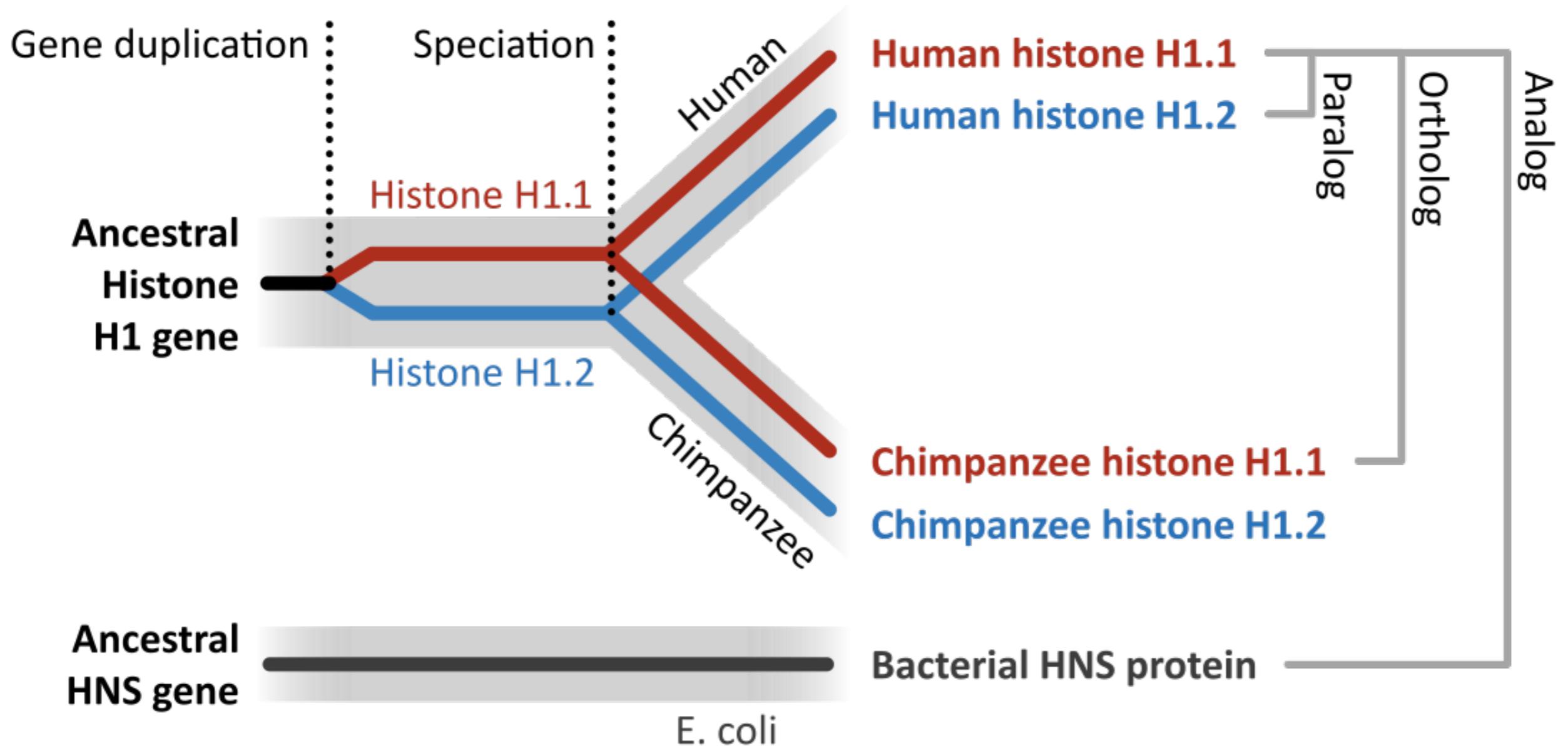
Gene contribution to genome size



Comparing gene evolution across species *finding orthologs*



Types of Homology



"The Ortholog Conjecture"

According to the "ortholog conjecture", or standard model of phylogenomics, protein function changes rapidly after duplication, leading to paralogs with different functions, while *orthologs retain the ancestral function*

OPEN ACCESS Freely available online

PLoS COMPUTATIONAL BIOLOGY

Resolving the Ortholog Conjecture: Orthologs Tend to Be Weakly, but Significantly, More Similar in Function than Paralogs

Adrian M. Altenhoff^{1,2}, Romain A. Studer^{2,3,4}, Marc Robinson-Rechavi^{2,3}, Christophe Dessimoz^{1,2,5*}

1 ETH Zurich, Department of Computer Science, Zürich, Switzerland, **2** Swiss Institute of Bioinformatics, Lausanne, Switzerland, **3** Department of Ecology and Evolution, University of Lausanne, Lausanne, Switzerland, **4** Institute of Structural and Molecular Biology, Division of Biosciences, University College London, London, United Kingdom, **5** EMBL-European Bioinformatics Institute, Hinxton, Cambridge, United Kingdom

Abstract

The function of most proteins is not determined experimentally, but is extrapolated from homologs. According to the "ortholog conjecture", or standard model of phylogenomics, protein function changes rapidly after duplication, leading to paralogs with different functions, while orthologs retain the ancestral function. We report here that a comparison of experimentally supported functional annotations among homologs from 13 genomes mostly supports this model. We show that to analyze GO annotation effectively, several confounding factors need to be controlled: authorship bias, variation of GO term frequency among species, variation of background similarity among species pairs, and propagated annotation bias. After controlling for these biases, we observe that orthologs have generally more similar functional annotations than paralogs. This is especially strong for sub-cellular localization. We observe only a weak decrease in functional similarity with increasing sequence divergence. These findings hold over a large diversity of species; notably orthologs from model organisms such as *E. coli*, yeast or mouse have conserved function with human proteins.

Citation: Altenhoff AM, Studer RA, Robinson-Rechavi M, Dessimoz C (2012) Resolving the Ortholog Conjecture: Orthologs Tend to Be Weakly, but Significantly, More Similar in Function than Paralogs. PLoS Comput Biol 8(5): e1002514. doi:10.1371/journal.pcbi.1002514

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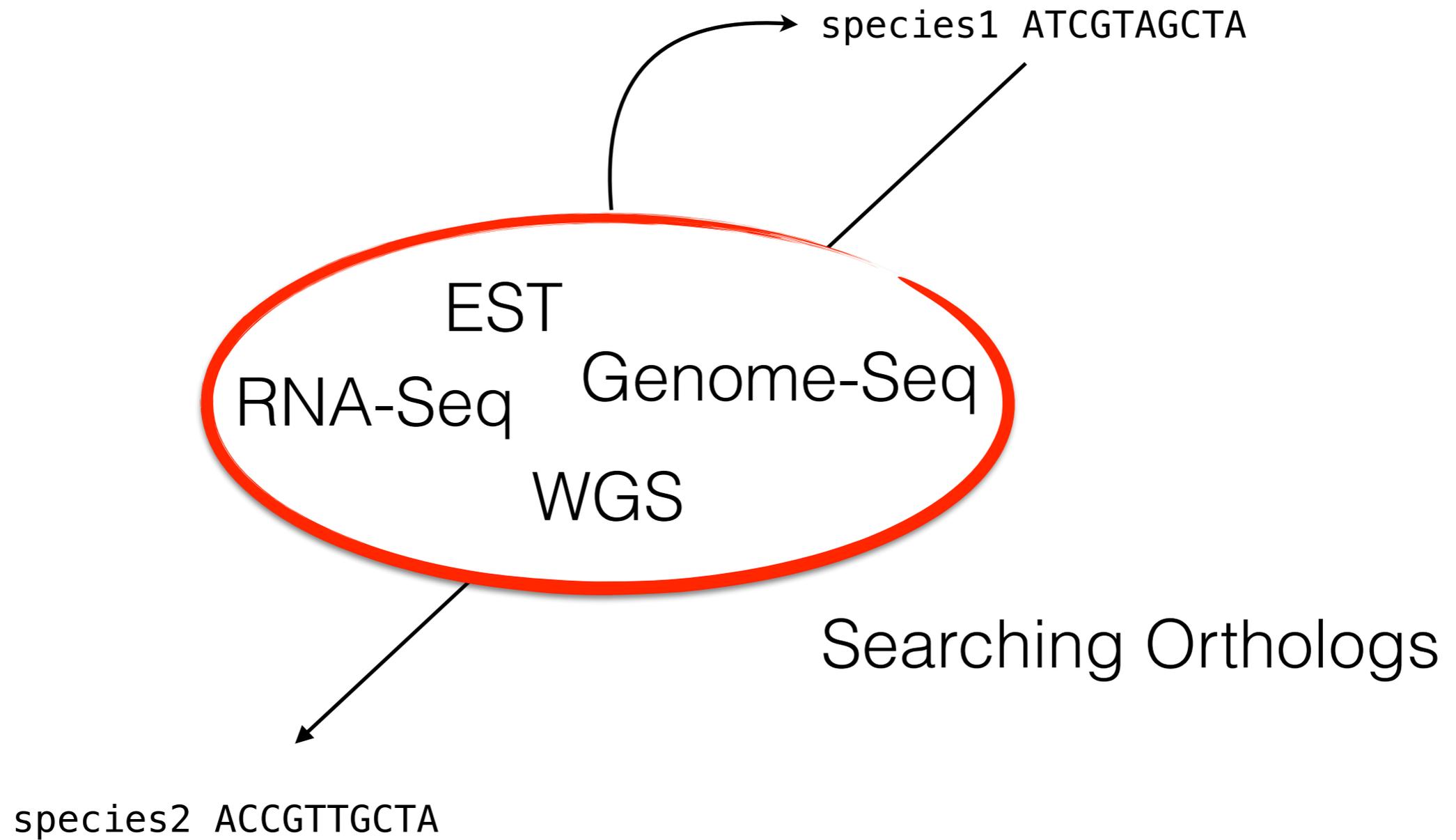
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Funding: RAS acknowledges funding from the Fondation du 450^{ème} anniversaire de l'Université de Lausanne and Swiss National Science Foundation grants 132476 and 136477. MR-R acknowledges funding from Etat de Vaud and Swiss National Science Foundation grant 133011. CD is supported by a fellowship from the Swiss National Science Foundation (grant 136461). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

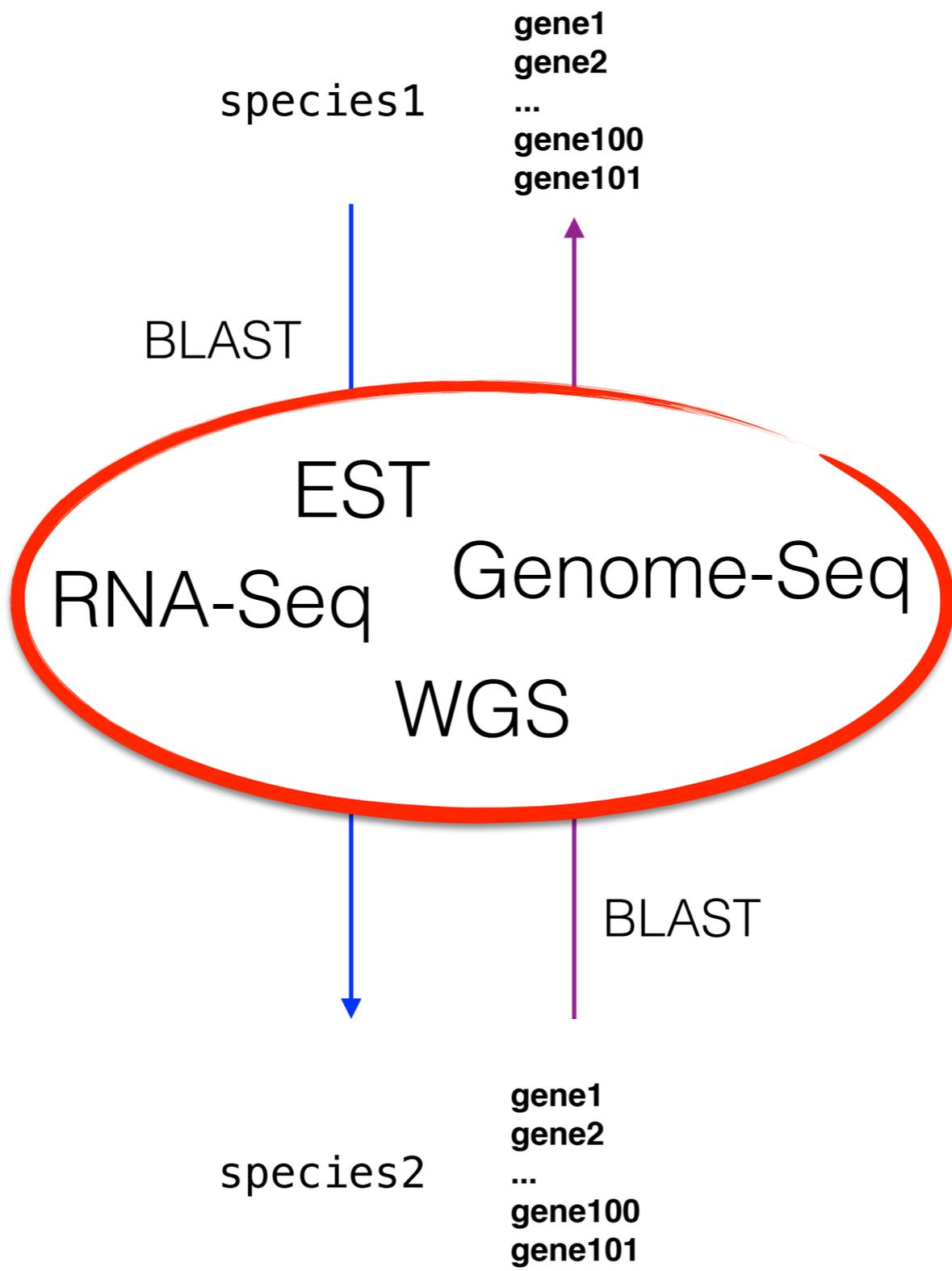
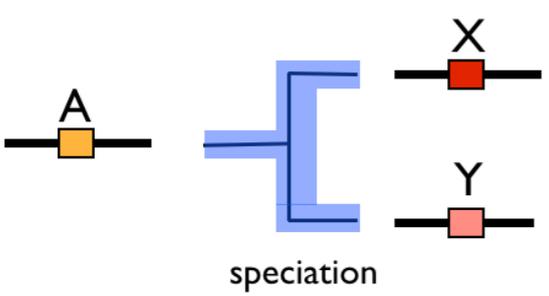
Competing Interests: The authors have declared that no competing interests exist.

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Genomic resources



Searching Orthologs



The simplest way:
reciprocal BLAST hit

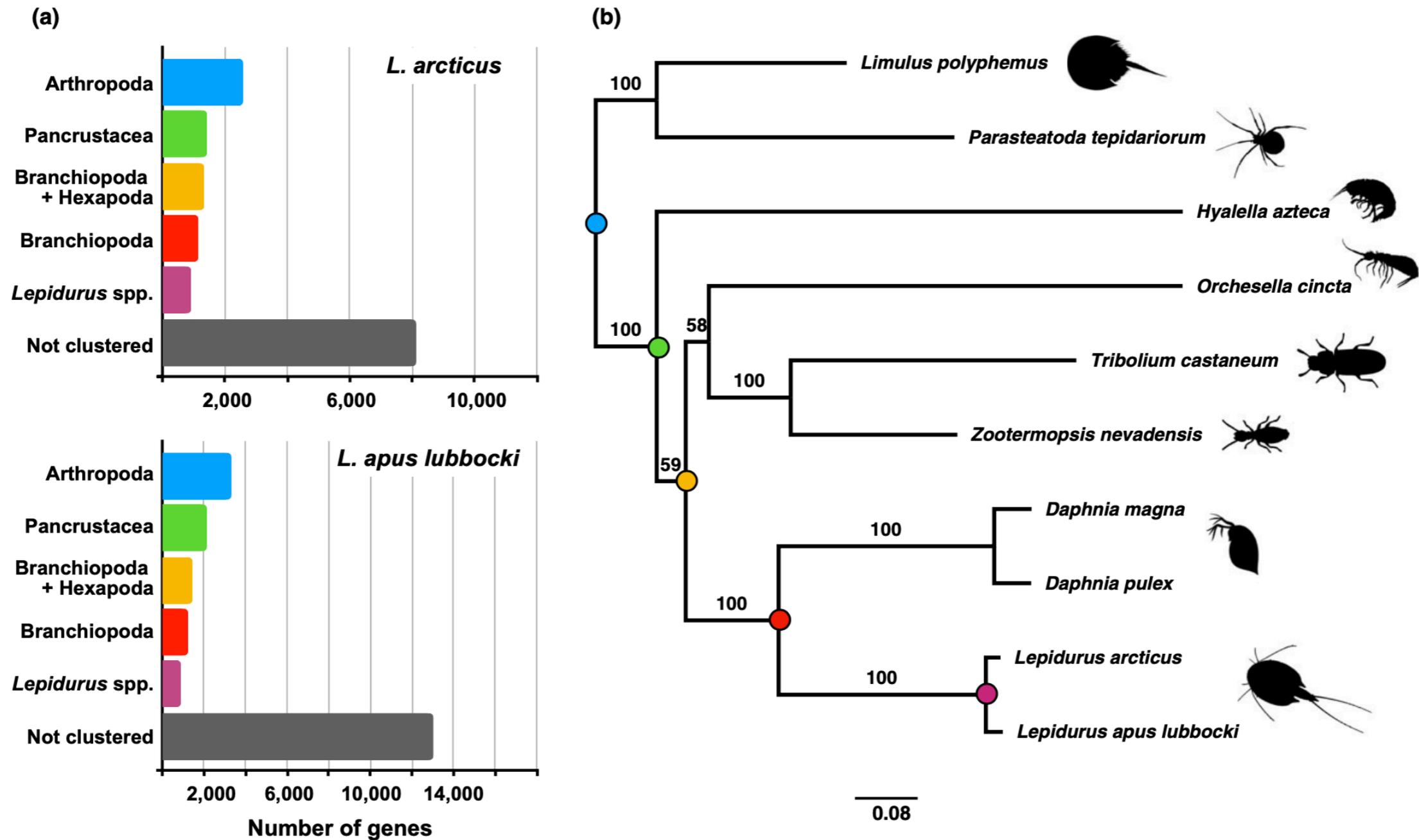
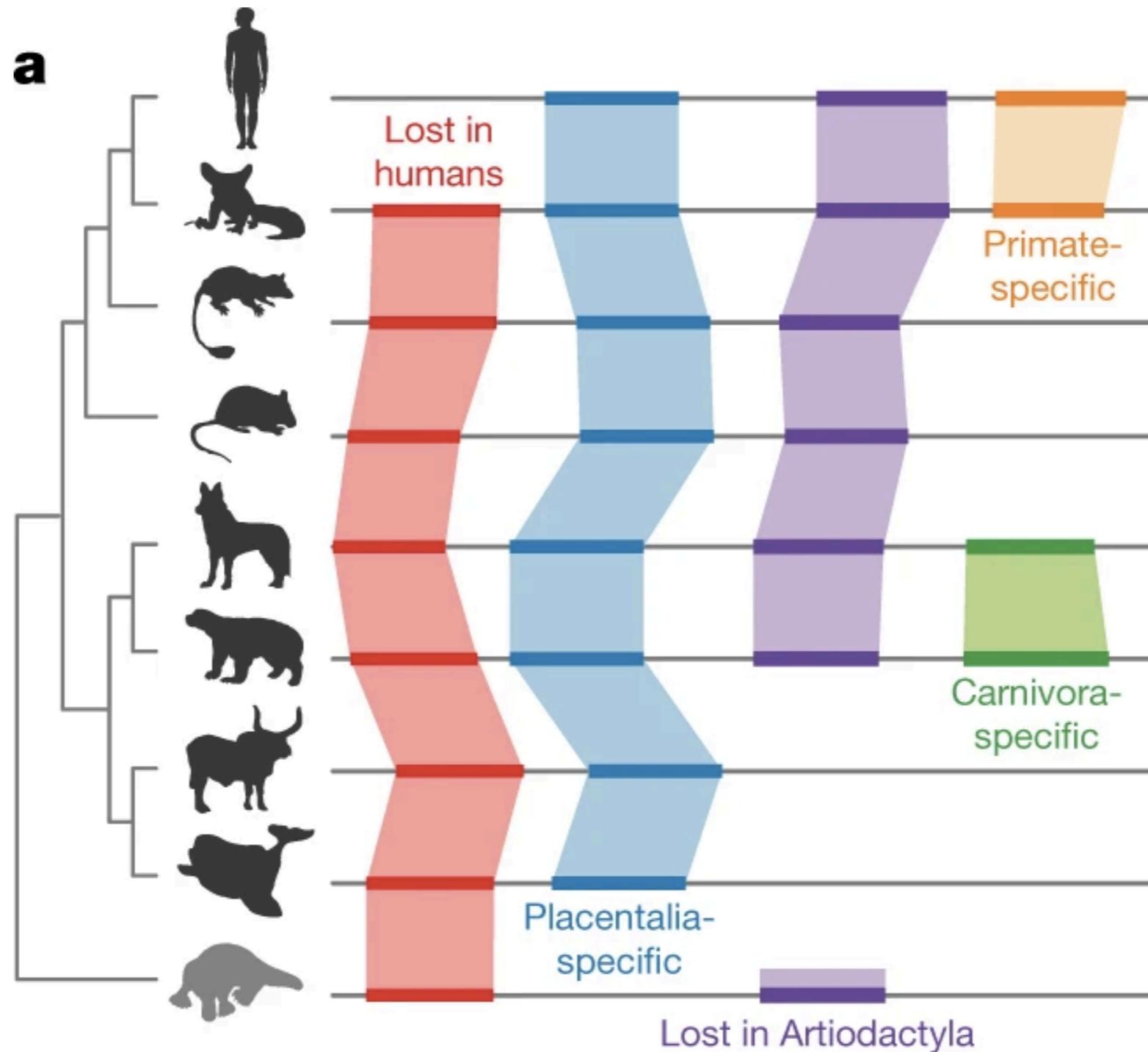
Draft genomes and genomic divergence of two *Lepidurus* tadpole shrimp species (Crustacea, Branchiopoda, Notostraca)Castrense Savojardo^{1,†} | Andrea Luchetti^{2,†}  | Pier Luigi Martelli¹ | Rita Casadio¹ | Barbara Mantovani²

FIGURE 2 Orthologous gene analysis. (a) Taxonomic distribution of orthologous genes. (b) Maximum-likelihood tree ($-\ln L = 1,502,204.92$) built on 432 orthologous proteins. The colour of squares at nodes corresponds to the taxonomic colour codes of the bins in the panel (a) bar plots; numbers above branches indicate bootstrap values [Colour figure can be viewed at wileyonlinelibrary.com]

Genes stratigraphy

Exploring the distribution of orthologs across lineages

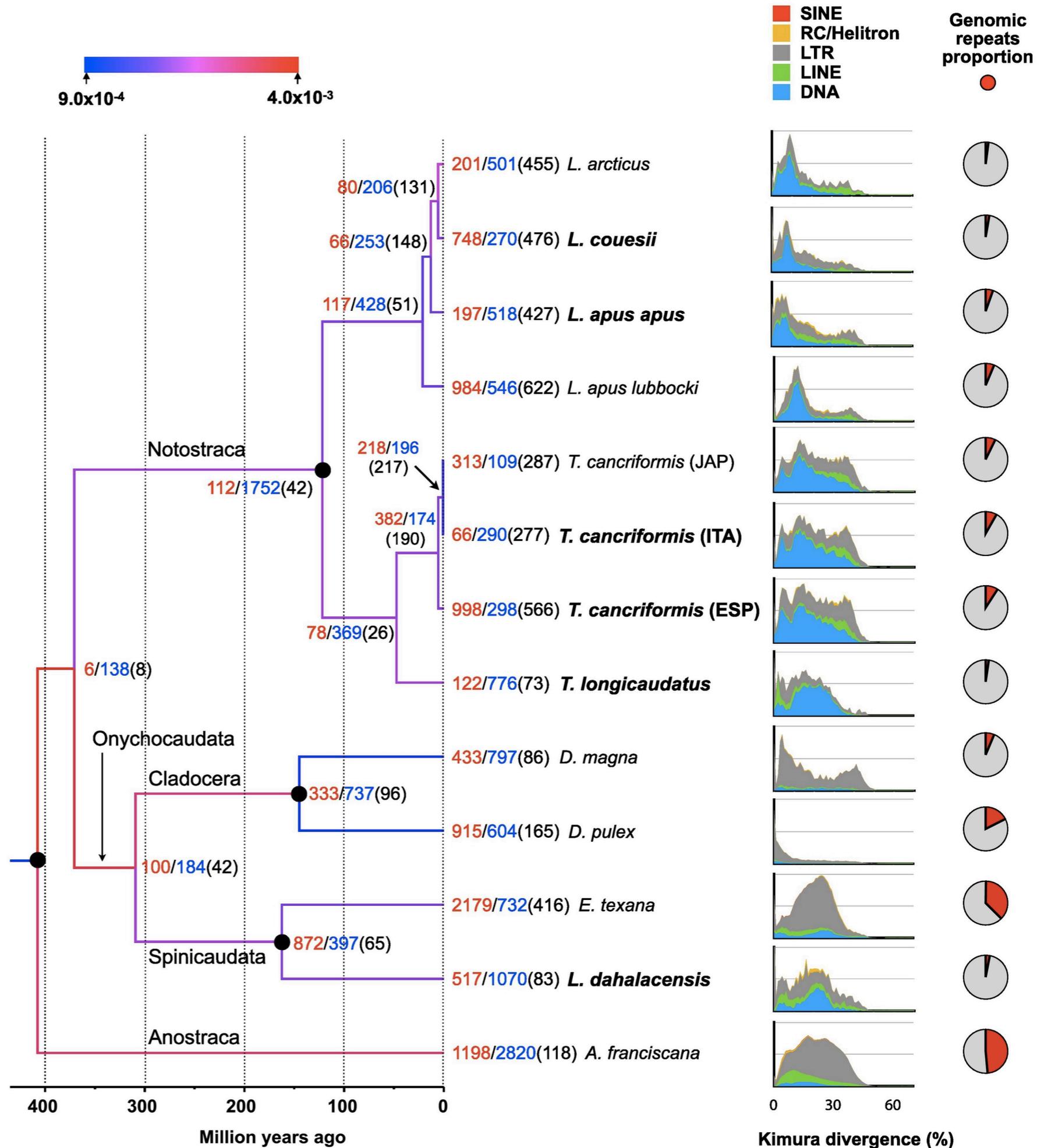


Gene families

evolution

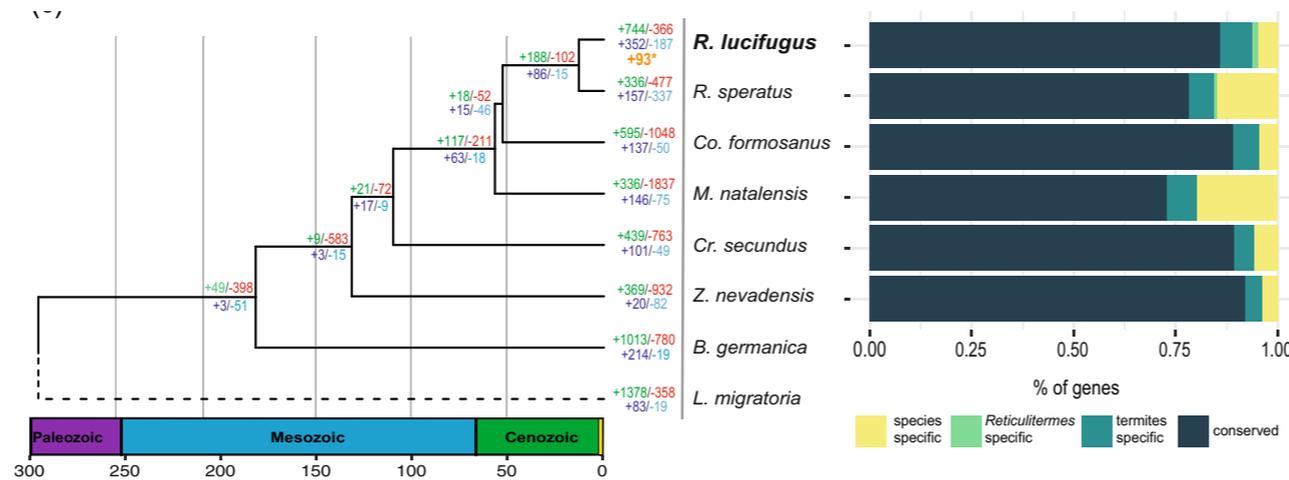
Gene families are groups of genes descended from a common ancestor that retain similar sequences and often similar functions.

exploring contractions and expansions of gene families

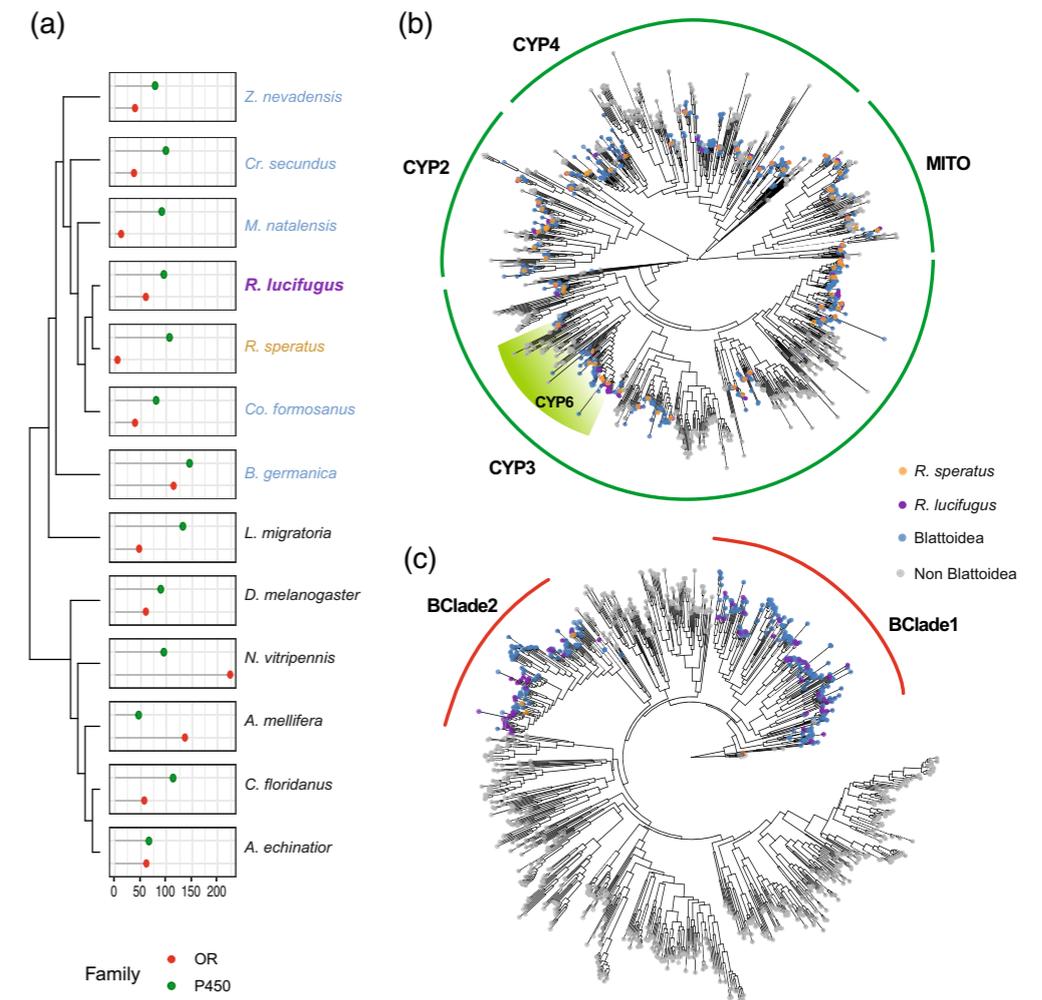
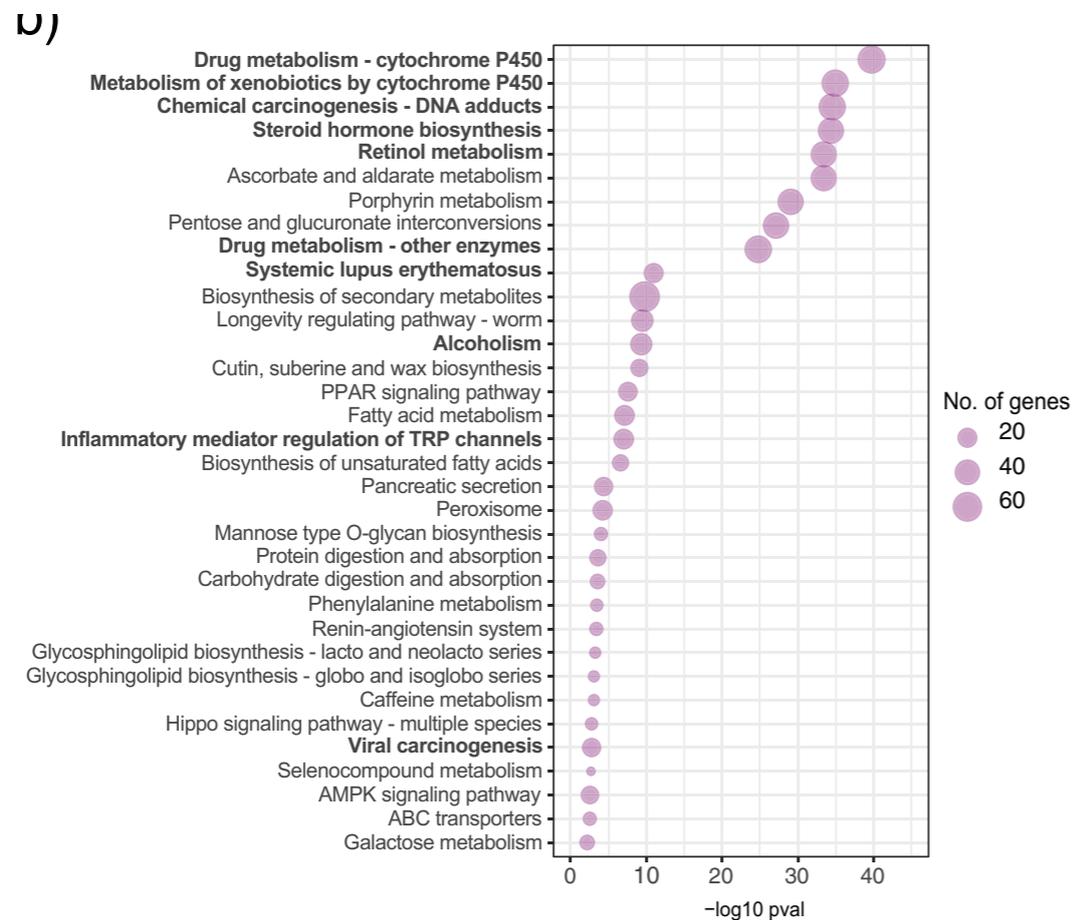


Gene families evolution

Comparative analysis across termite species



genes & gene families evolution

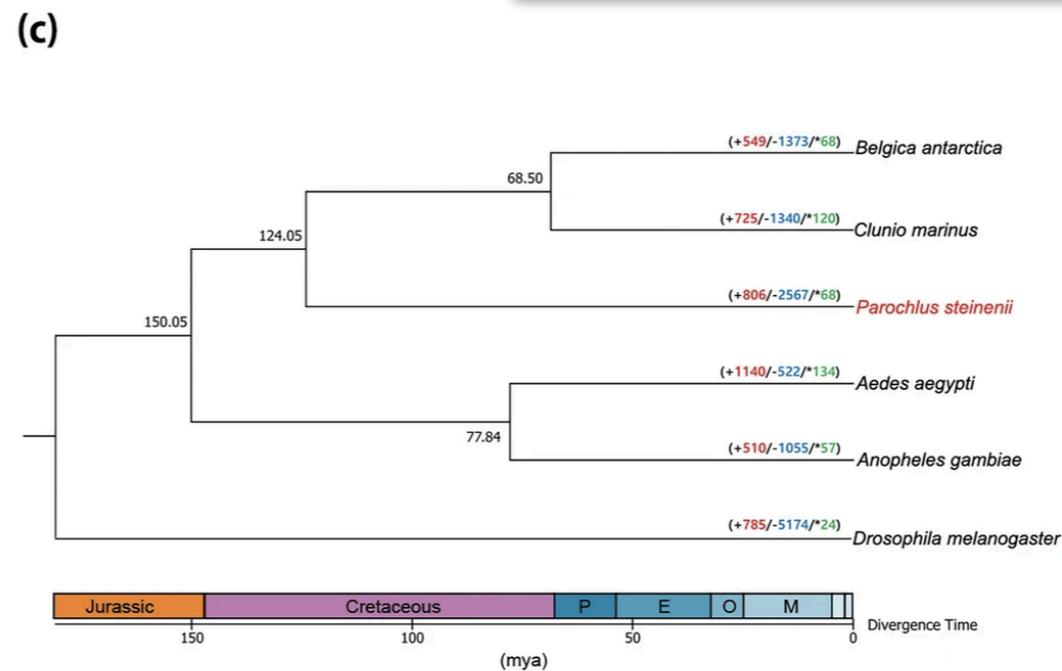
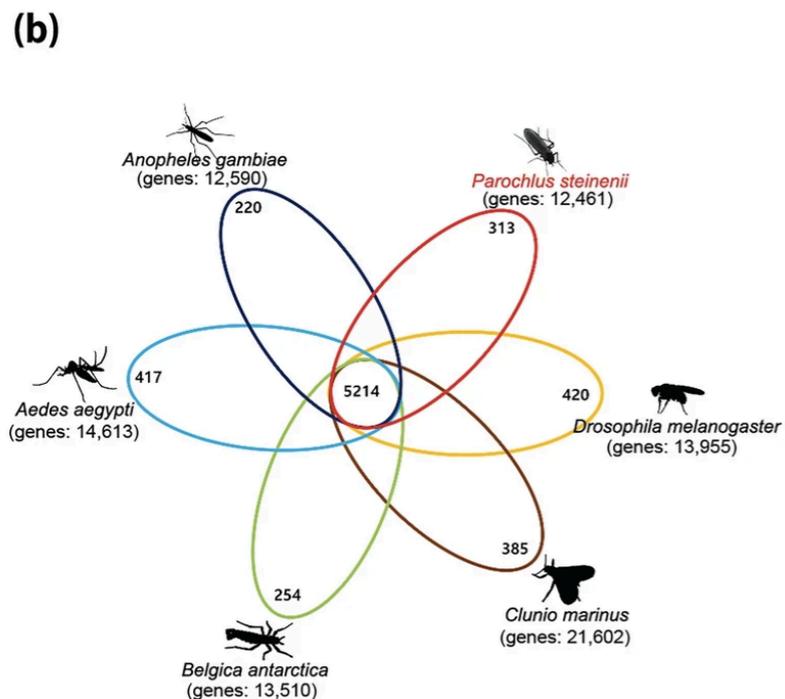
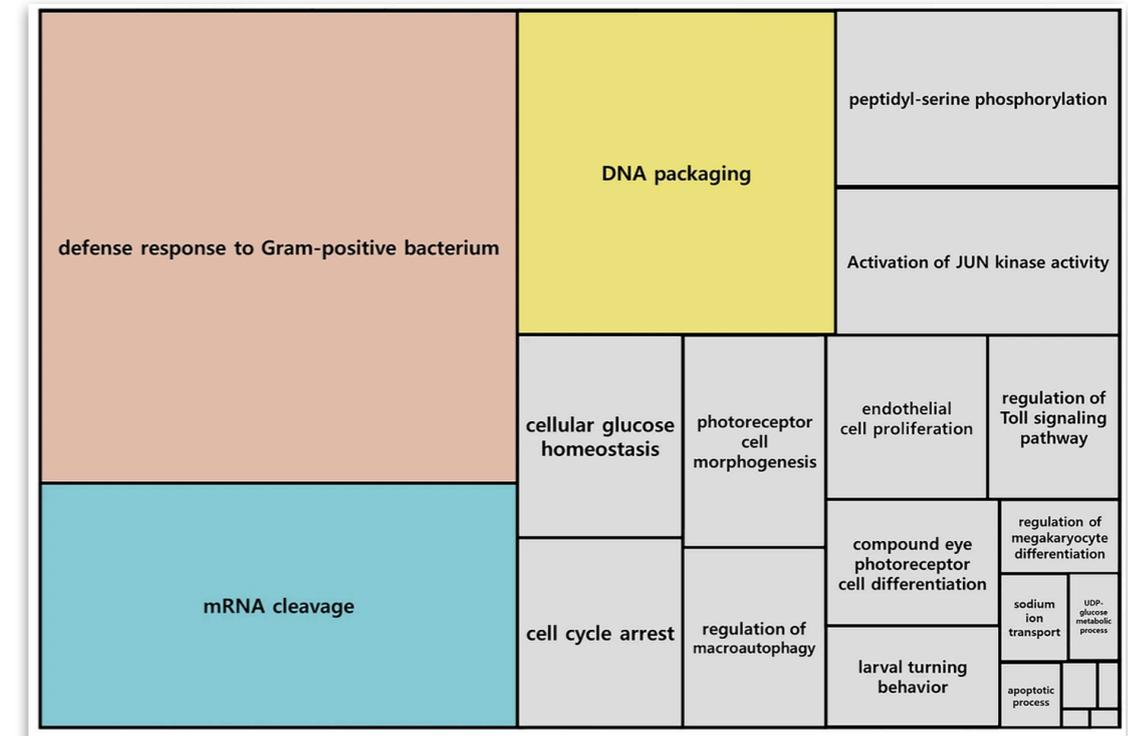
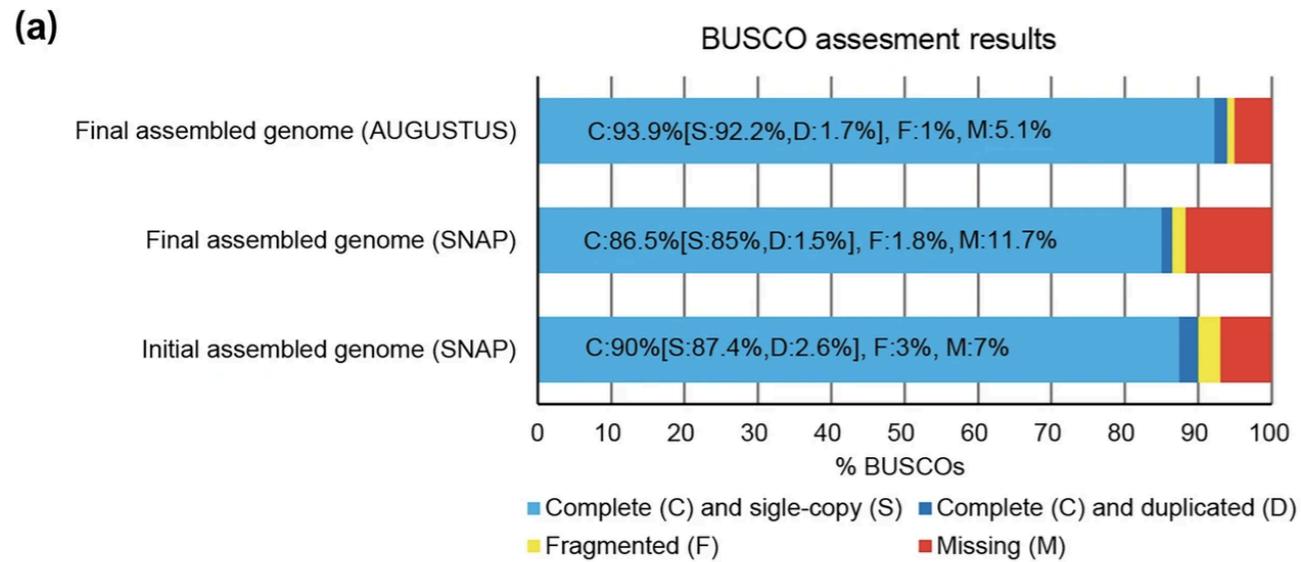


functional annotation of expanded families

detailed analysis of OR and P450 families

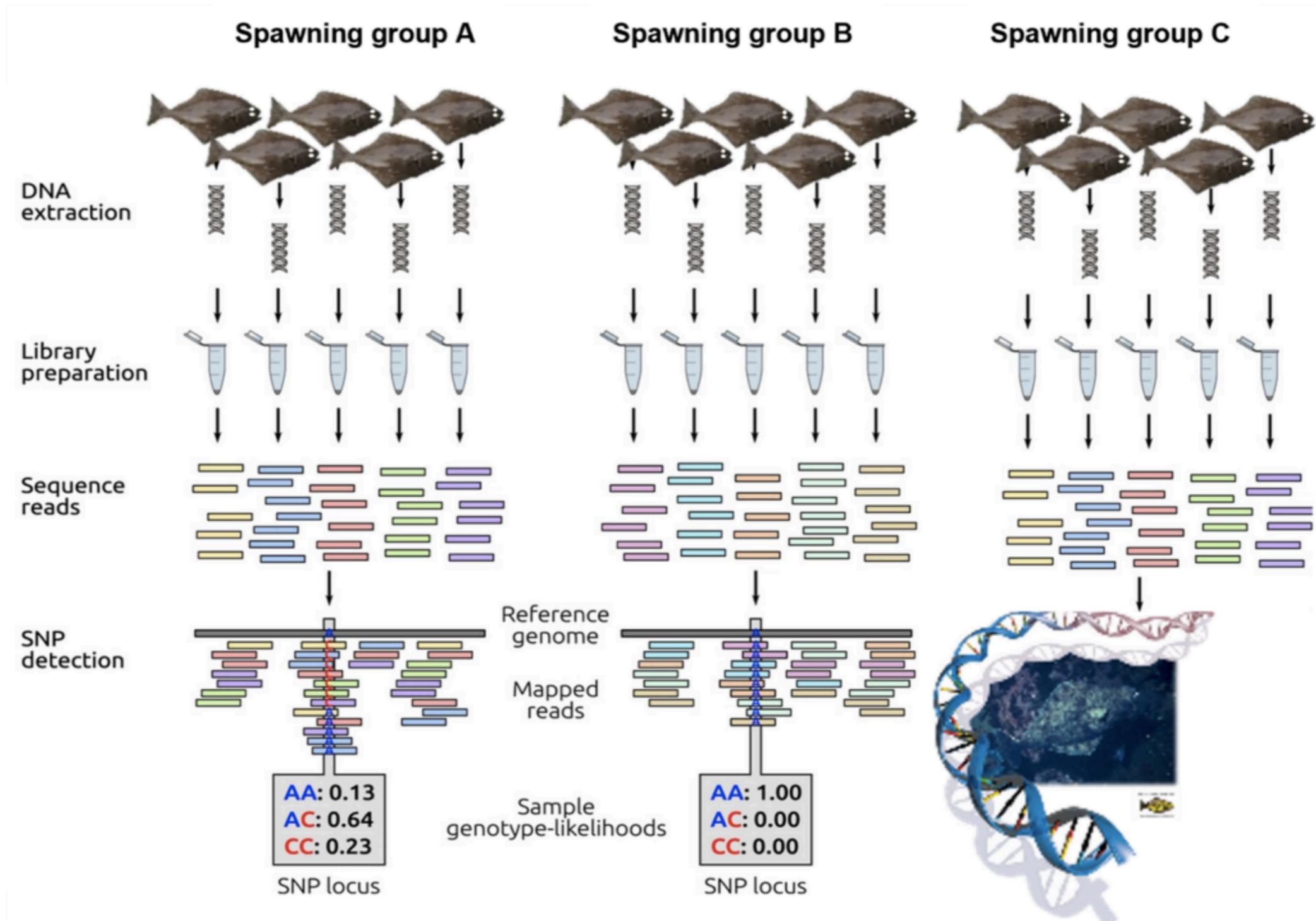
Gene families evolution

Comparative analysis of a cold-adapted dipteran

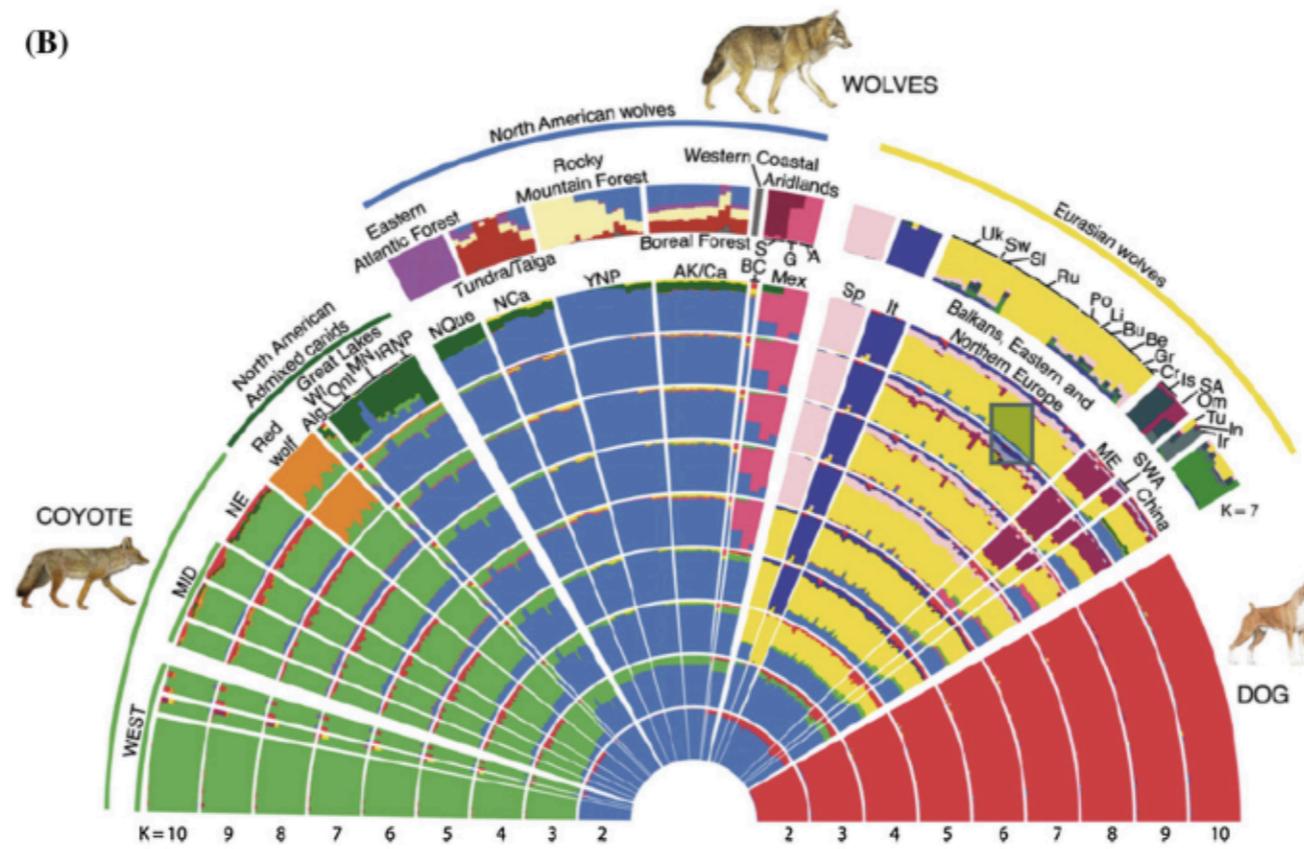
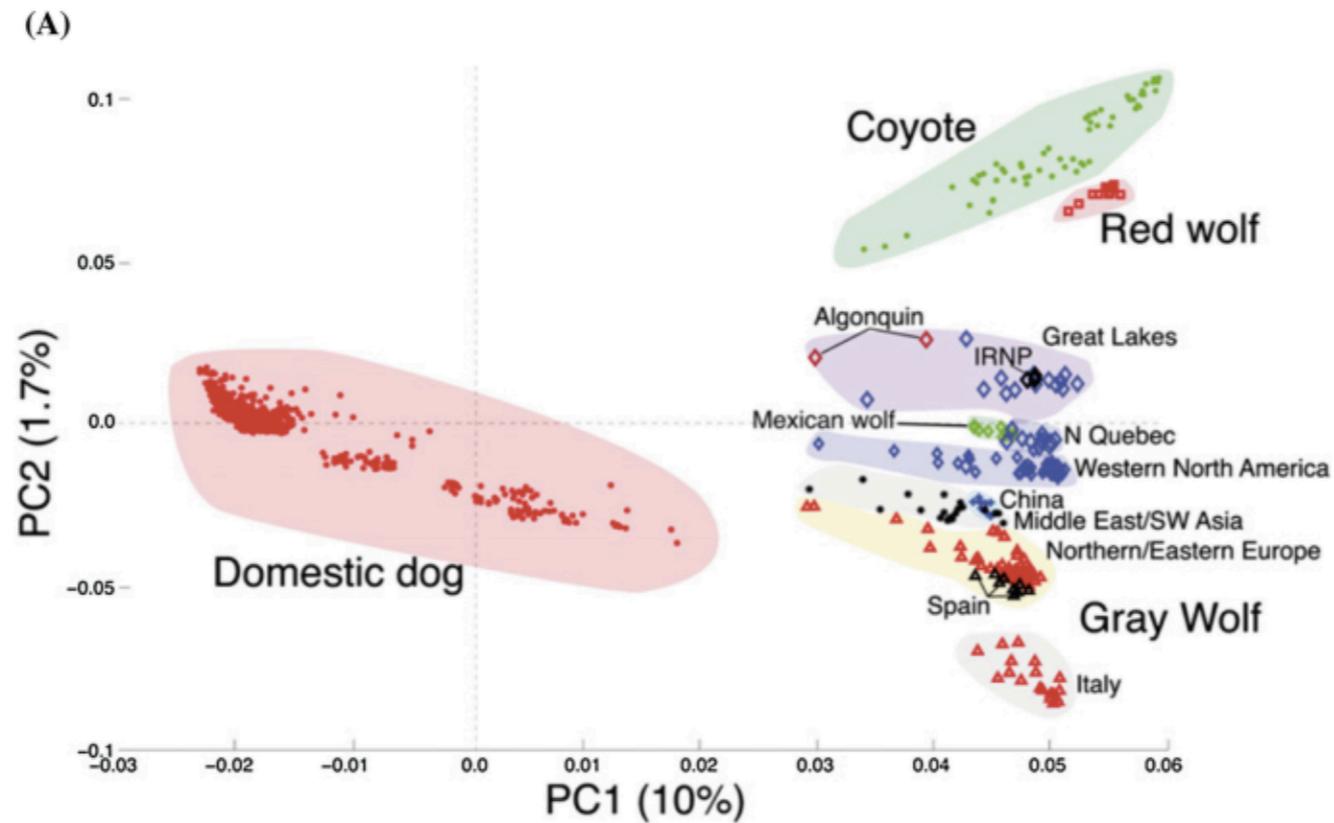


Population genomics

Short reads mapping on a reference genome



Population genomics



finding
divergence,
gene flow and
hybridization

Writing a small project

1. Biological question (organism evolution/divergence; biological process; etc)
2. Biological system (organism-s) & sampling strategy
3. Genomic approach (de novo assembly & compGen; reads mapping & popGen)
4. Expected results