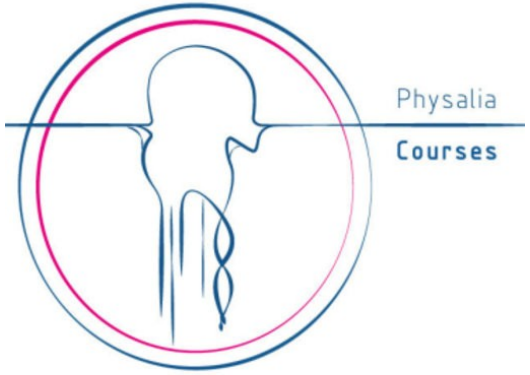

Adaptation Genomics Course

Anna Tigano, Ph.D. & Claire Mérot, Ph.D. & Yann Dorant , Ph.D.

June 26- 30, 2023

Claire Mérot

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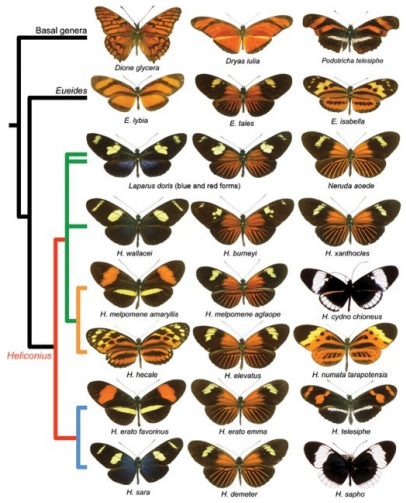
http://www.normalesup.org/~cmerot/index_en.html



Speciation in *Heliconius* butterflies

Mimicry

Evolution

Ecology

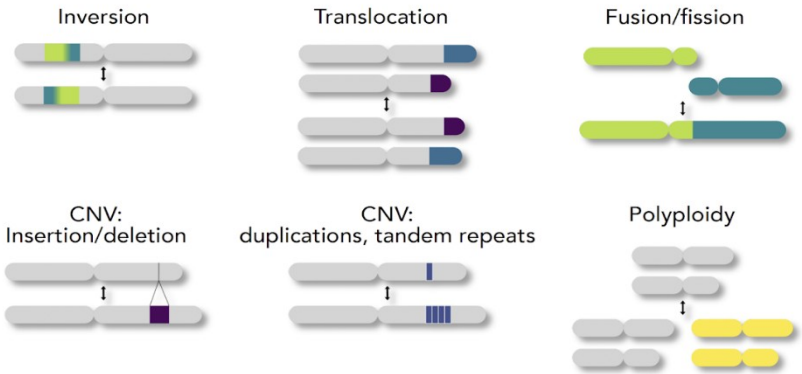
The evolution of biological diversity

Genomic

Environmental adaptation

Inversion polymorphism in *Coelopa frigida* seaweed flies

Structural Variants



LEMAR laboratoire des sciences de l'environnement marin UBO | CNRS | IRD | Ifremer

iuem INSTITUT UNIVERSITAIRE EUROPÉEN DE LA MER

Yann Dorant, Ph.D

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- Population genetic structure
- Genome architecture and adaptation to environment
- Seascape genomics
- Transcriptomics and functional genomics
- Genomics for fisheries and aquaculture
- Linkage map and genome assembly

UBC OKANAGAN

Anna Tigano, Ph.D

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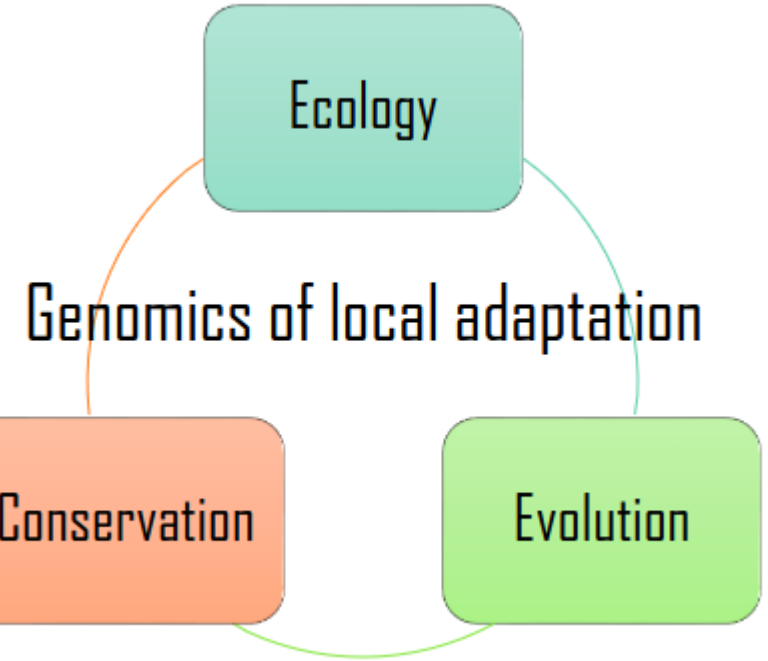


- Genomics of local adaptation with and without gene flow
- Genomic basis and architecture of adaptive traits
- Adaptation to extreme environments
- Structural variation and adaptation
- Conservation genomics

Claire **Yann** **Anna**

Schedule

CET (Europe)	PST (West America)	Monday	Tuesday	Wednesday	Thursday	Friday
14:30-17h	5h30-8h	Introduction/ Practical 1	Lecture 2-1/ Practical 2	Lecture 3-1/ Practical 3	Lecture 4-1/ Practical 4	Lecture 5-1/ Practical 5
		Break	Break	Break	Break	Break
18h-20h30	9h-11h30	Lecture 1-2/ Practical 2	Lecture 2-2/ Practical 2	Lecture 3-2/ Practical 3	Lecture 4-2/ Practical 4	Lecture 5-2/ Q&A

The instructors will take a break between the two periods but otherwise be available for questions and support (depending on time zone)
You are welcome to work at your own pace and when it’s most convenient to you

You have access to the AWS server from 12:30 to 22:30 (CET)
*** In case of particular needs ask @Carlo for a time extension ***

Outline of the course

Day 1

Intro to adaptation genomics

Bioinformatics and sequencing approaches

Population genomics for adaptation

Practical

Connect to the server

From raw data to variant calling

Outline of the course

Day 2

Population structure as a confounding factor

Genomic signatures of selection

Practical

Genetic diversity, population differentiation and structure

Outline of the course

Day 3

Outlier analyses and genotype-environment associations

Confounding factors of signatures of selection

Practical

Outlier analyses and genotype-environment associations

Outline of the course

Day 4

Detecting structural variation

Evolutionary significance of structural variation

Practical

Analysis of haploblocks

Analysis of structural variants

Outline of the course

Day 5

Other methods to study the genomics of adaptation

Validation of candidate loci

Practical

Functional annotation of candidate loci for adaptation

Q & A

THE END!

Objectives

To get you familiar with bioinformatics, sequencing and analytical methods through the integration of *theory and empirical examples* to select the most appropriate approach to study the genomics of **adaptation** in your species of interest.

Adaptation genomics

The main goal of adaptation genomics is to understand the genomic basis and architecture of adaptive traits

Adaptation genomics

The main goal of adaptation genomics is to understand the genomic basis and architecture of adaptive traits

- Genetic basis of traits = loci that control the adaptive trait
- Genetic architecture = the interactions among alleles (dominance, epistasis, pleiotropy, polygeny)
- Genomic architecture = position of alleles and structural variants associated

Adaptation genomics

The main goal of adaptation genomics is to understand the genomic basis and architecture of adaptive traits

Ecology

Often local adaptations are not apparent, and we use a top-down approach to understand what species/populations are adapted to

Adaptation genomics

The main goal of adaptation genomics is to understand the genomic basis and architecture of adaptive traits

Ecology

Evolution

By identifying the genes underpinning local adaptation we can gain insights into the process of adaptation and the interplay among evolutionary forces

Adaptation genomics

The main goal of adaptation genomics is to understand the genomic basis and architecture of adaptive traits

Ecology

Evolution

Conservation

Understanding how organisms have adapted in the past can help us predict their potential to future changes in their environment

Adaptation genomics

The main goal of adaptation genomics is to understand the genomic basis and architecture of adaptive traits

Ecology

Evolution

Conservation

Management

Assessment of adaptive differentiation ensures appropriate management of population/species of socio-economic importance (e.g., fish stocks, game species)

Adaptation genomics

The main goal of adaptation genomics is to understand the genomic basis and architecture of adaptive traits

Ecology

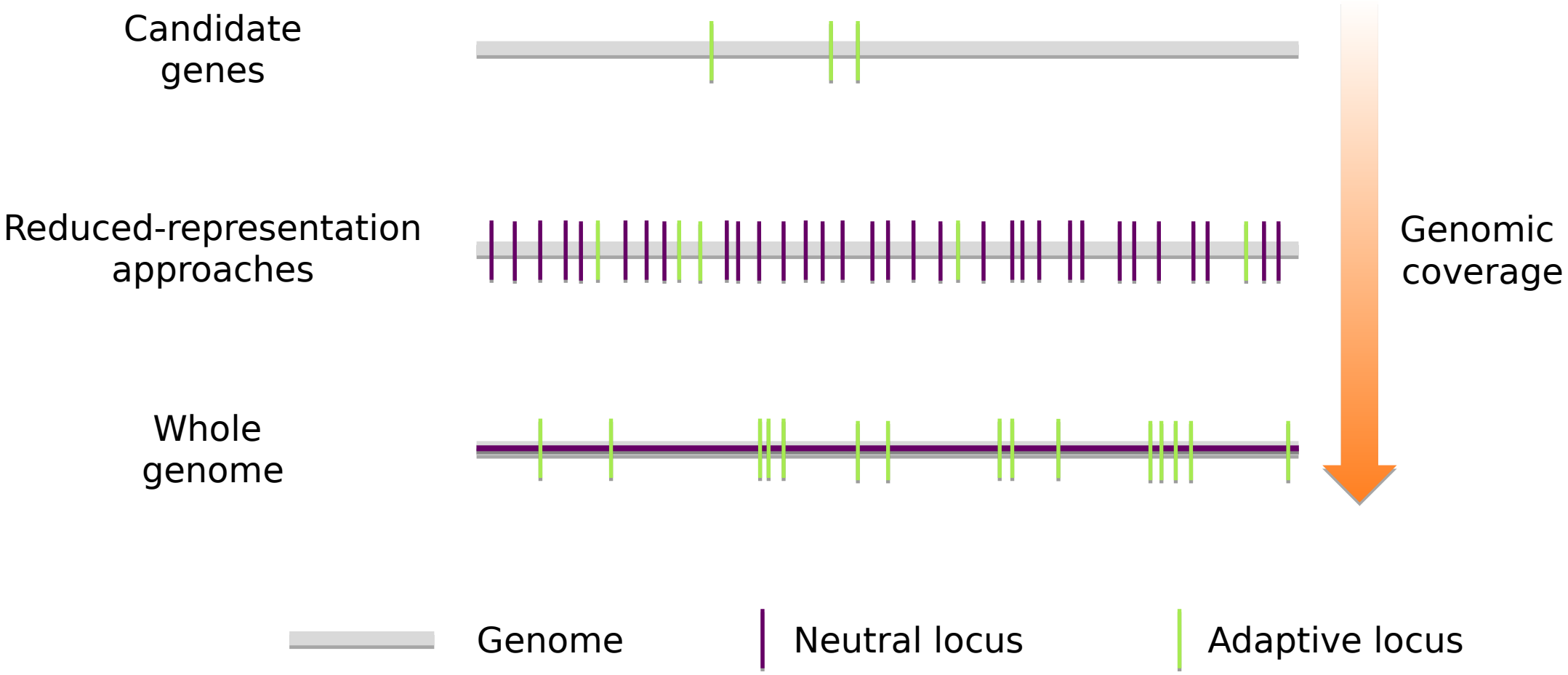
Evolution

Conservation

Management

Physiology, molecular evolution, biodiversity, speciation…

Sequencing approaches



Genetics

Fraction of genome

Sanger sequencing

Genomics

Whole genome re-sequencing

RADtag (Baird 2008)

ddRAD

Phylogeny

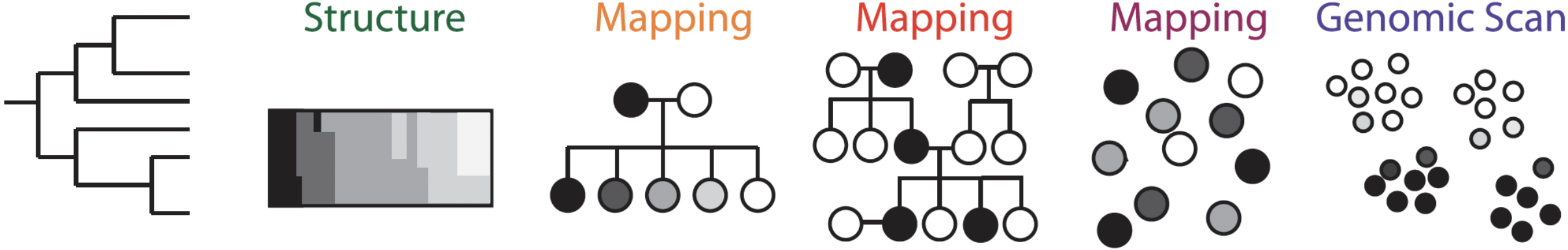
Population Structure

QTL Mapping

Pedigree Mapping

Association Mapping

Population Genomic Scans



Divergence limited

Recombination limited

Linkage Diseq. limited

Peterson et al. 2012, PlosOne

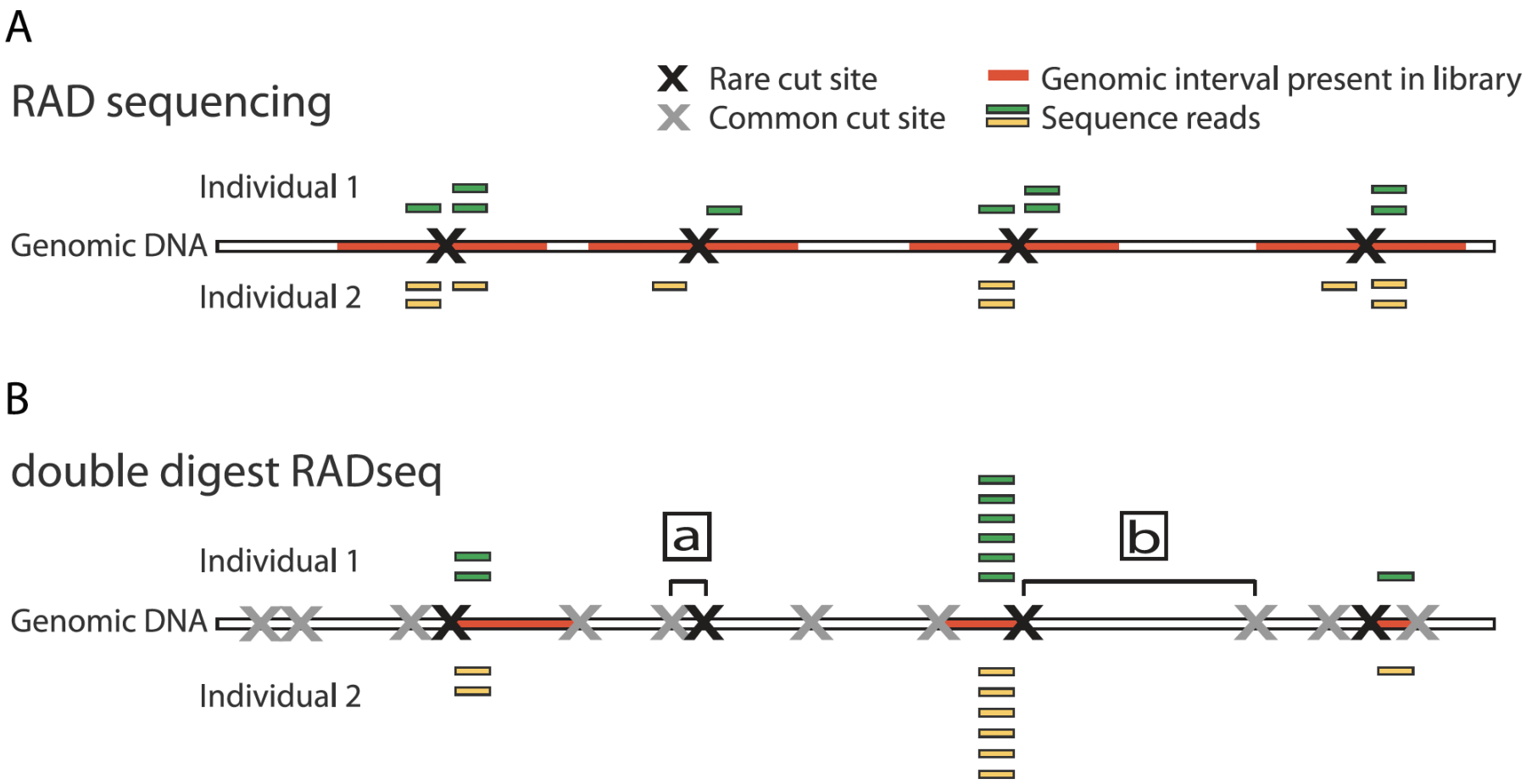
Reduced-representation approaches

- RADseq/GBS
- Exome/exon capture
- SNP chip

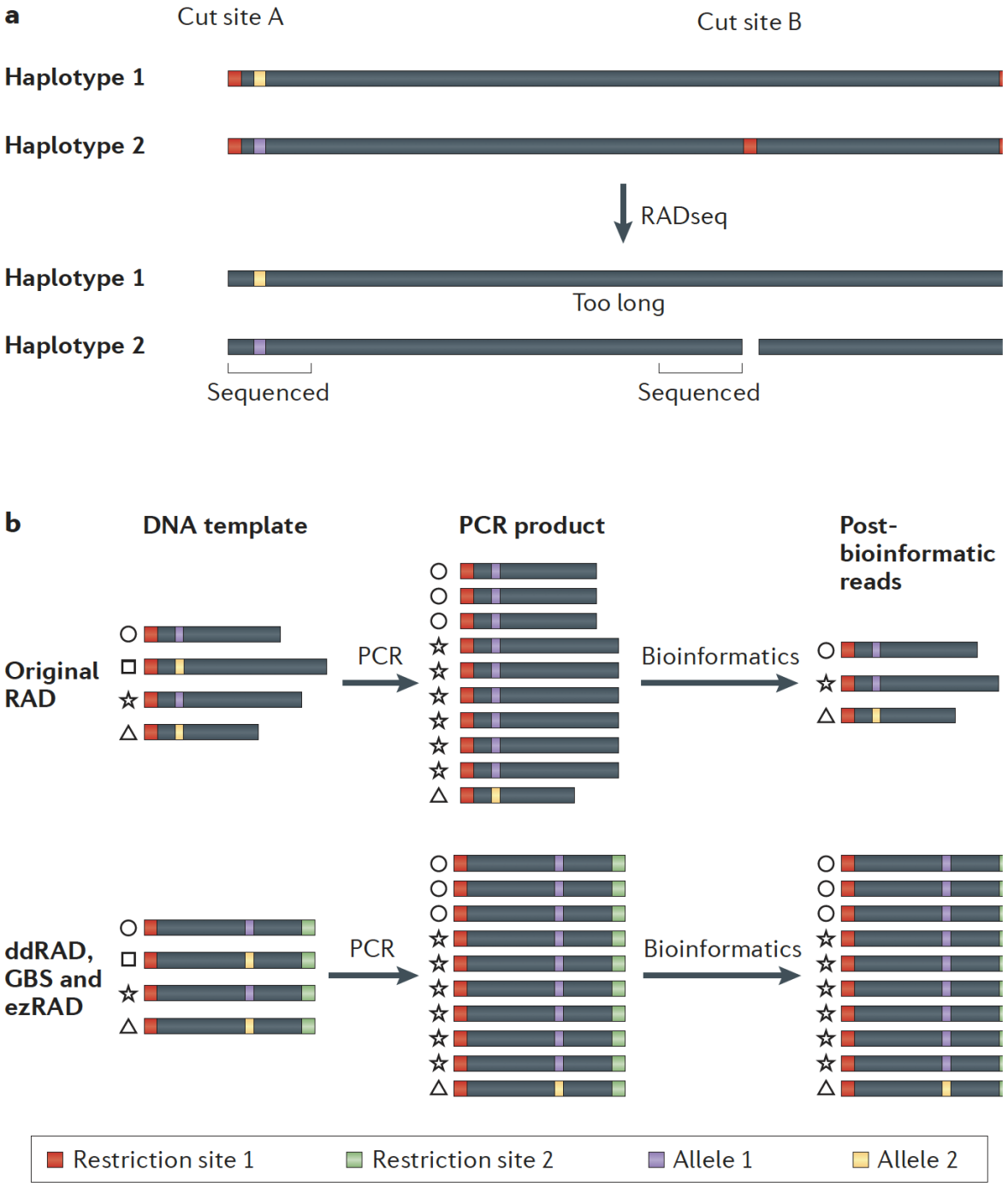
Random sampling of the genome

Targeted capture of loci of interest

RADseq



Peterson et al. 2012, PlosOne



Single vs. double digestion

Andrews et al. 2016, Nature Gen. Rev.

Many different RADseq protocols

	mbRAD	ddRAD	ezRAD	2bRAD
Restriction cut sites per 10 kb*	~0.2–2.4	~3.7×10^{-5}–39	~39	~2.4
Postdigest fragment reduction	Size selection	Size selection	Size selection	Selective adapters
Contigs > 200 bp†	Yes	No	Some	No
Ability to blast/annotate *de novo* contigs	High	Mid	Mid	Low
Protocol complexity (# Steps)‡	6	4	4–6	3
Level of technical difficulty	High	Mid	Low	Low
Level of technical support	Low	Low	Mid-high	Low
Insert complexity (first × bases)	Low	Low	Very low	High
PCR AT/GC content, copy number Bias among loci	Yes	Yes	Yes, No§	Yes
ID of PCR duplicates	Yes	No	No§	No¶
Uniform locus length	No	No	No	Yes
Oligos required to uniquely identify and build 96 libraries	196**	31	20–22	37
Target insert size range	200–600 bp	Customizable	Customizable	33–36 bp

*These numbers represent only theoretical calculations for one enzyme (or enzyme combination). The number of fragments sampled will depend on size selection, genome composition, the number of enzymes used and the use of restrictive adapters (see 2bRAD).
†When performing 100 bp reads such as on a HiSeq platform.
‡Not counting clean-up steps.
§ezRAD can be used with a PCR-free library preparation kit, thus removing the need to detect PCR duplicates.
¶2bRAD can detect PCR errors by mismatch among forward and reverse reads on individual strands.
**With some effort, the indexing for mbRAD can be modified to reduce the oligo counts to 22–37.

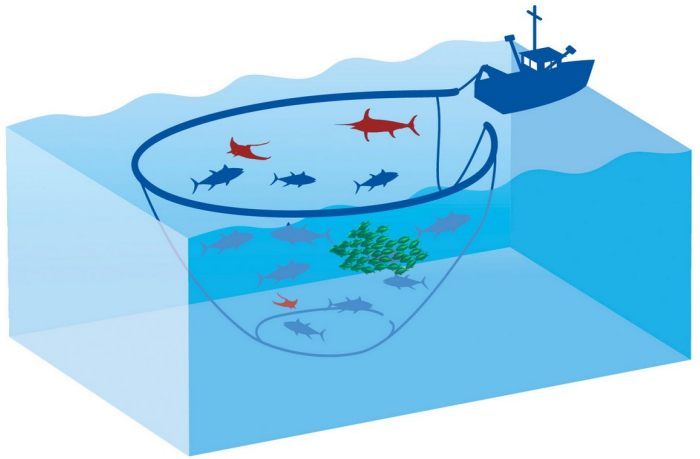
Puritz et al. 2014, Molecular Ecology

Targeted approaches

Advantages:

- Scalable and cost-effective
- Lower variance in target coverage
- More accurate SNP calling
- Higher reproducibility
- Can be combined with other reduced-representation approaches

RADseq

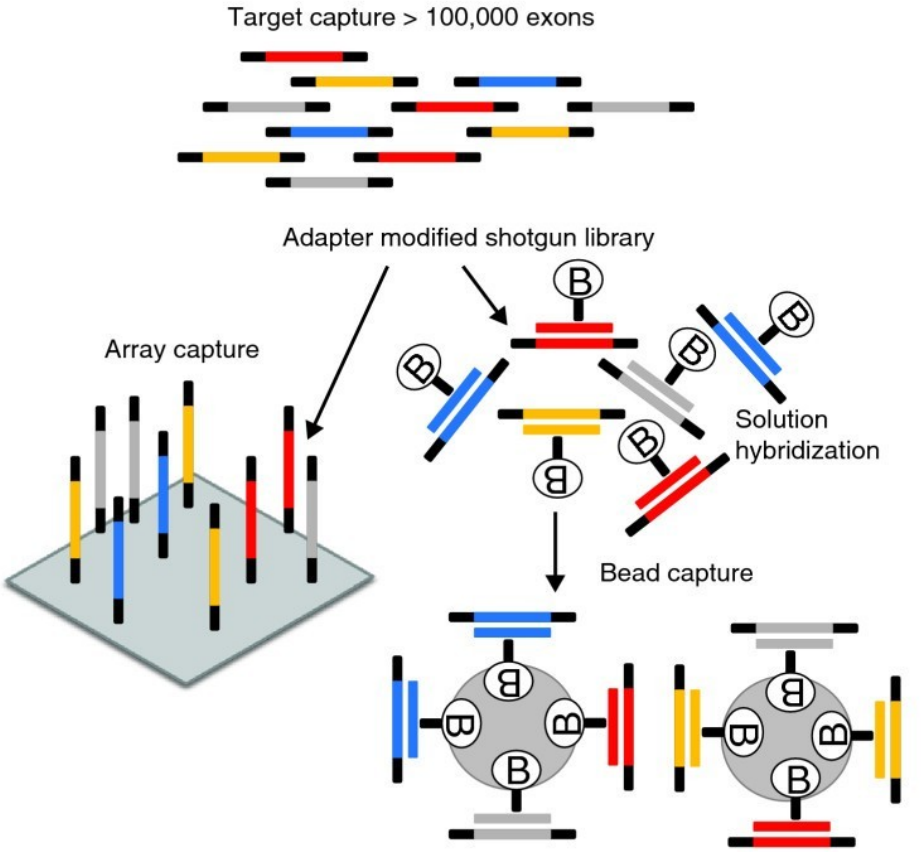


Targeted sequencing - RAPTURE

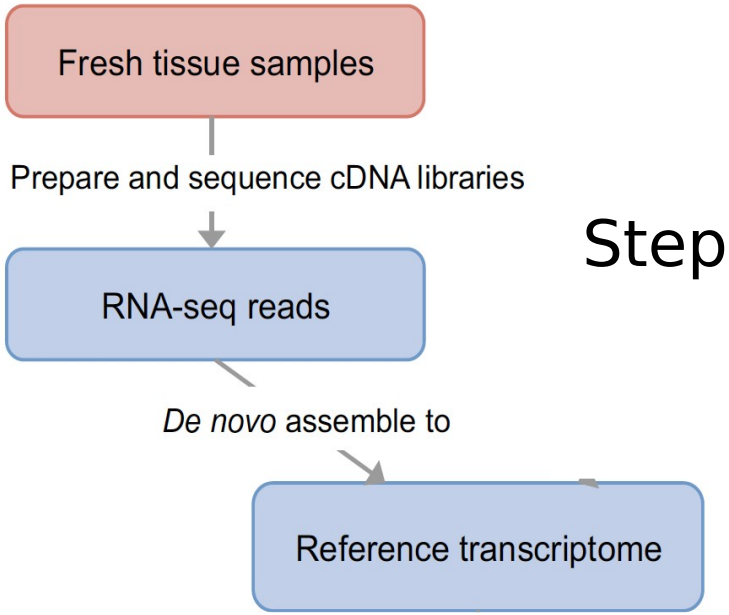
Targeted approaches - Exome/exon capture

Used to sequence protein coding genes (or other sequences as well).

While probes are generally available for some model species (human, mouse), they have to be designed for other species.



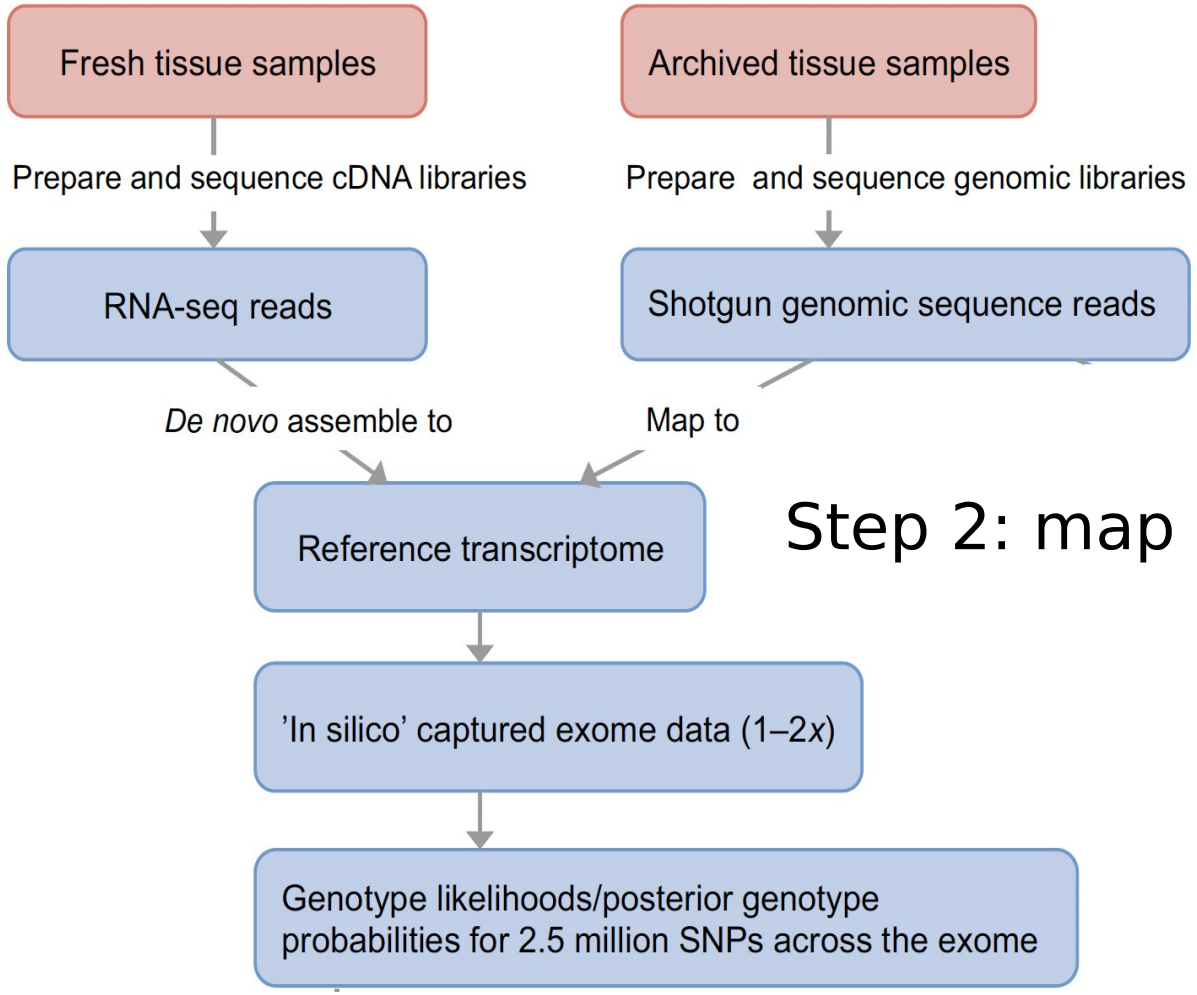
Targeted approaches - Exome capture (*in silico*)



Step 1: build a reference transcriptome

Therkildsen & Palumbi 2017, Mol. Ecol. Res

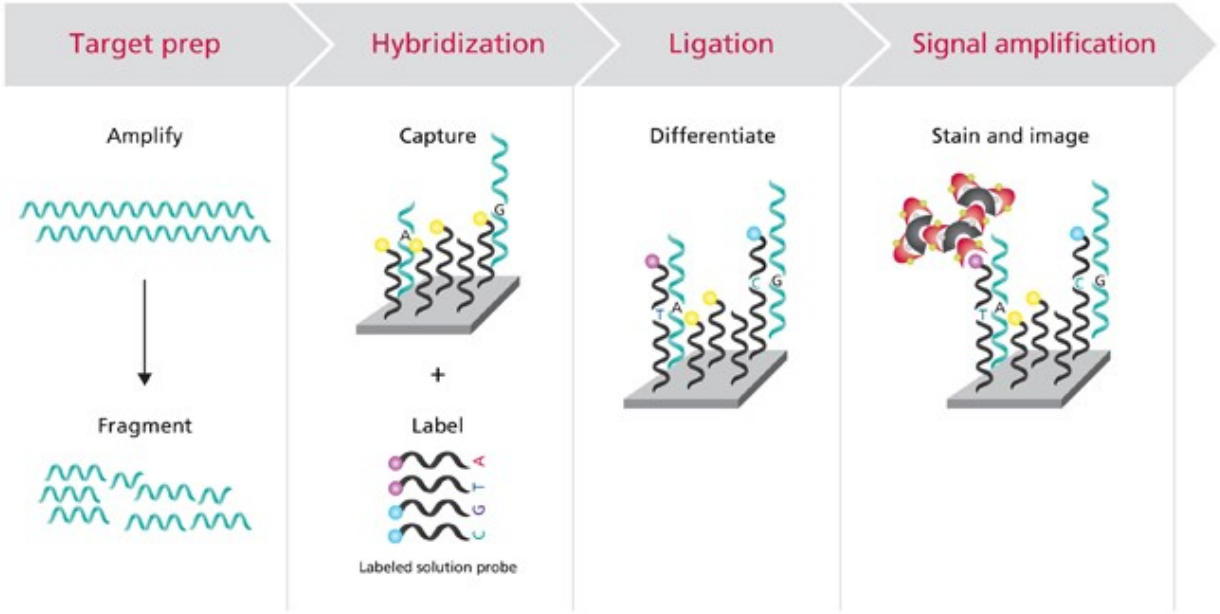
Targeted approaches - Exome capture (*in silico*)



Step 2: map data to reference

Therkildsen & Palumbi 2017, Mol. Ecol. Res

Targeted approaches - SNP chip array



Cost-effective to genotype high number of SNPs in large number of samples.

Targeted approaches - SNP chip array

Antarctic fur seal

85k Affymetrix Axiom genotyping array includes SNPs from

- Previous RADseq markers
- transcriptome markers
- MHC loci

☾ To identify loci of adaptive importance and monitor levels of standing genetic variation

Humble et al. 2020, G3

Whole genome resequencing

Short-read sequencing

Long-read sequencing

Linked-reads technology
(synthetic long reads)

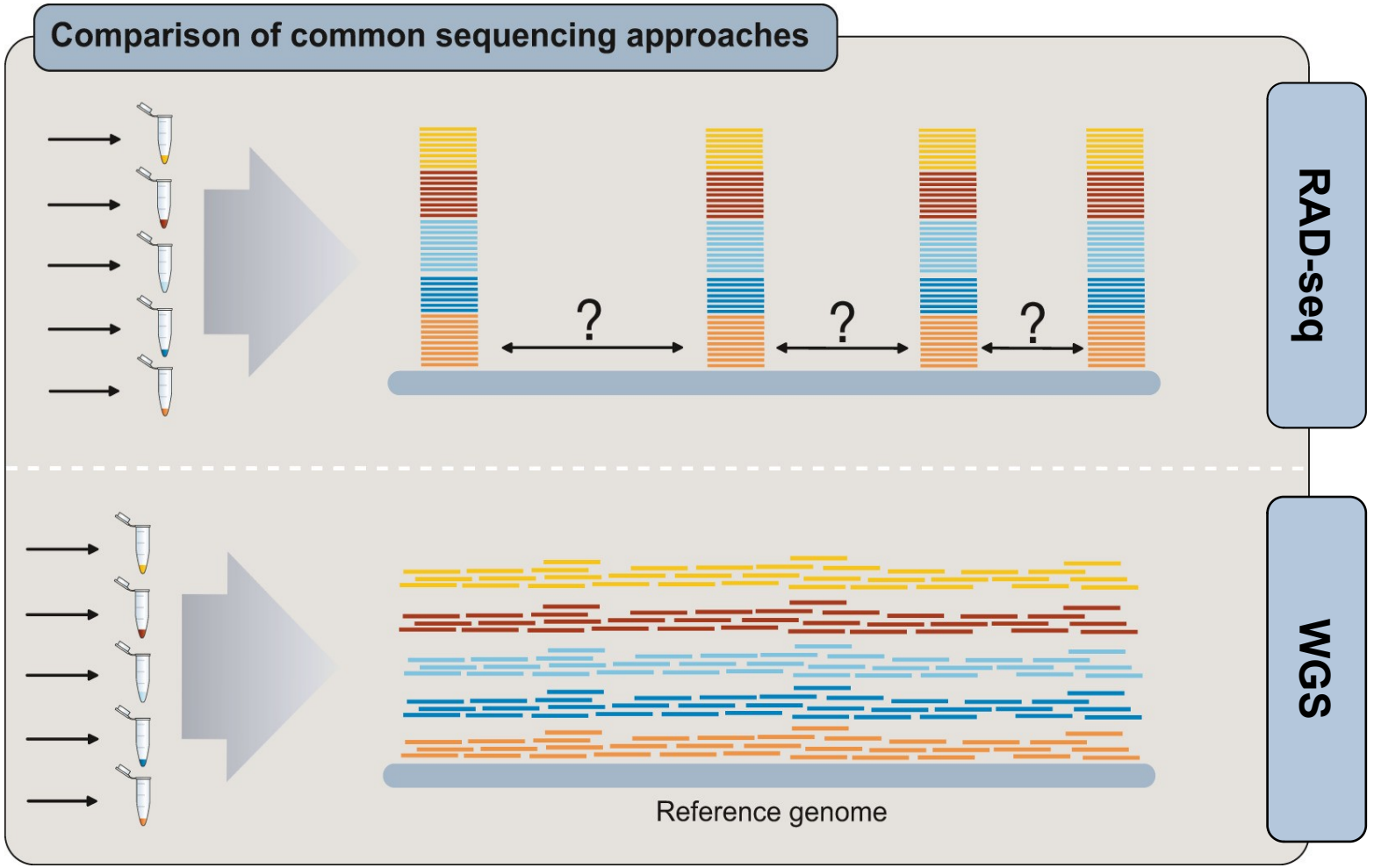
???

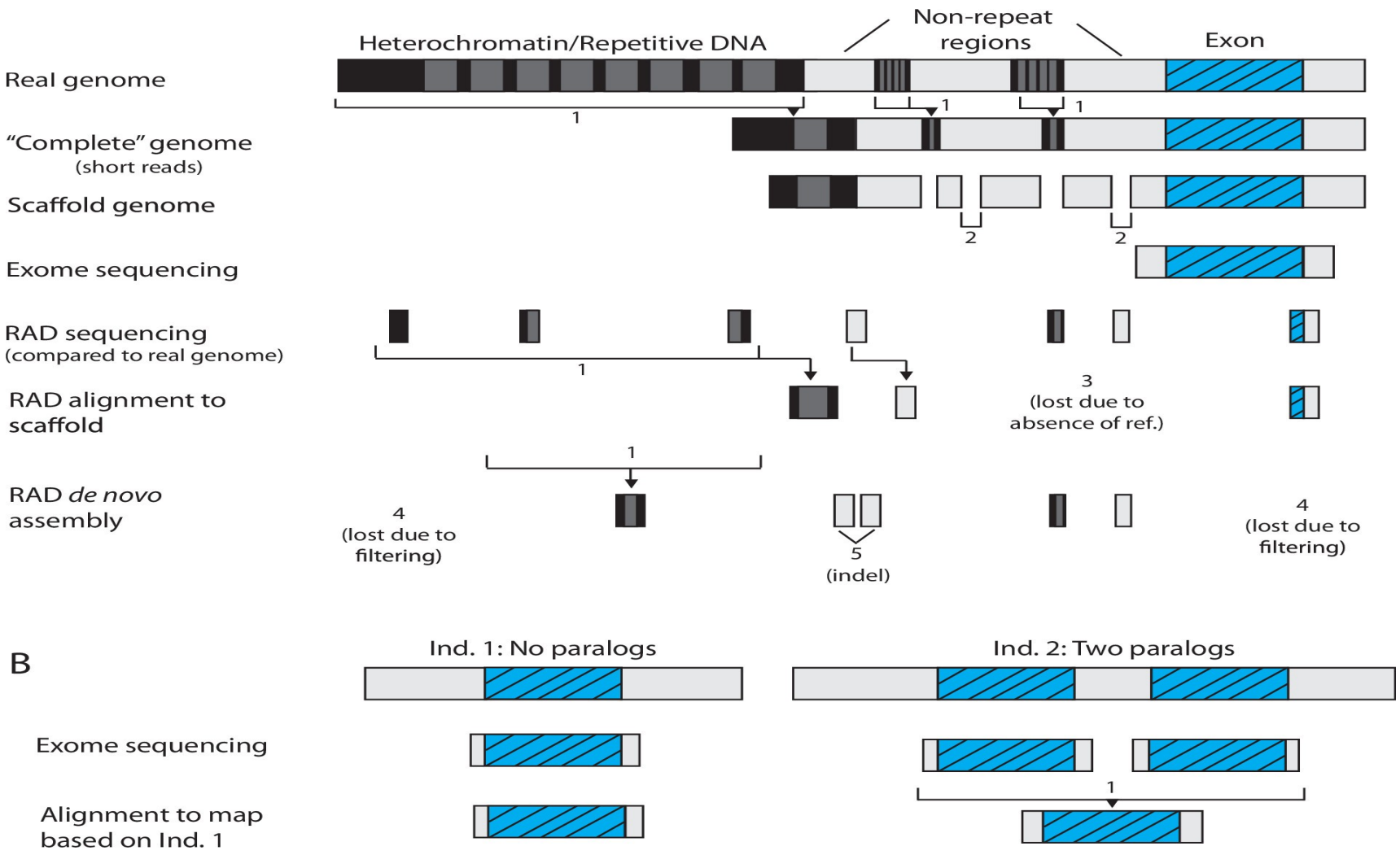
Tell-seq
Haplotagging
Stlfr…

= short-reads + barcodes by molecules

Whole genome resequencing

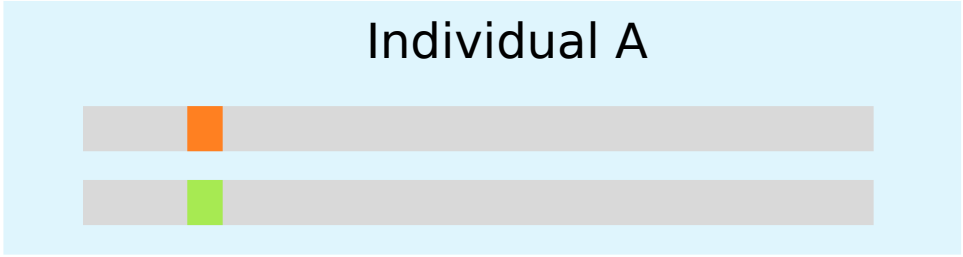
Short-read sequencing



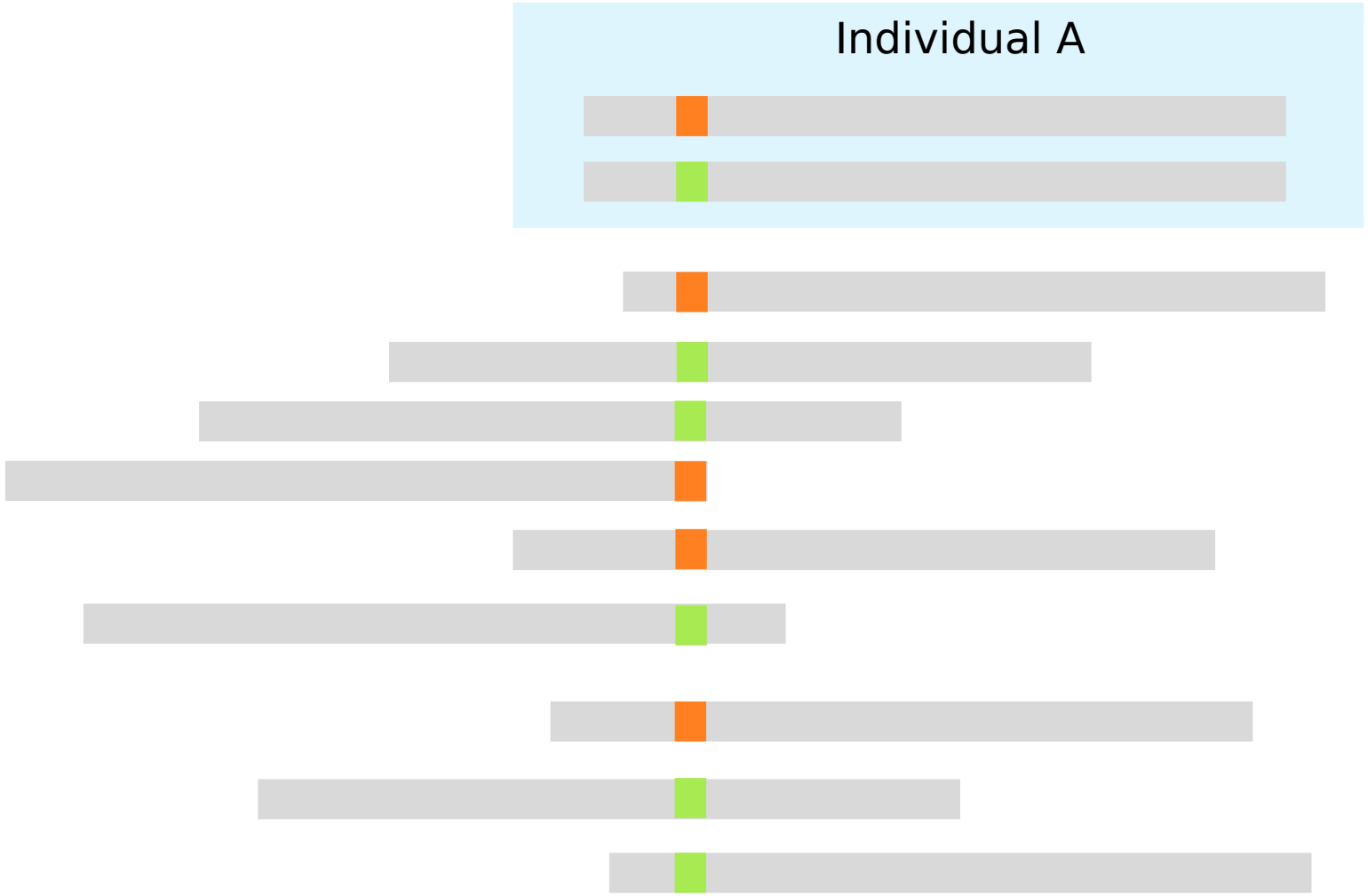


Hoban et al. 2016, American Naturalis

Sequencing depth = the number of reads covering a given site



Sequencing depth = the number of reads covering a given site

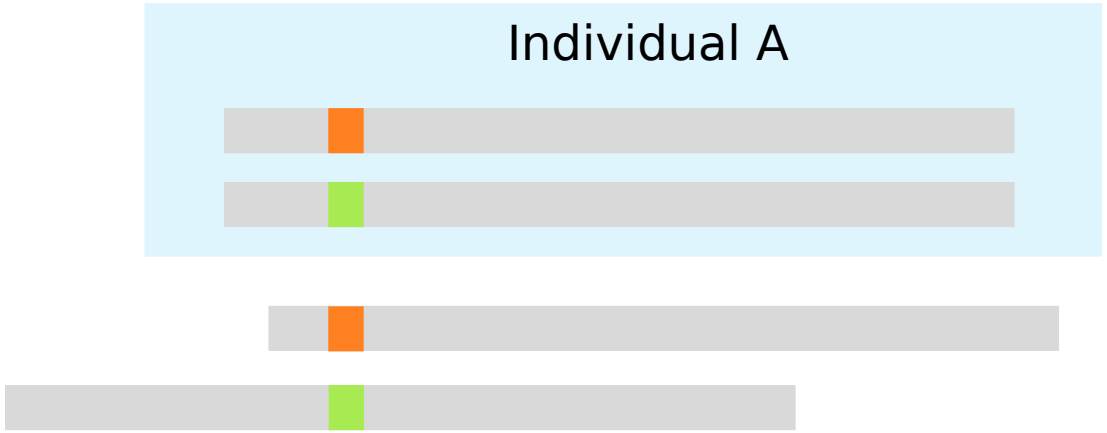


Short reads – moderate depth (10x)

↓

Heterozygous site

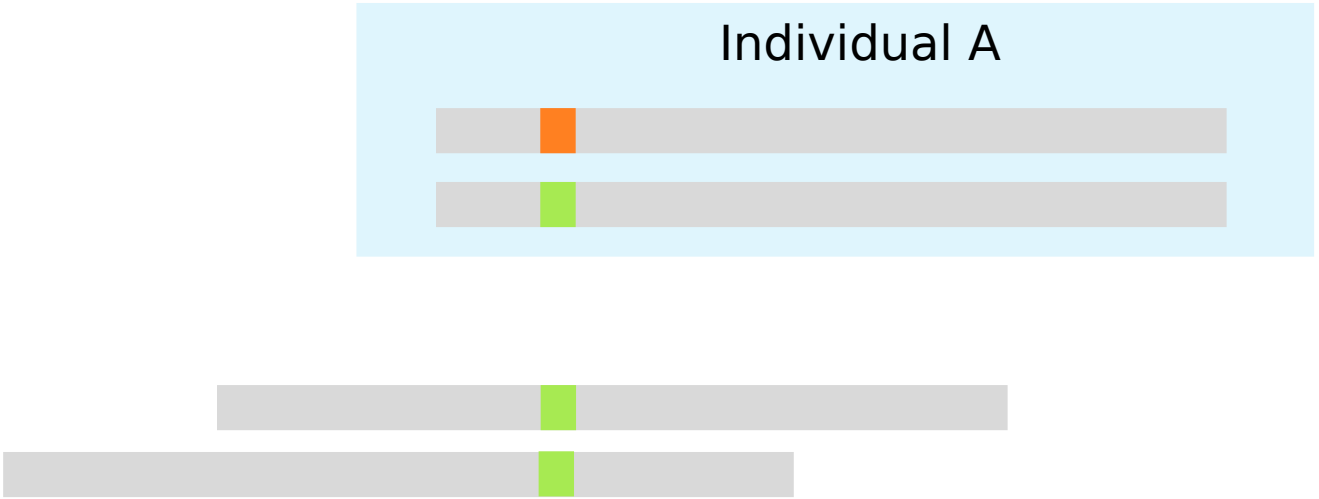
Sequencing depth = the number of reads covering a given site



Short reads – low depth (2x)

Heterozygous site

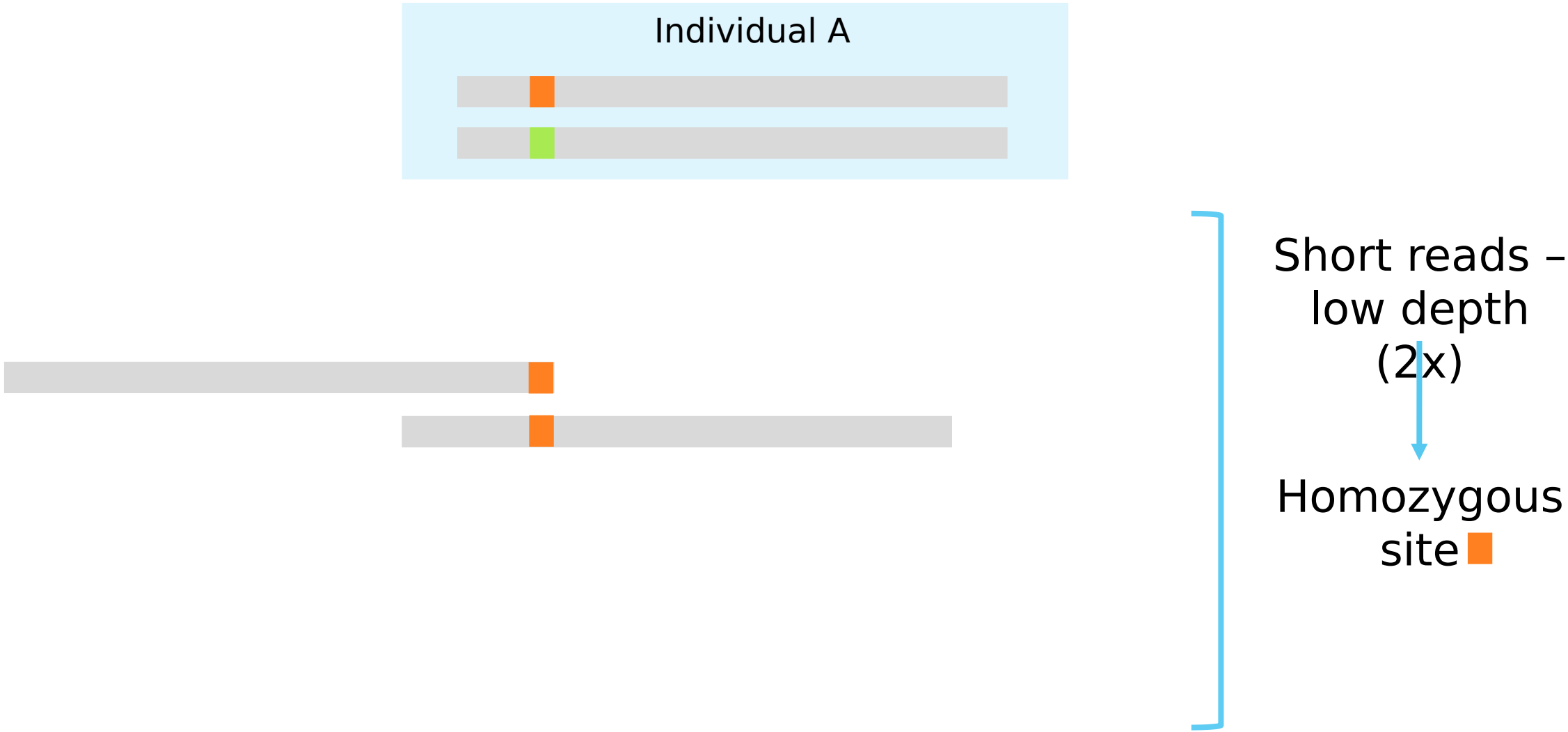
Sequencing depth = the number of reads covering a given site



Short reads – low depth (2x)

Homozygous site

Sequencing depth = the number of reads covering a given site

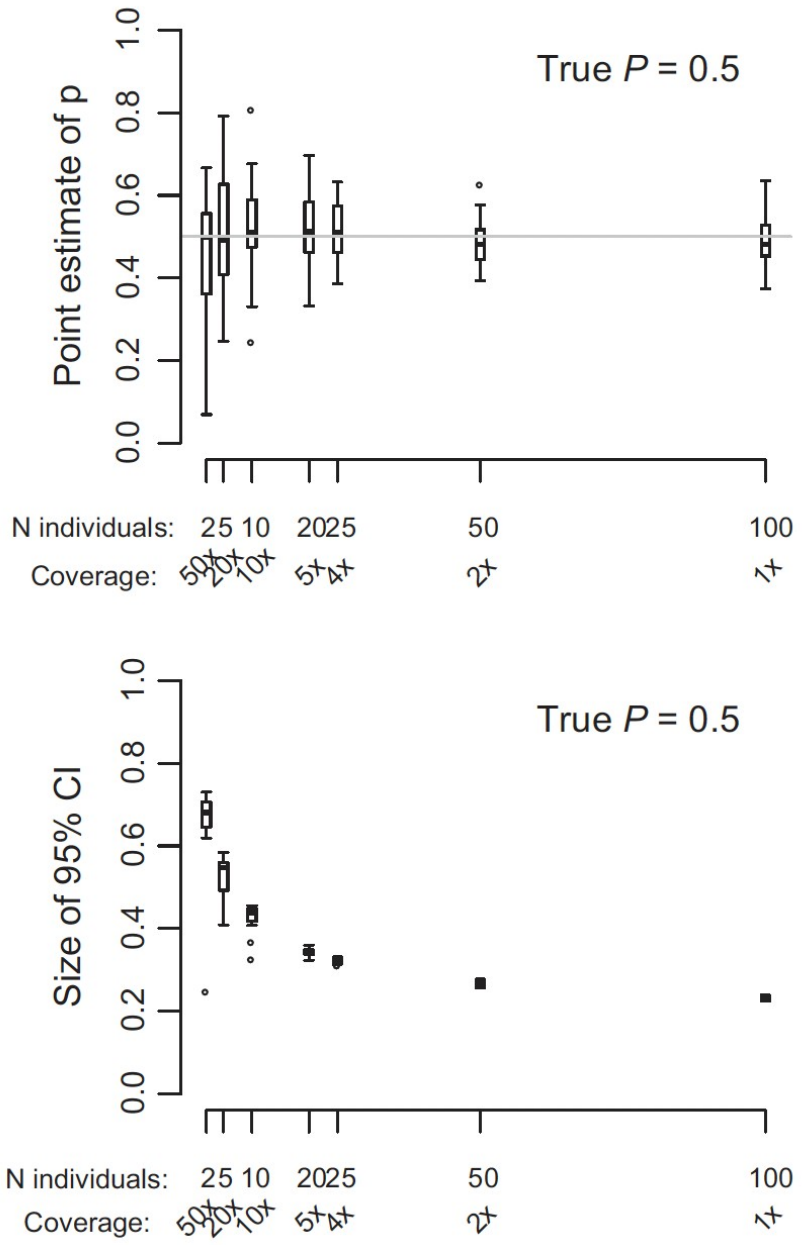


Low-coverage sequencing

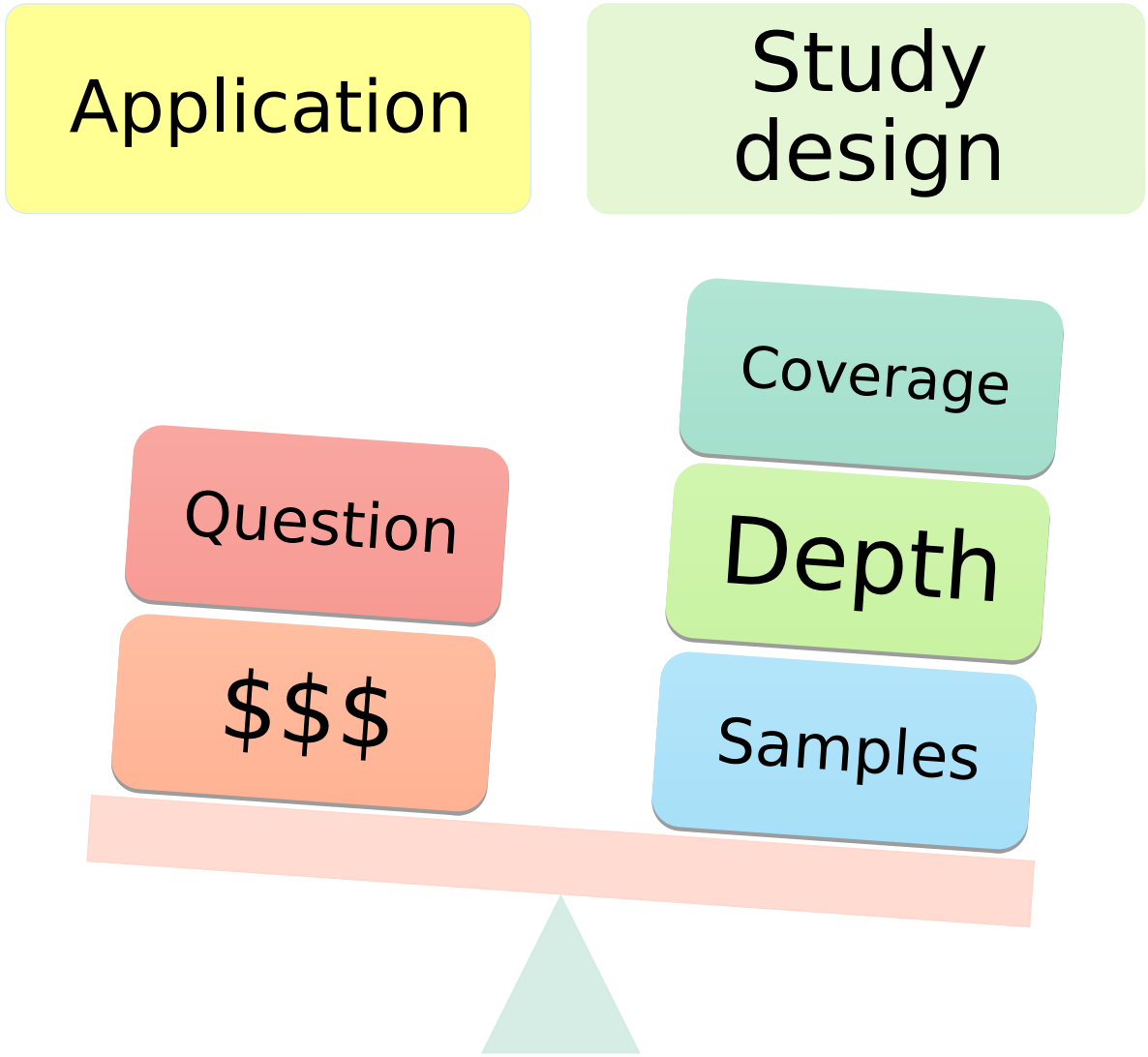
However, most population genomics analyses collapse genotypes to population allele frequencies.

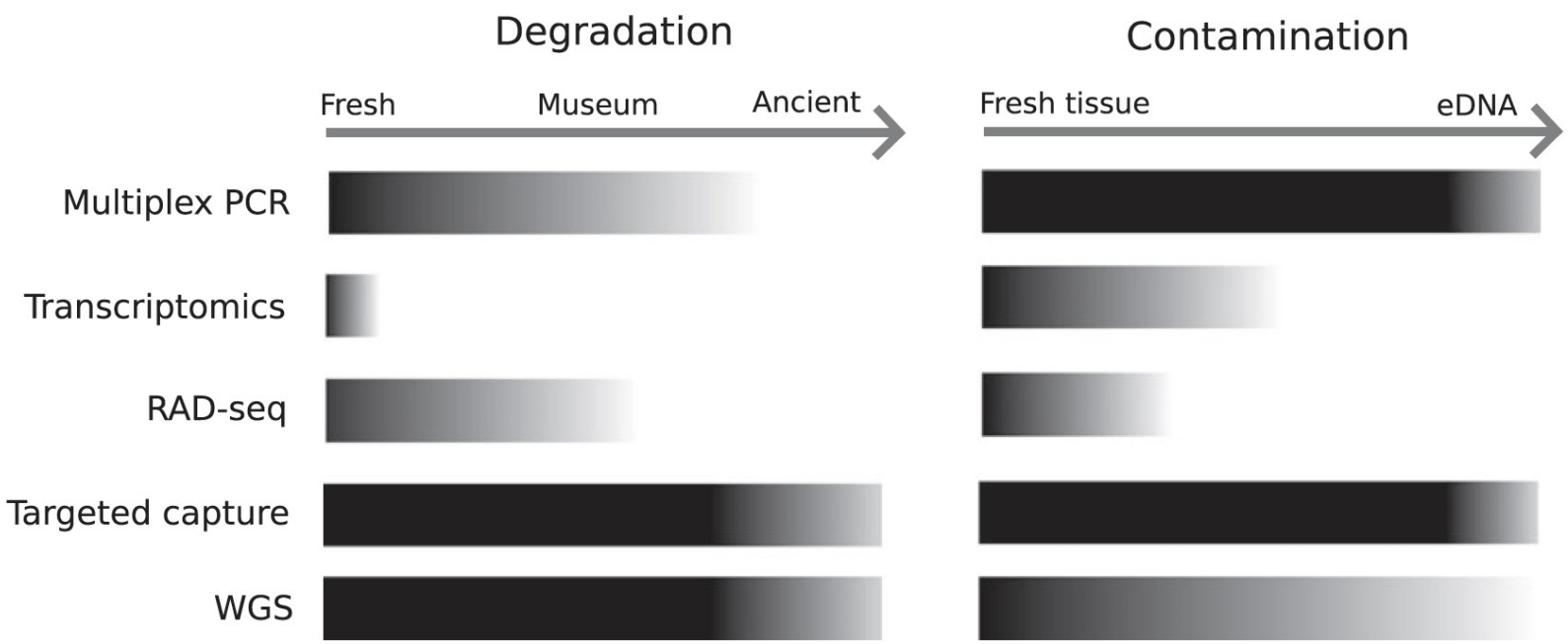
In those cases, high number of individuals at low depth provide more accurate estimates than a few individuals sequenced at higher depths.

When genotypes are necessary, they can be associated with genotype uncertainty in a probabilistic framework



Buerkle and Gompert 2013, Molecular Ecolog


Application
Study design
Coverage
Question
Depth
$$$
Samples



Jones & Good 2016, Molecular Ecology

In addition to all these technical aspects, there are many evolutionary and molecular factors to consider to choose the most appropriate sequencing approach for your study.

We will explore those throughout the rest of the week.

The end.