BIOL 502 Population Genetics Spring 2017

Lecture 1 Genomic Variation

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What is Population Genetics?

Population Genetics

`Population Genetics` is the study of how evolutionary forces of natural selection, gene flow, genetic drift and mutation have influenced historical and contemporary patterns of genomic variation, and the processes by which this variation changes in space and time.

T. Dobzhansky (1973)

Nothing in biology makes sense except in the light of evolution.

M. Lynch (2005)

Nothing in evolution makes sense except in the light of population genetics.

G.E.P Box (1987)

All models are wrong, but some are useful.

Course Logistics

- Syllabus
- Textbook - Principles of Population Genetics, 4th Edition by Hartl and Clark (Sinauer)[1]
- Additional notes will be posted on Cougar Courses
- Office Hours: Mondays 2pm-4pm, or by appointment
- The “white” paper
- WORK IN GROUPS!
- Work out assigned problems, do additional readings as required, practice!
- Two midterm exams, one final exam.
- Absolute grading scale (see syllabus)

Vocabulary Recap

General Vocabulary

- Genotype
- Phenotype
- Genome
- Genetic Locus/Loci
- Chromosome
- Recombination
- Mutation
- Linkage
- Ploidy
- Chromosome
- Gamete
- Population
- Segregation
- Mendelian Trait
- Dominance
- Evolution

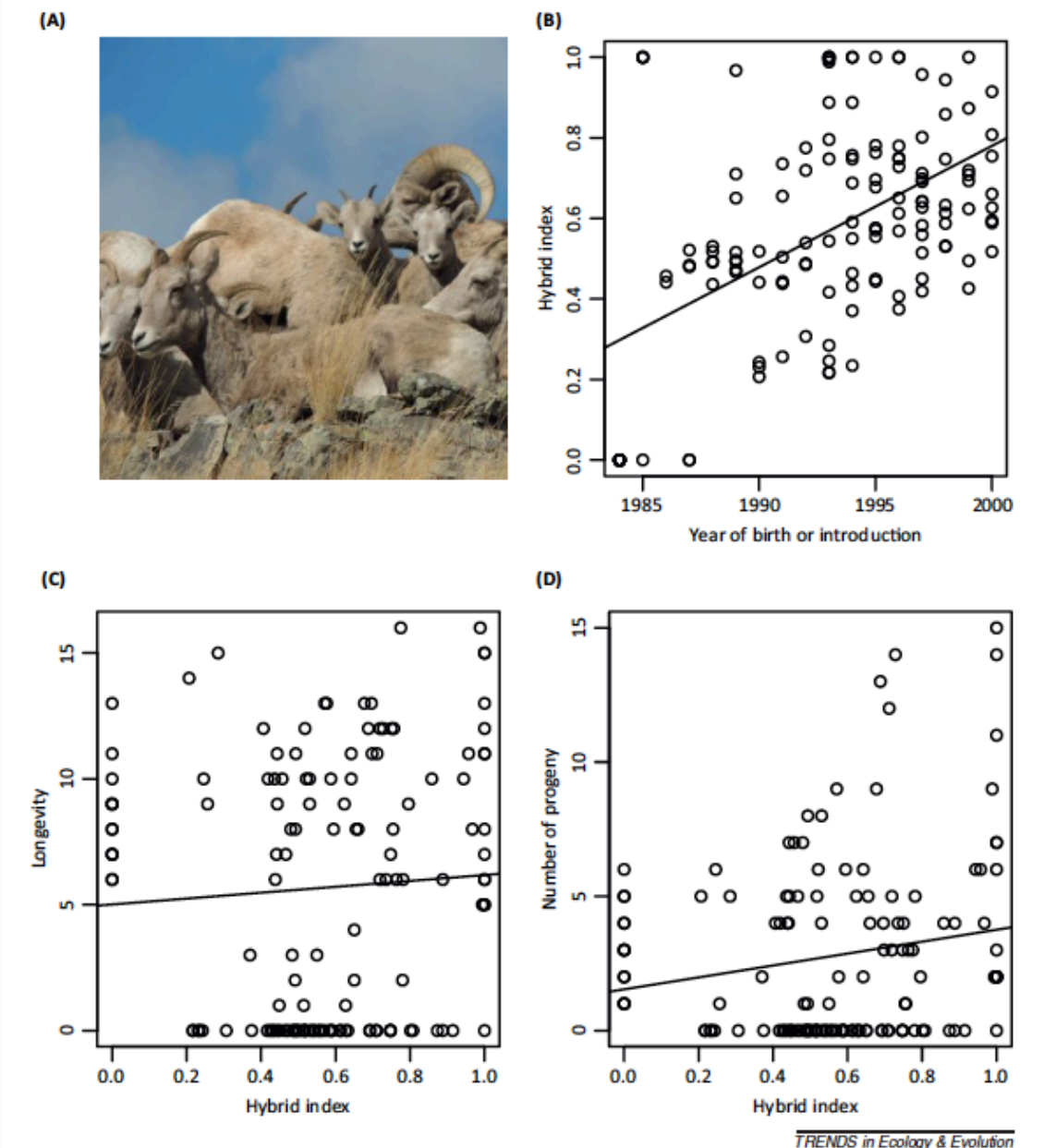
Population Genetics Vocabulary

- Population
- Allele
- Frequency
- Genetic Drift
- Hybridization
- Speciation
- Phylogenetic Tree
- Inbreeding
- Gene Flow
- Heterozygosity
- Homozygosity
- Random mating
- Natural Selection

Relevance

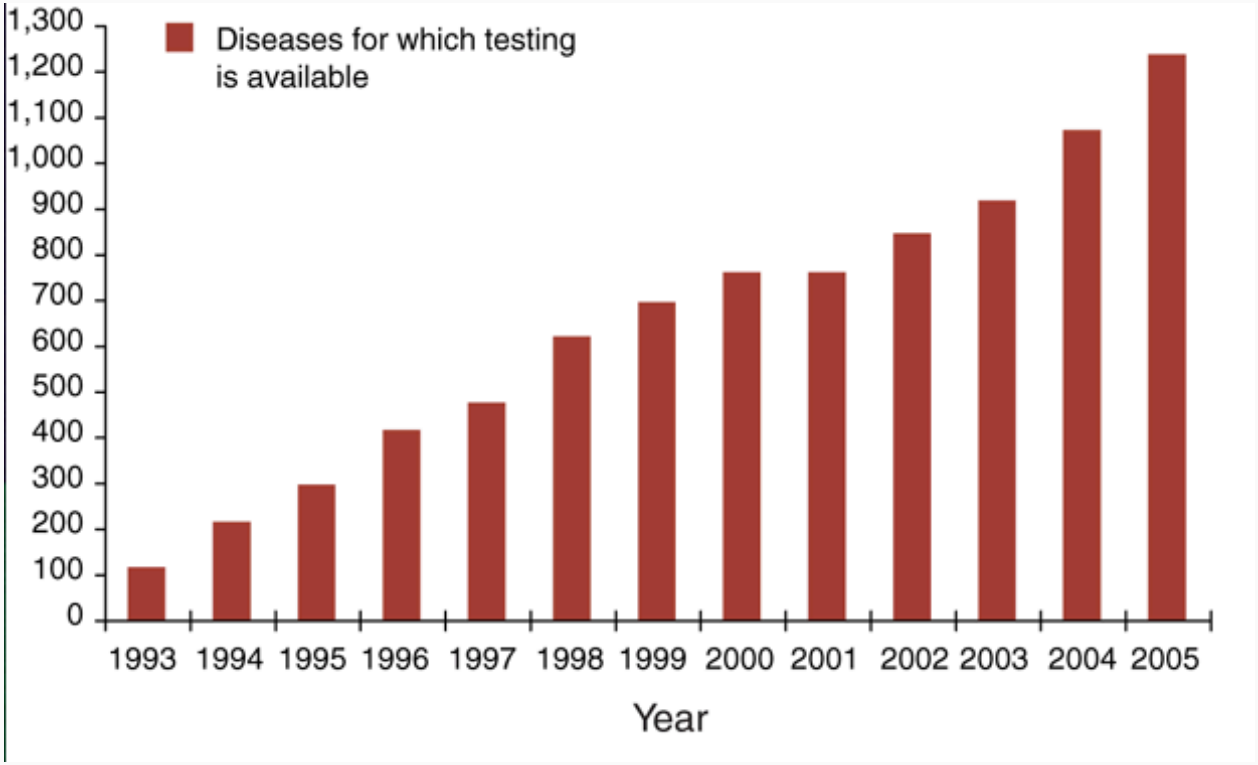
Conservation

Example - genetic rescue of big horn sheep (*Oviscanadensis*) at the National Bison Range, MT. Two separate introductions successfully increased genetic diversity and reversed negative effects of inbreeding. [2]



Human Health and Counseling

Rapid increase in genetic testing since 1993. Citation: Pray, L. (2008) Questionable prognostic value of genetic testing. Nature Education 1(1):74[7]



Forensics

Secure https://www.fbi.gov/services/laboratory/biometric-analysis/codis

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Combined DNA Index System (CODIS)

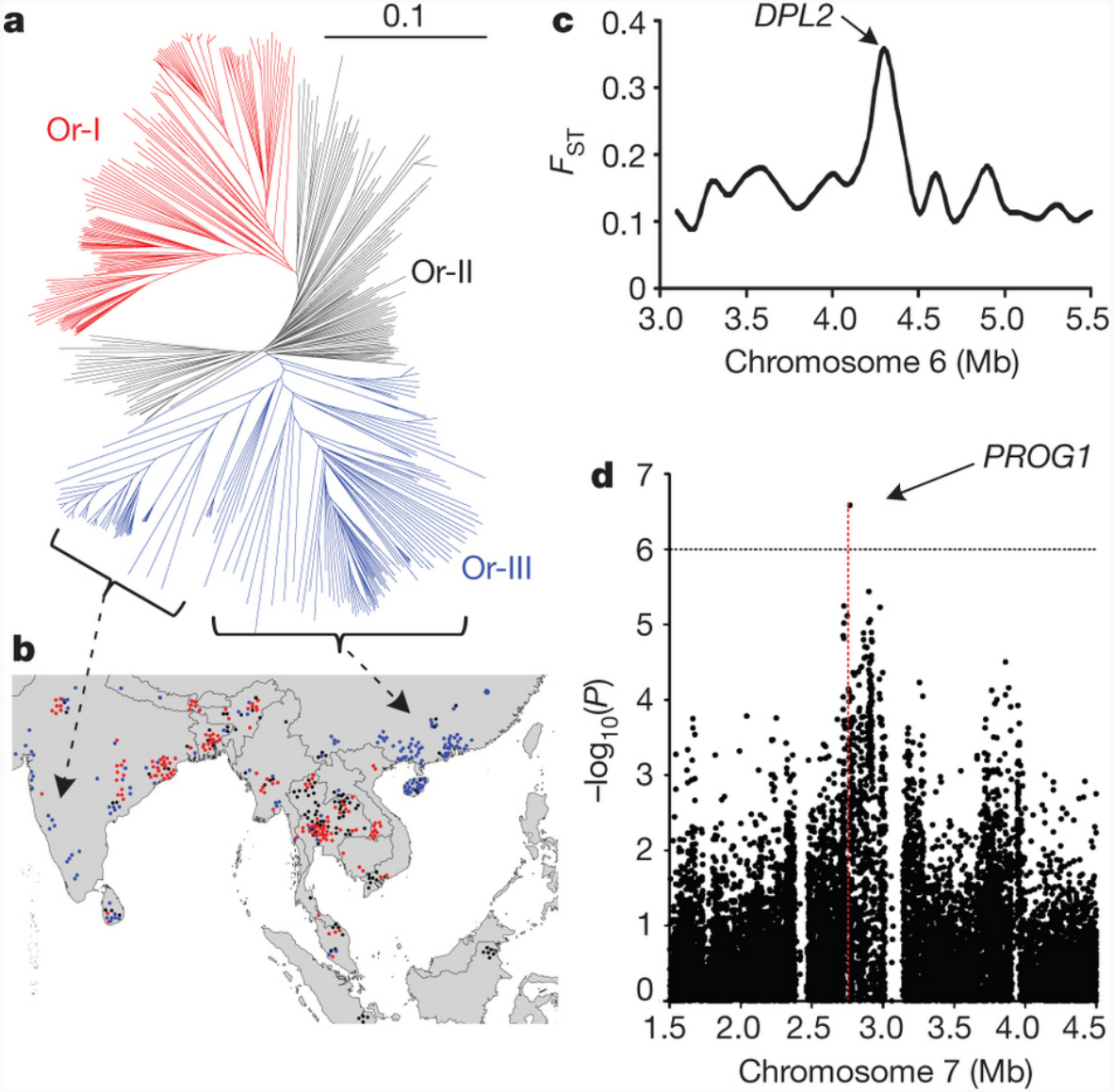
The Combined DNA Index System, or CODIS, blends forensic science and computer technology into a tool for linking violent crimes. It enables federal, state, and local forensic laboratories to exchange and compare DNA profiles electronically, thereby linking serial violent crimes to each other and to known offenders. Using the National DNA Index System of CODIS, the National Missing Persons DNA Database also helps identify missing and unidentified individuals.

Overview

CODIS generates investigative leads in cases where biological evidence is recovered from the crime scene. Matches made among profiles in the Forensic Index can link crime scenes together, possibly identifying serial offenders. Based upon a match, police from multiple jurisdictions can coordinate their respective investigations and share the leads they developed independently. Matches made between the Forensic and Offender Indexes provide investigators with the identity of suspected perpetrators. Since names and other personally identifiable information are not stored at NDIS, qualified DNA analysts in the laboratories sharing matching profiles contact each other to confirm the candidate match.

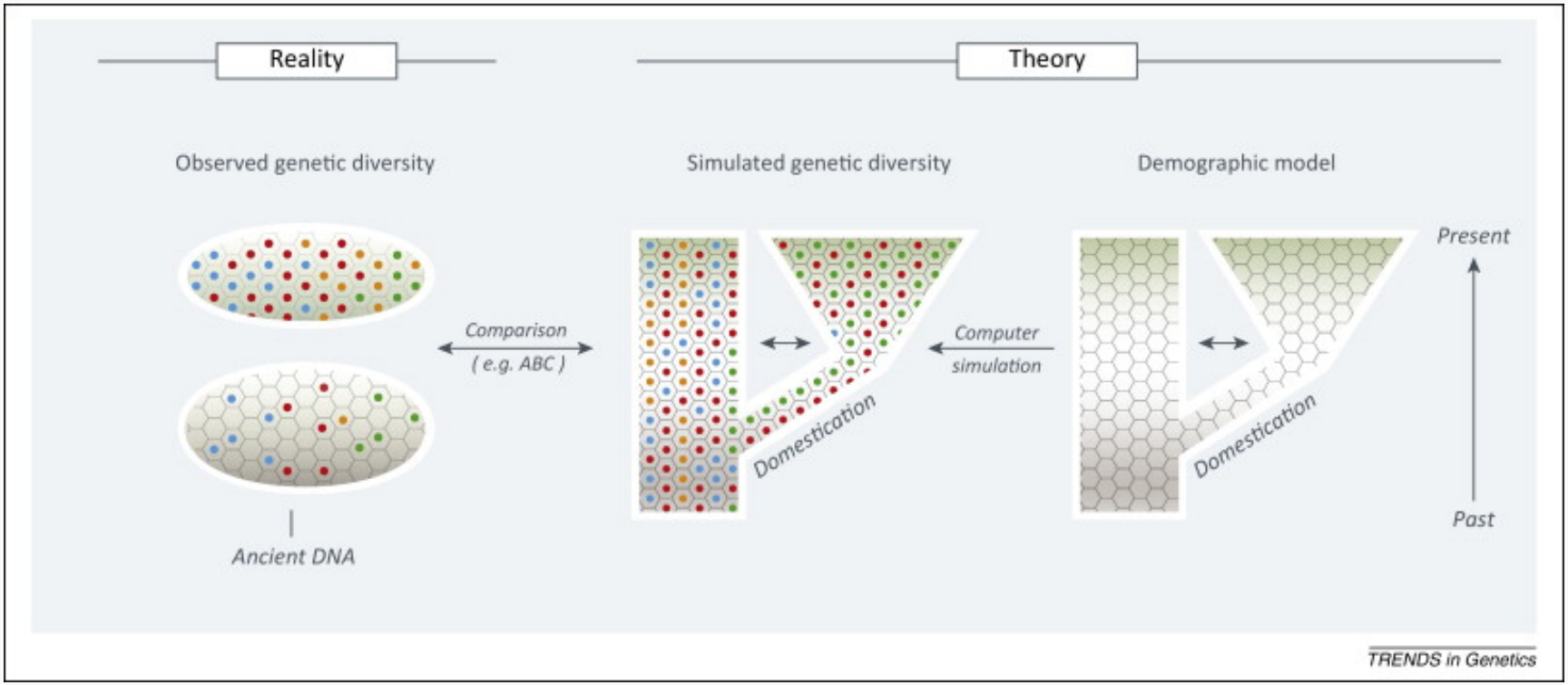
Agriculture

Huang, Xuehui, et al. "A map of rice genome variation reveals the origin of cultivated rice." Nature 490.7421 (2012): 497-501.[3]



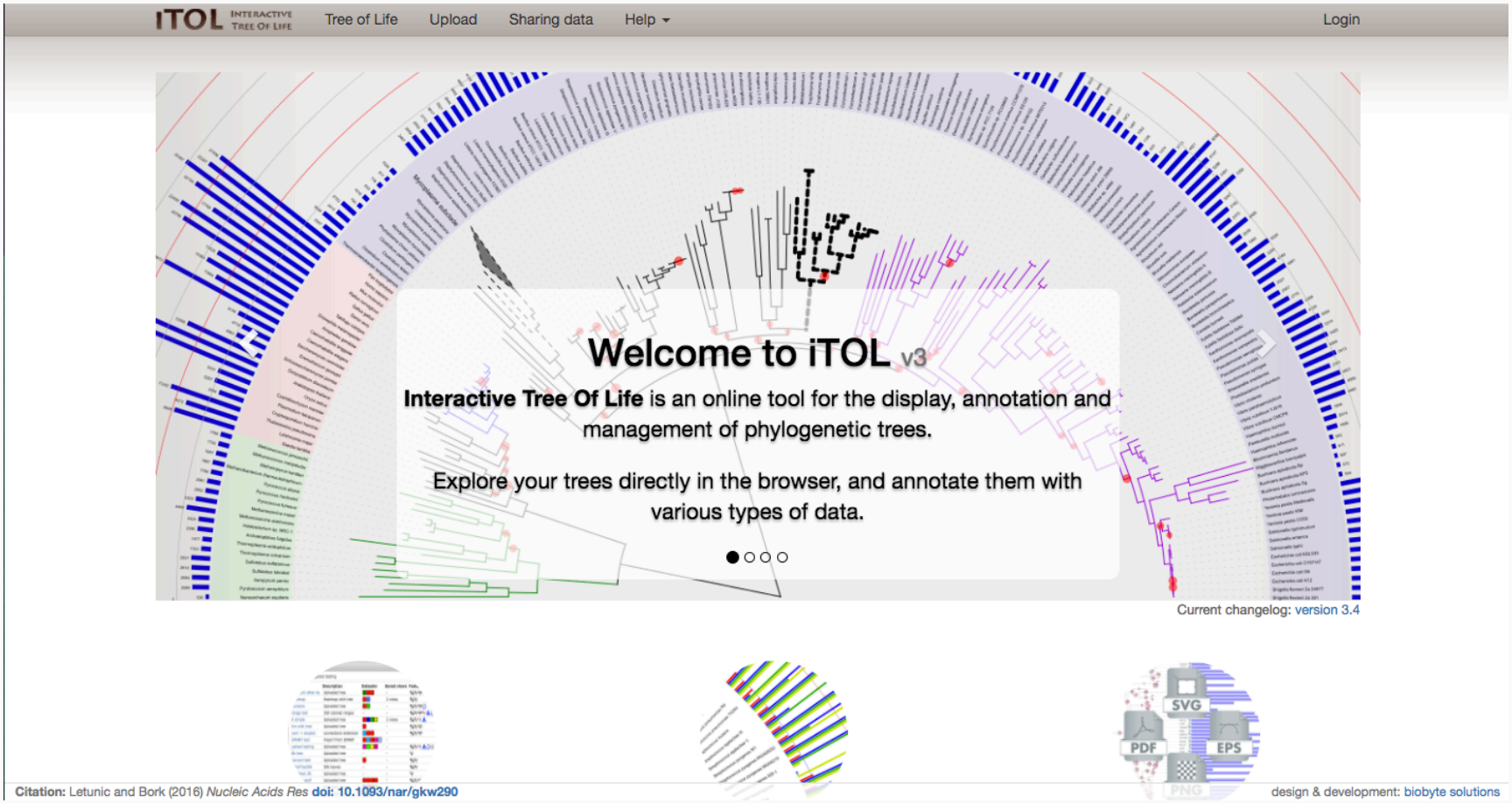
Animal Husbandry/Domestication

Larson, G. and Burger, J., 2013. A population genetics view of animal domestication. Trends in Genetics, 29(4), pp.197-205.[4]



Constructing the Tree of Life

Letunic, I. and Bork, P., 2016. Interactive tree of life (iTOL) v3: an online tool for the display and annotation of phylogenetic and other trees. Nucleic acids research, p.gkw290.[6]



Other Applications

- Biological Control
- Epidemiology
- Genetic Ancestry
- Speciation/Evolution
- Paternity/Relatedness
- Ancient Genomics

Genetic Variation

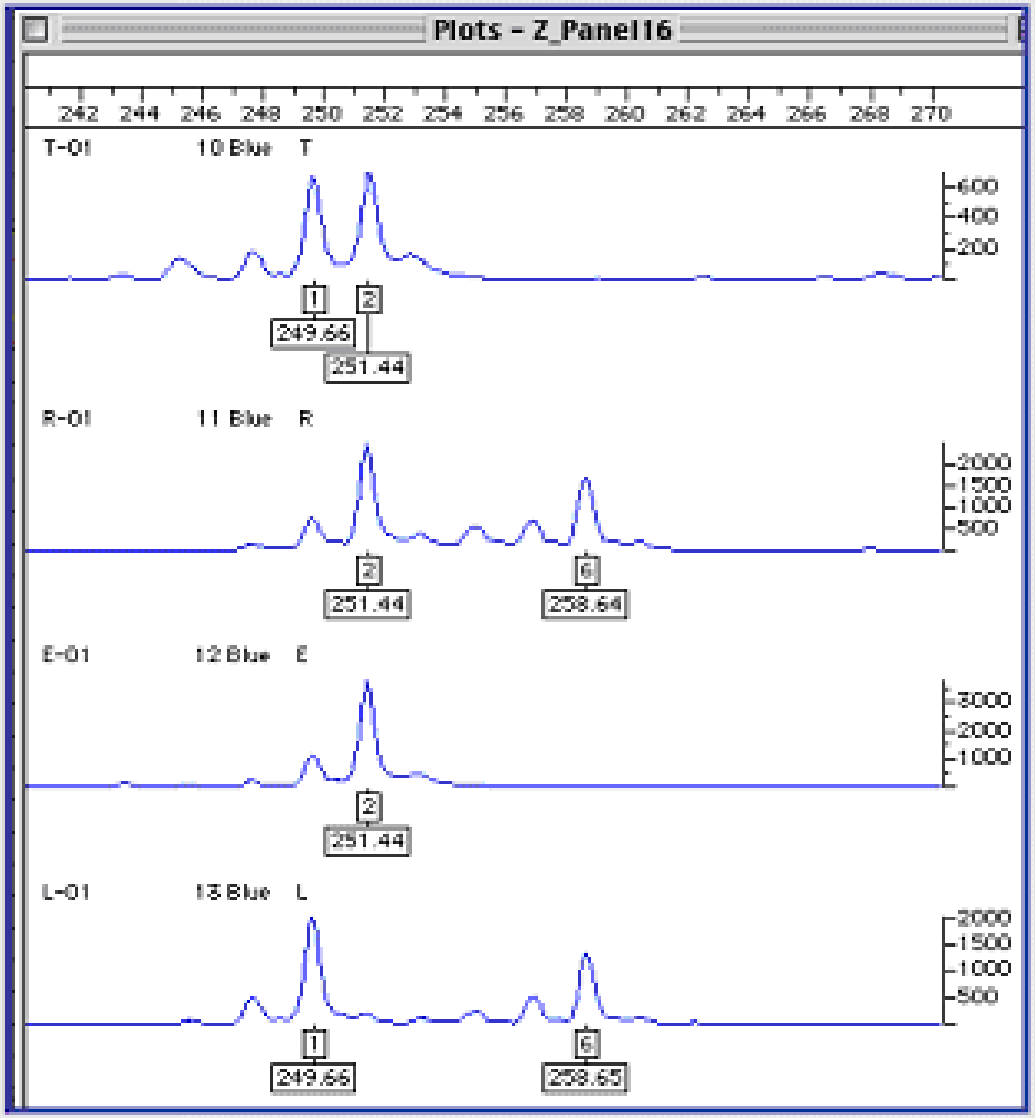
Microsatellite

Father alleles of sizes 249.66 and 251.44 (heterozygous)

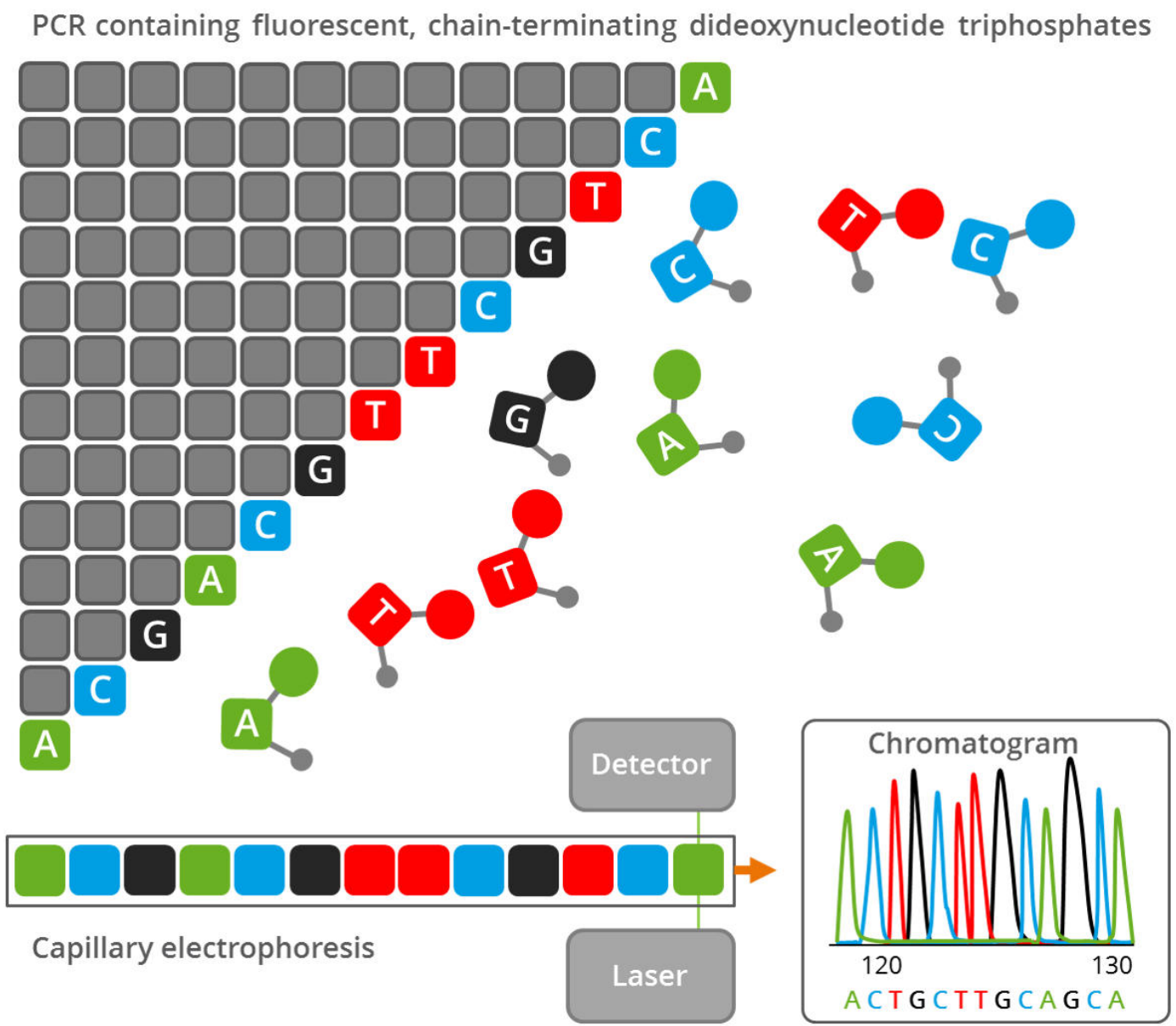
Mothers alleles of sizes 251.44 and 258.64 (heterozygous)

Child 1 alleles both of Size 251.44 (homozygous)

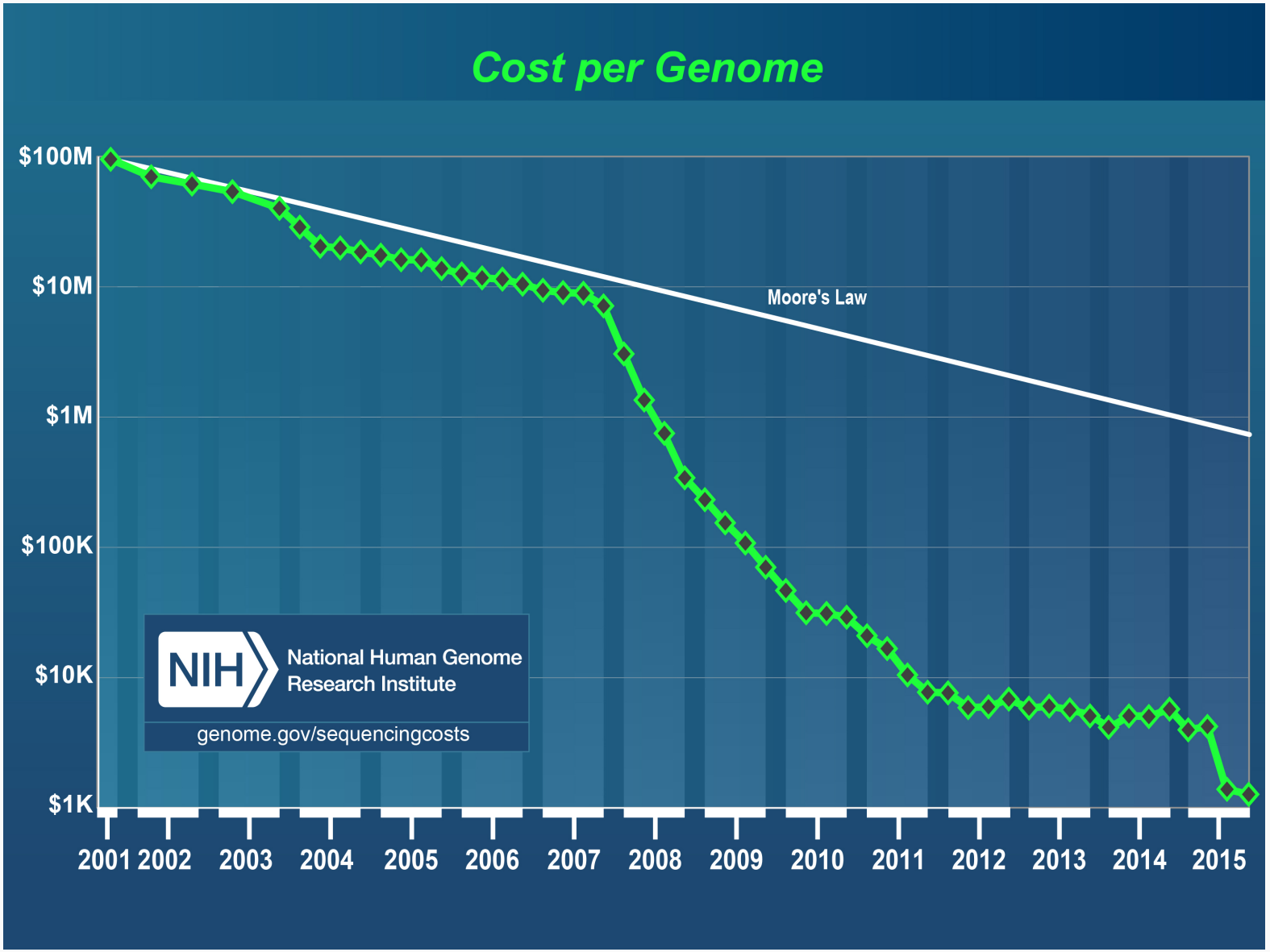
Child 2 alleles of sizes 249.66 and 258.65 (heterozygous)



Sanger Sequencing



Whole Genome Sequencing



What's interesting?

Similarities

Why are genomic sequences similar?

Differences

Why are genomic sequences different?

Hierarchy

- Locus-level
- Individual-level
- Population-level
- Regional-level
- Species-level

Descent with Modification

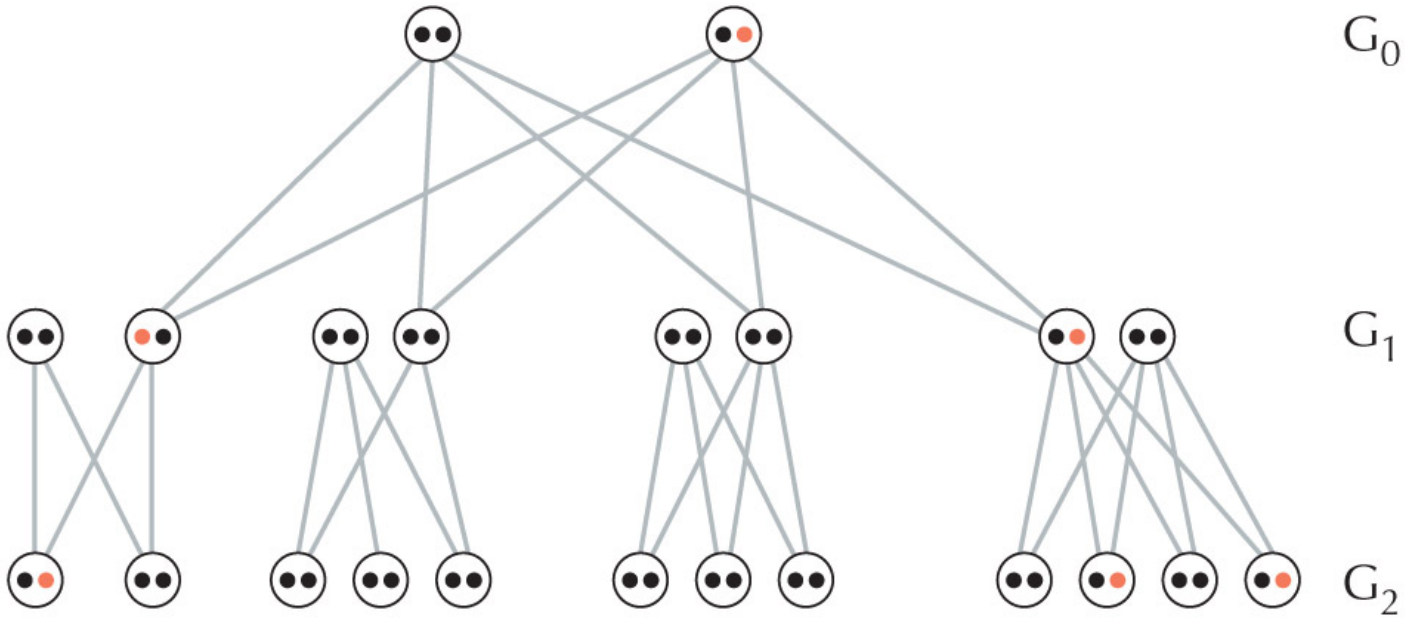
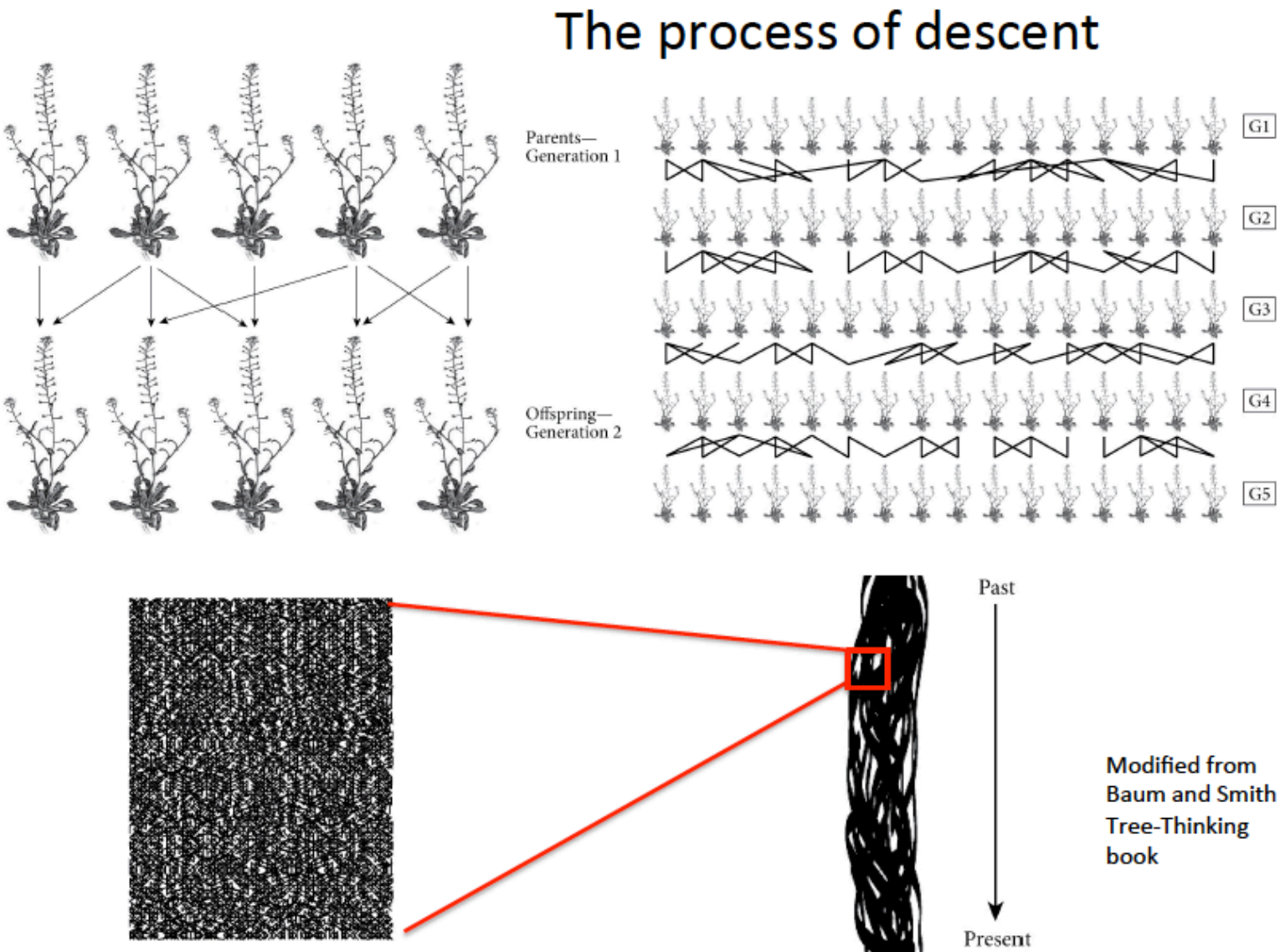


FIGURE 21.20. Identity by descent.

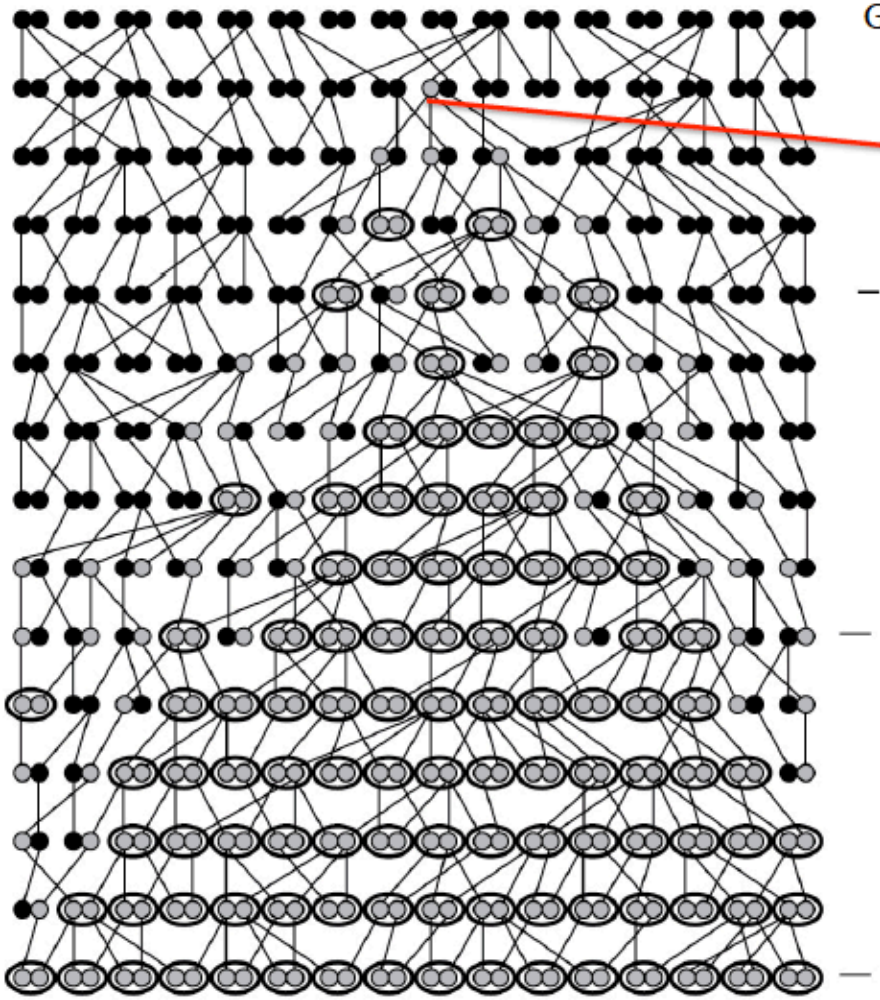
Identity By Descent

Tree-thinking images courtesy Graham Coop (UC Davis)



Identity By Descent

Descent with modification



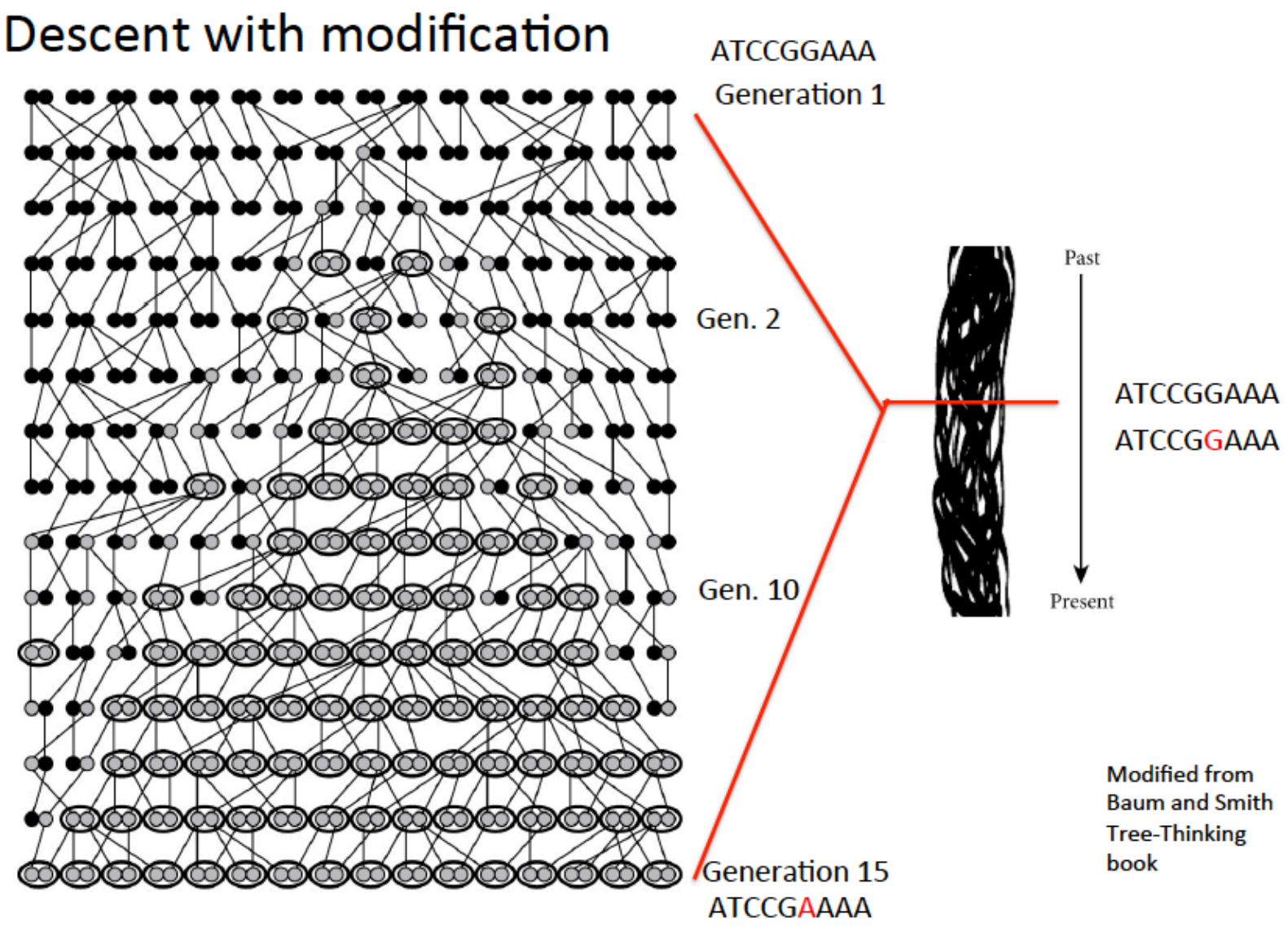
Generation 1 ATCCGGAAA

Mutation from G->A position 6.
Creates a polymorphism
G/A in population

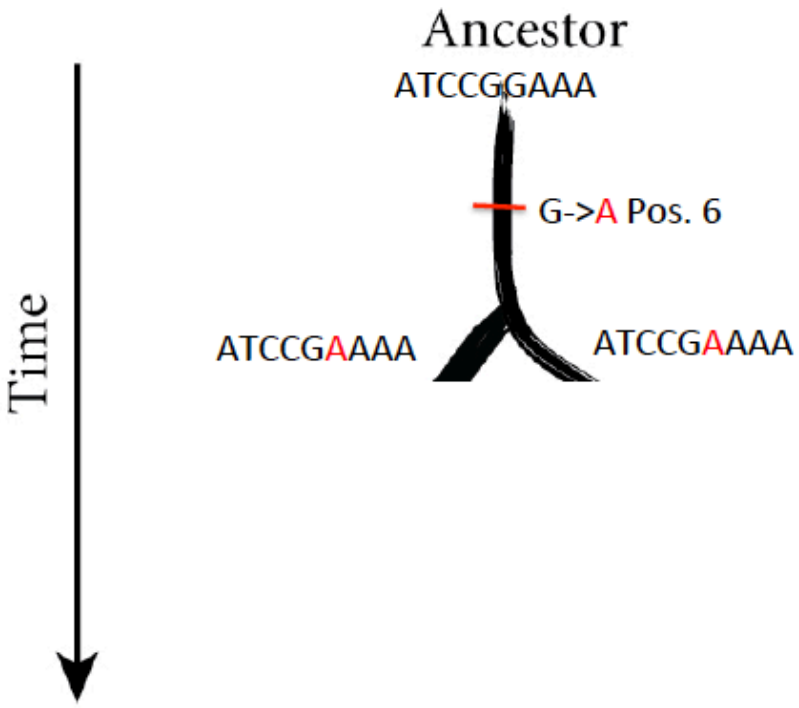
ATCCGAAAA

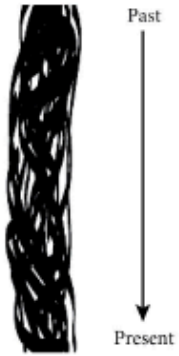
Modified from
Baum and Smith
Tree-Thinking
book

Identity By Descent



Identity By Descent

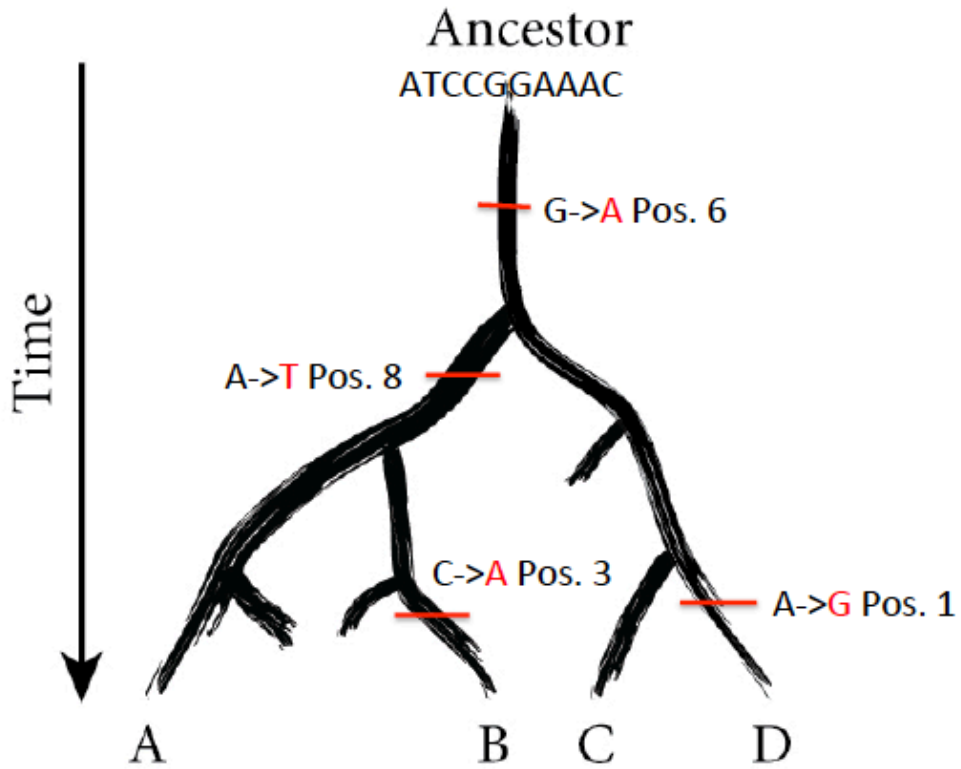




A: ATCCGAAAA
B: ATCCGAAAA
C: ATCCGAAAA
D: ATCCGAAAA

Modified from Baum and Smith Tree-Thinking book

Identity By Descent



A: ATCCGAATA
B: ATACGAATA
C: ATCCGAAAA
D: GTCCGAAAA

Modified from Baum and Smith Tree-Thinking book

Quantifying Similarities and Differences

Genomic Sequences

Haplotype/Locus

Allele:

ATG CAG CGT ATT TCA CAT TTG GGA CAT GTA TTT ACG GCT GAT

Genotype

Orthologous sequences:

ATG CAG CGT ATT TCA CAT TTG GGA CAT GTA TTT ACG GCT GAT

ATG CAG CGT ATT TCA CAT TTG GGA CAT GTA TTT ACG GCT TAT

Population Genetic Data

Multiple Sequence Alignment

Population 1:

ATG CAG CGT ATT TCA CAT TTG GGA CAT GTA TTT ACG GCT GAT

ATG CAG CGT ATT TCA CAT TTG GGA CAT GTA TTT ACG GCT TAT

ATG CAG CGT ATT TCA CAT TTG GGA CAT GTA TTT ACG GCT TAT

ATG CAG CGT ATT TCA CAT TTG GGA CAT GTA TTT ACG GCT TAT

ATG CAG CGT ATT TCA CAT TTG GGA CTT GTA TTT ACG GCT GAT

ATG CAG CGC ATT TCA CAT TTG GGA CAT GTA TTT ACG GCT GAT

ATG CAG CGC ATT TCA CAT TTG GGA CAT GTA TTT ACG GCT GAT

ATG CAG CGT ATT TCA CAT TTG GGA CAT GTA TTT ACG GCC TAT

Population 2:

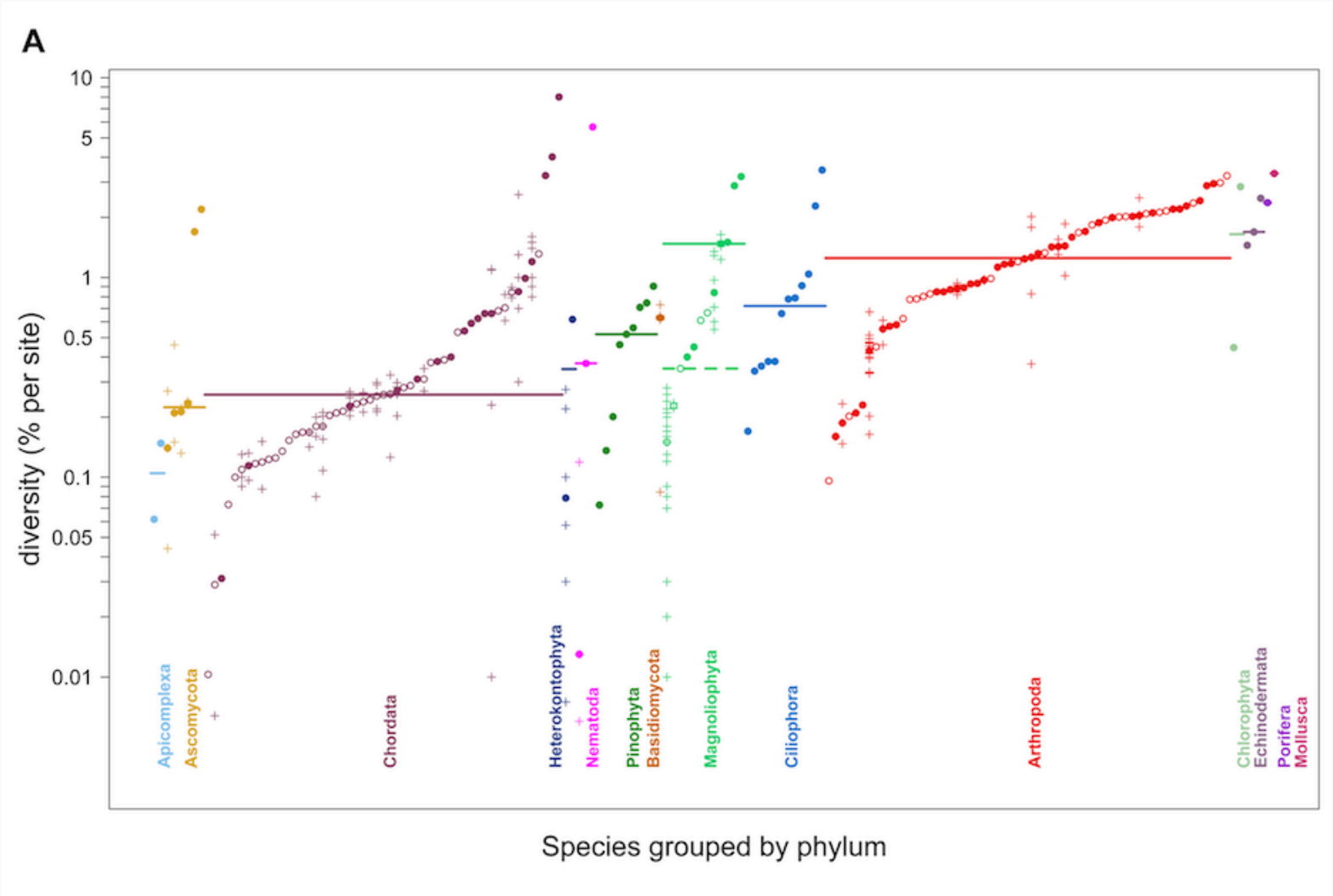
ATG CGG CGT ATT TCG CAT TTG GGA CAT GTA TTC ACG GCT TAT

Summary Statistics

- Homozygosity/heterozygosity
- Frequency
- Polymorphism
- Segregating Sites
- Nucleotide Diversity

How much diversity?

Leffler, Ellen M., et al. "Revisiting an old riddle: what determines genetic diversity levels within species?." PLoS Biol 10.9 (2012): e1001388.[5]



Conclusion

Summary

- Mendelian traits - monogenic, predictable expectations
- Not all traits are Mendelian!
- Evolution = descent with modification
- Ultimate level of variation consists of similarities and differences in the nucleotide sequence of DNA
- Polymorphisms can be synonymous, non-synonymous
- Summary statistics can be used to quantify variation
- Population genetics, empirical and theoretical, have applications in numerous fields.

Questions?

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J. T. Hogg, S. H. Forbes, B. M. Steele, and G. Luikart.
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