Comparative Genomics and Visualisation
BS32010
1.Introduction

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These slides, and supporting material including exercises, are available at https://github.com/widdowquinn/Teaching-2015-03-17-UoD_compgenvis

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What Is Comparative Genomics?

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Comparative genomics is...

The combination of genomic data, and comparative and evolutionary biology, to address questions of genome structure, evolution, and function.

Evolution is the central concept

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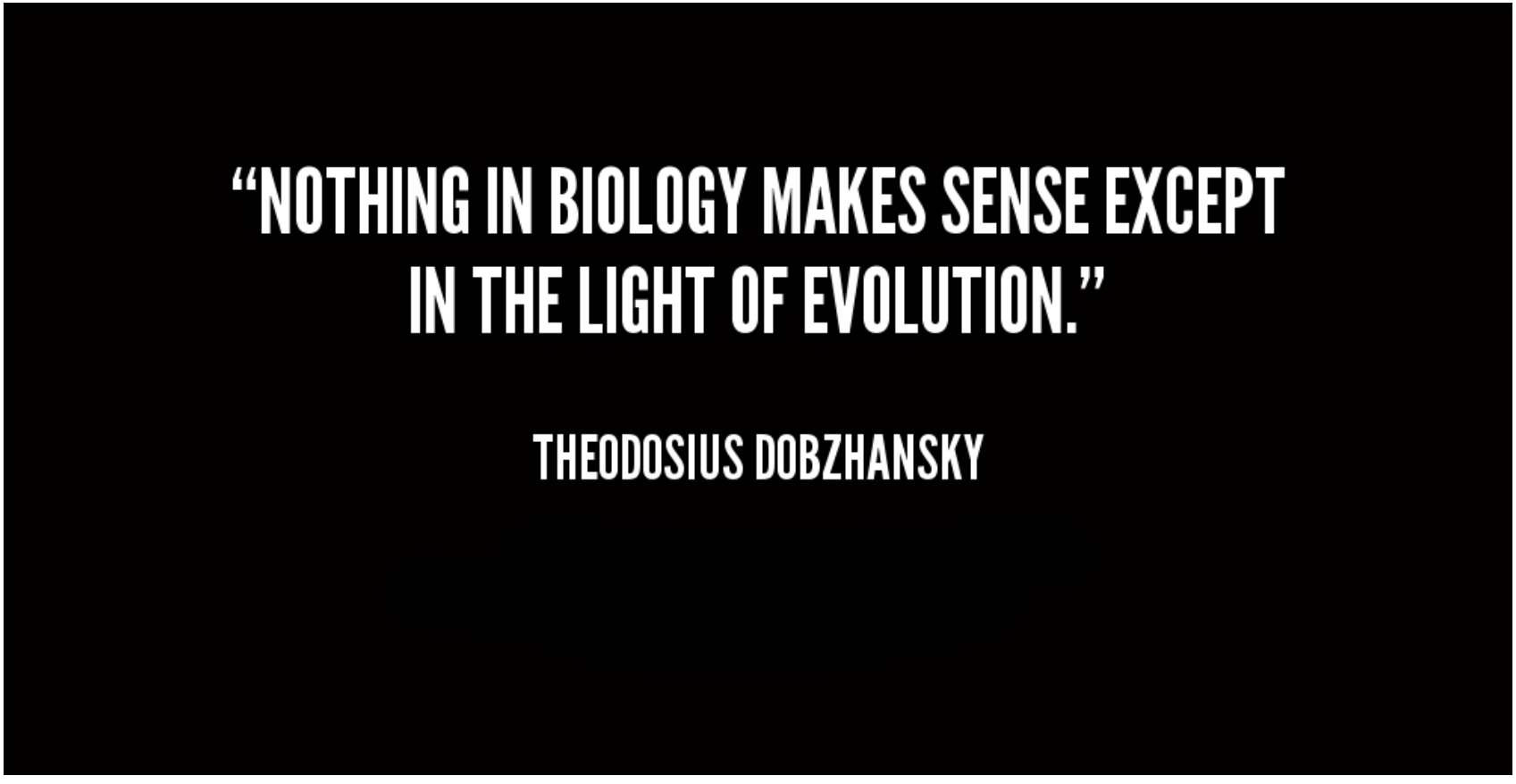

Comparison of physical features

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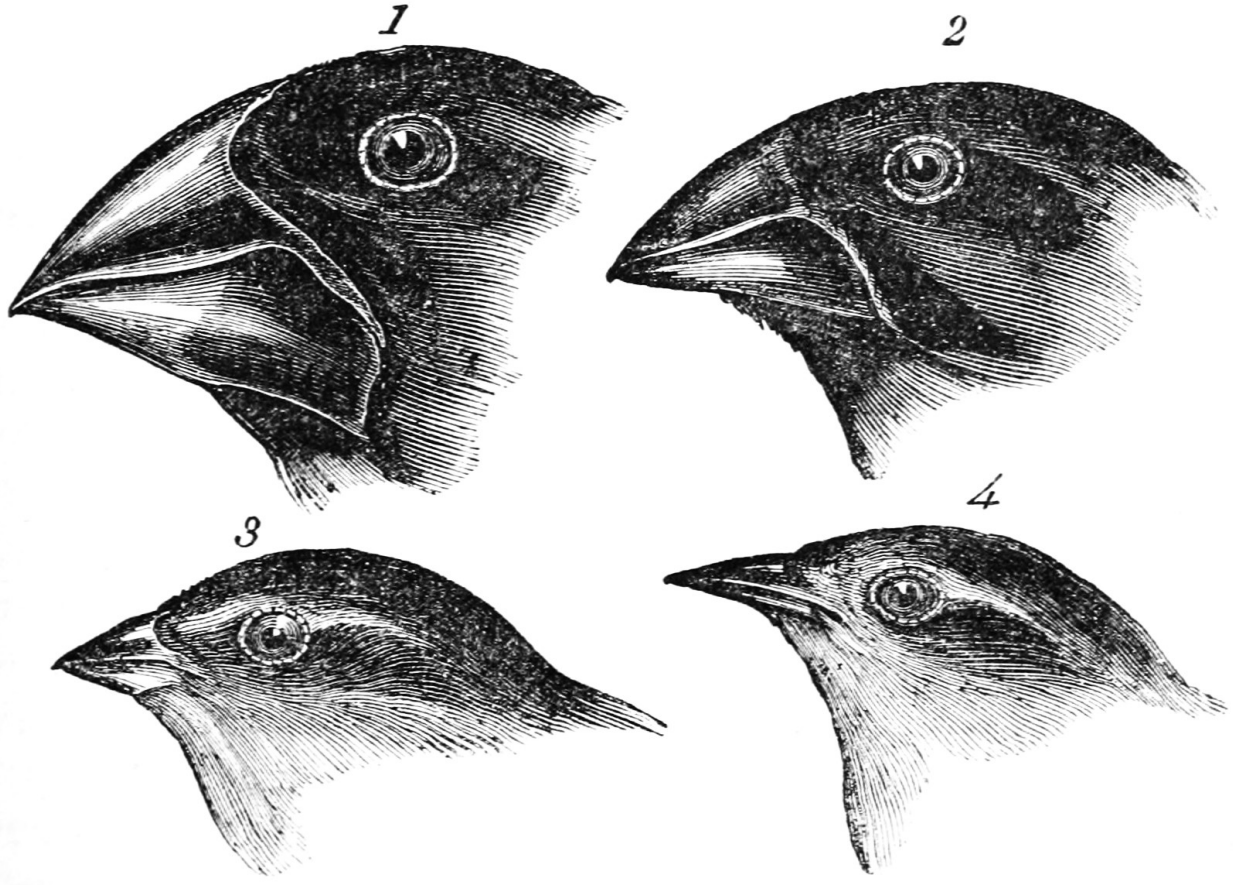
How do we determine that features are related, and evolved?



1. Geospiza magnirostris.
2. Geospiza fortis.
3. Geospiza parvula.
4. Certhidea olivasea.

Comparison of sequence features

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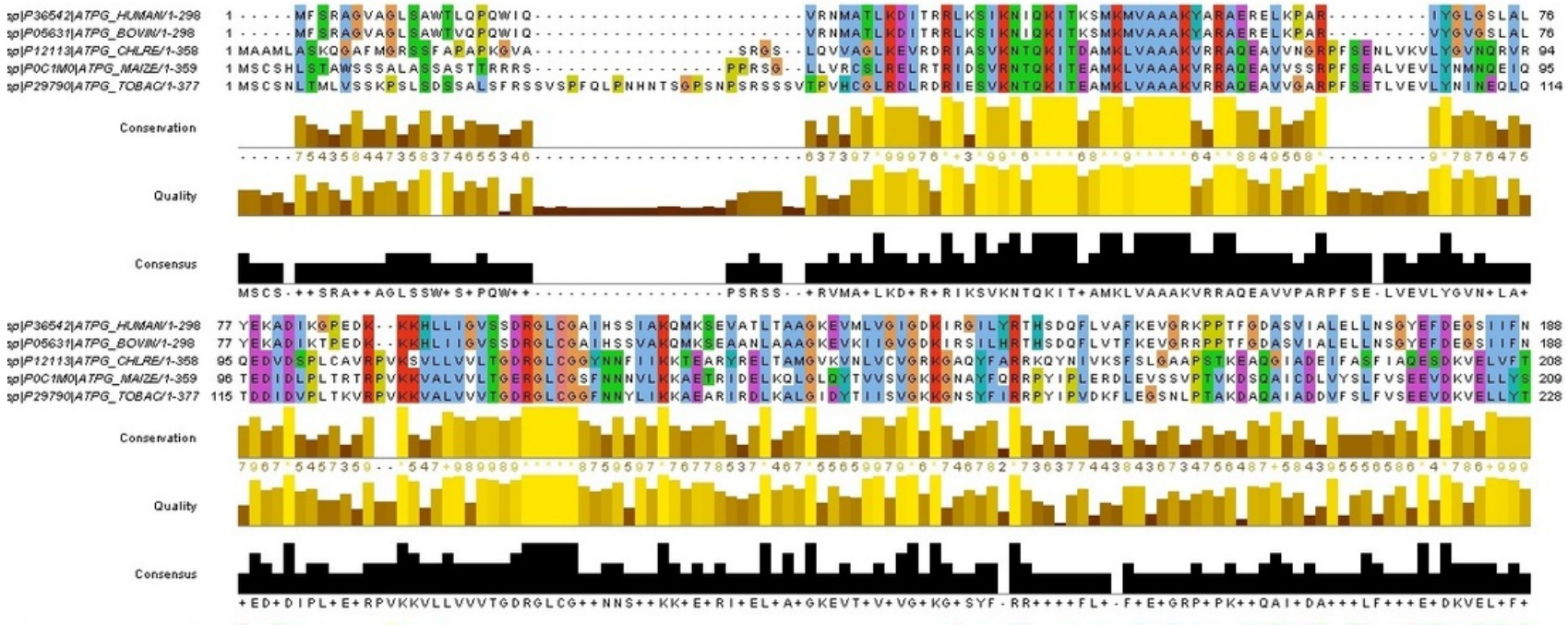
Multiple alignment of ATP synthase



Comparison of genome features

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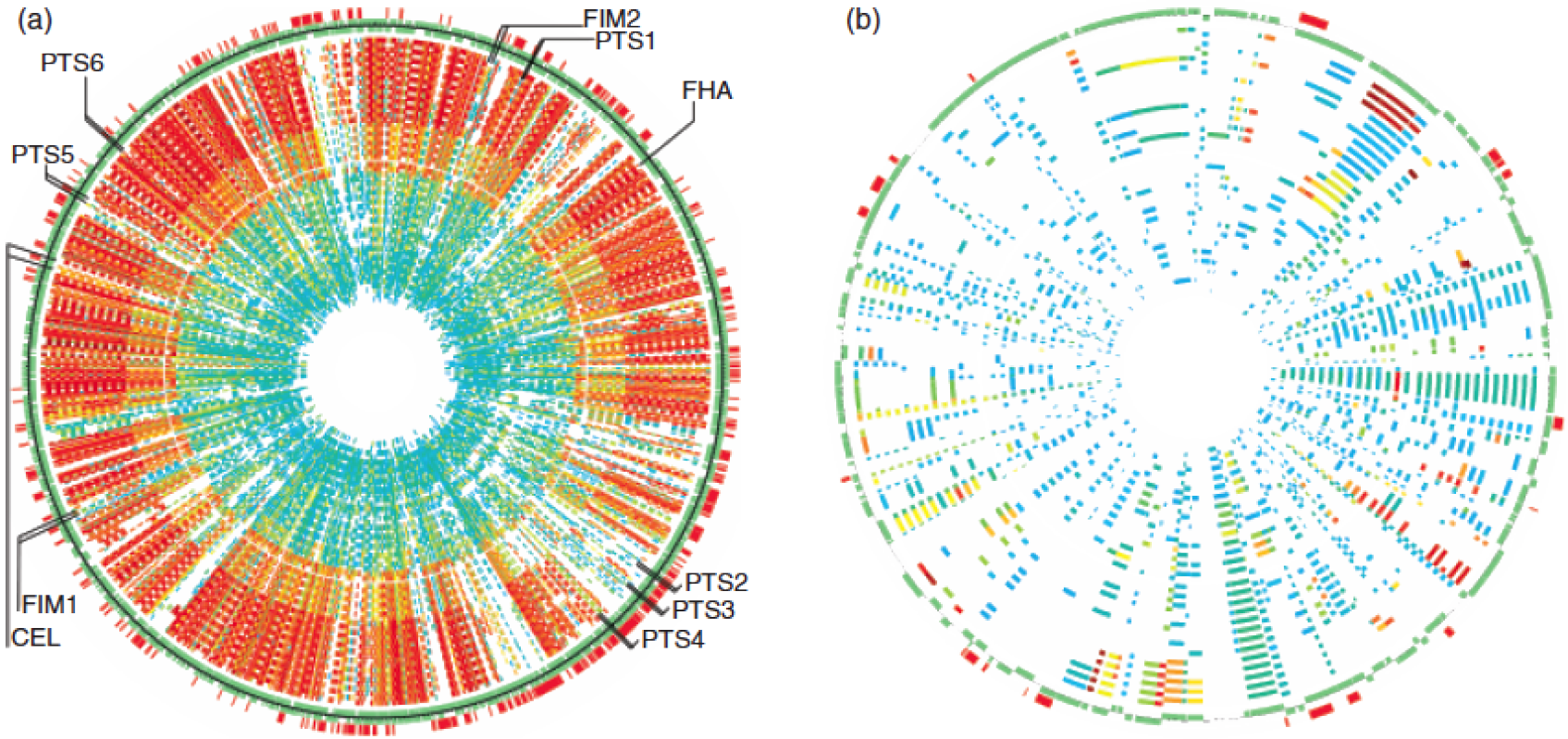
Sequence similarity of individual features



Comparison of genome features

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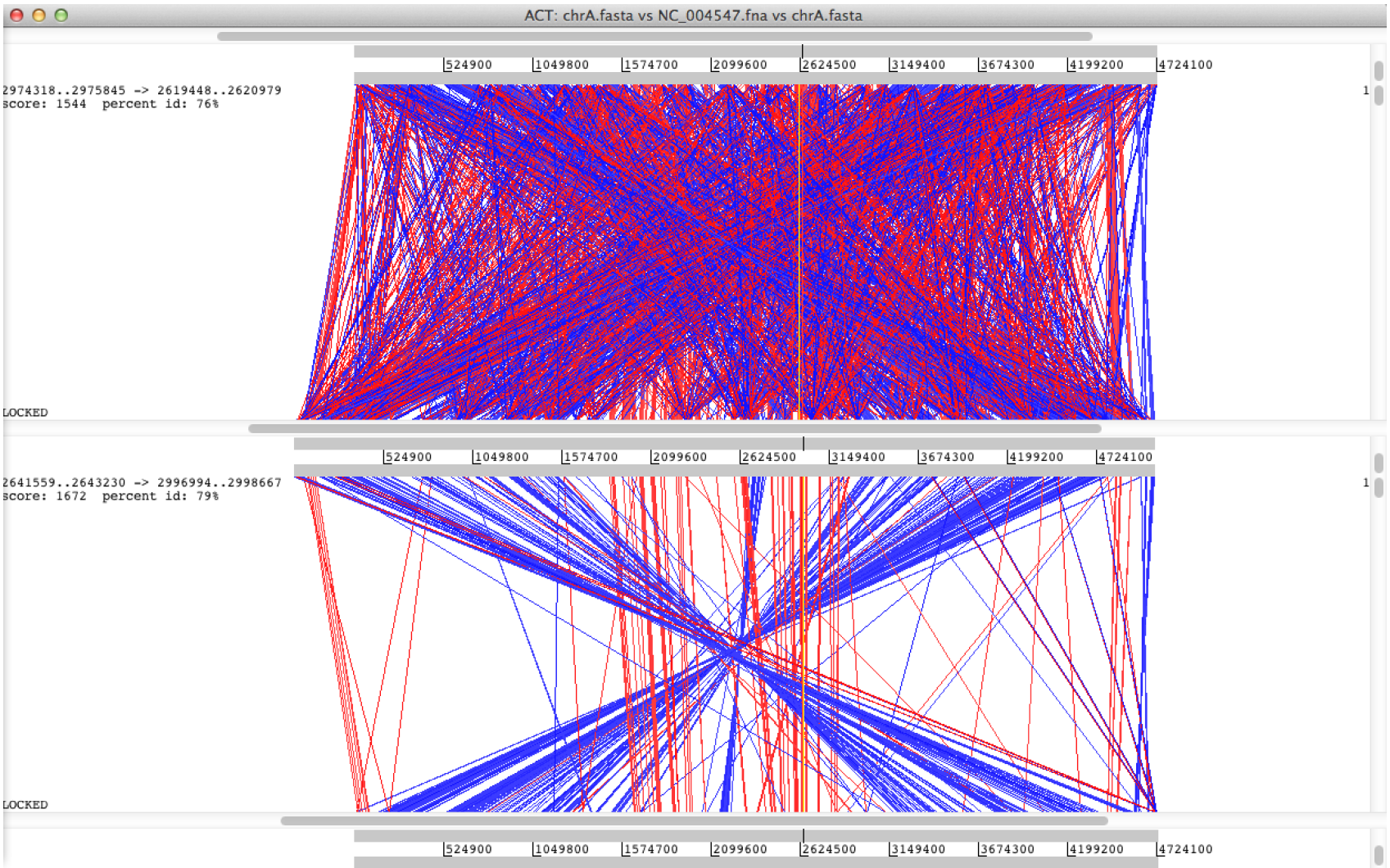
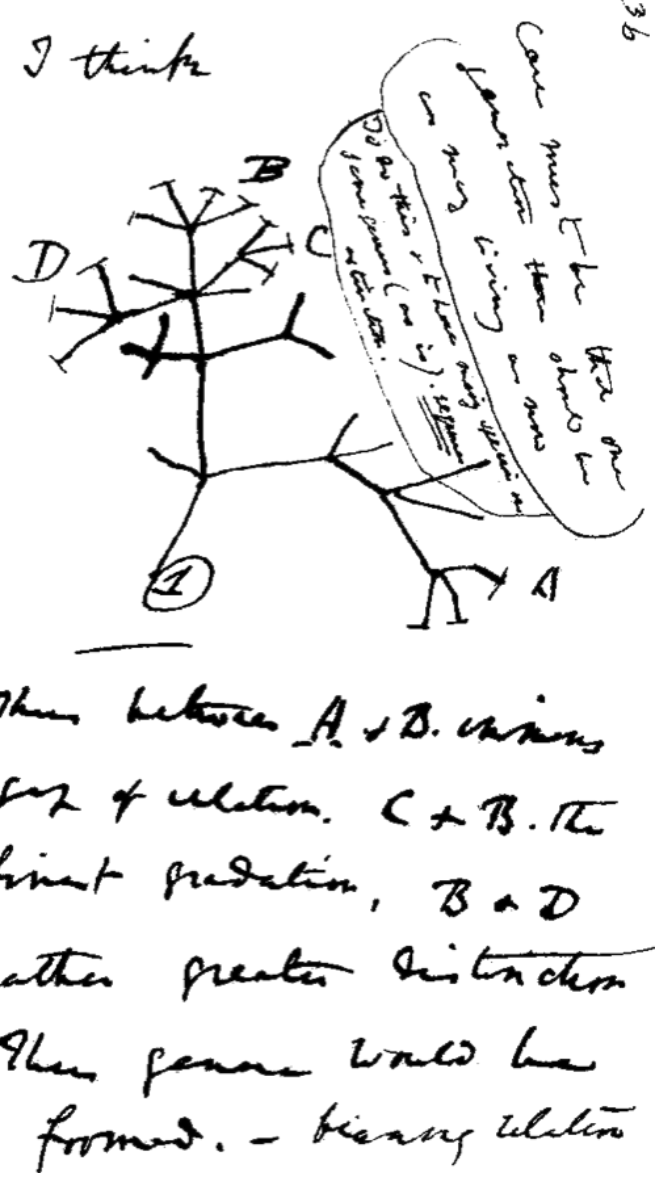
Genome structural rearrangements



Why comparative genomics?

- Genomes describe heritable characteristics
- Related organisms share ancestral genomes
- Functional elements encoded in genomes are common to related organisms



Why comparative genomics?

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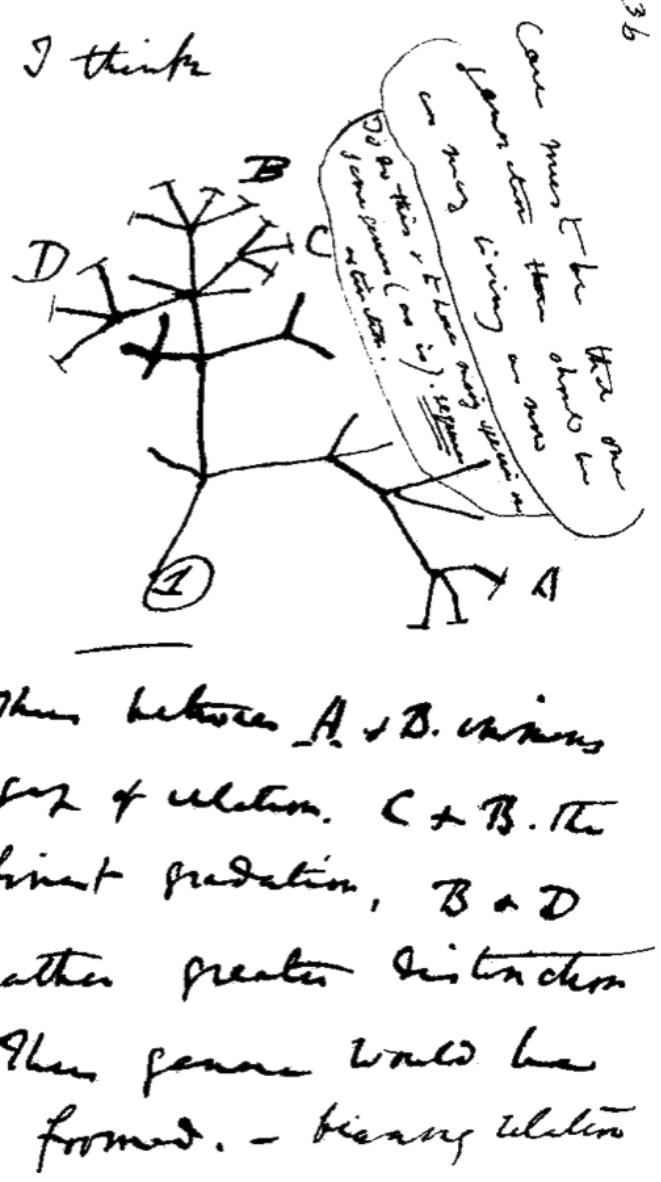
- Transfer of functional understanding from model systems (*E. coli*, *A. thaliana*, *D. melanogaster*) to non-model systems
- Genome comparisons can be informative, even for distantly-related organisms



Genomes are informative, but...

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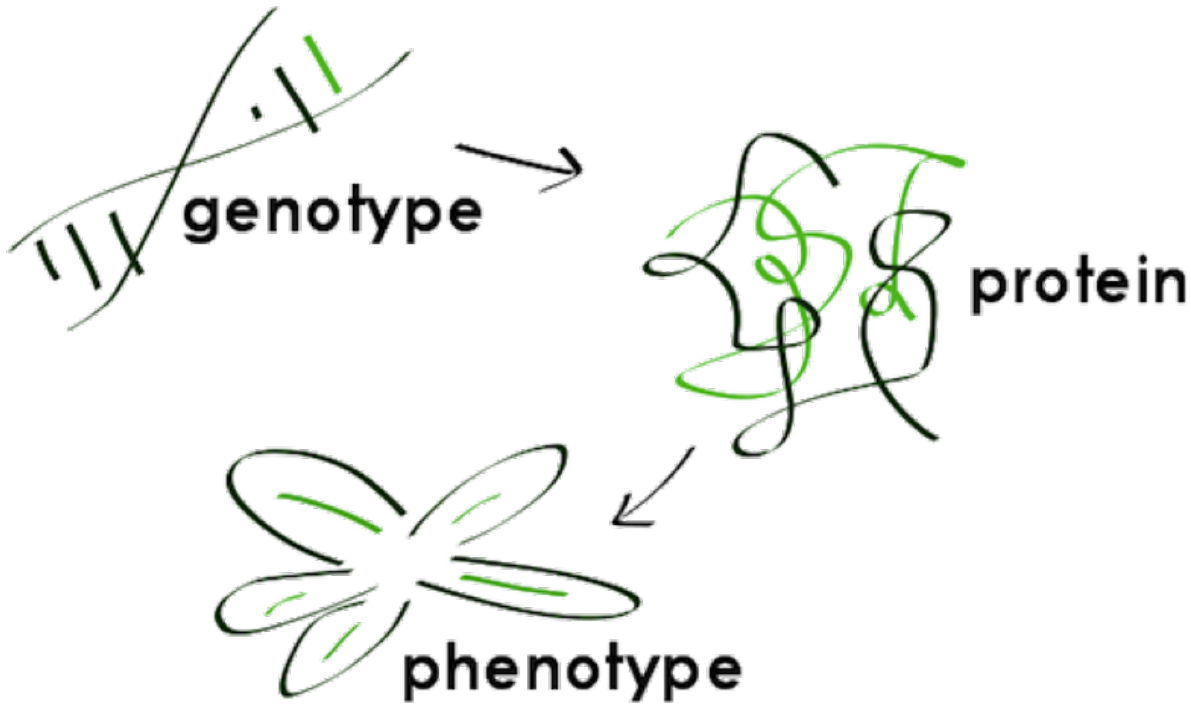
CONTEXT: epigenetics, tissue differentiation, mesoscale systems, etc.



PHENOTYPIC PLASTICITY: responses to temperature, stress, environment, etc.

Genomes to systems

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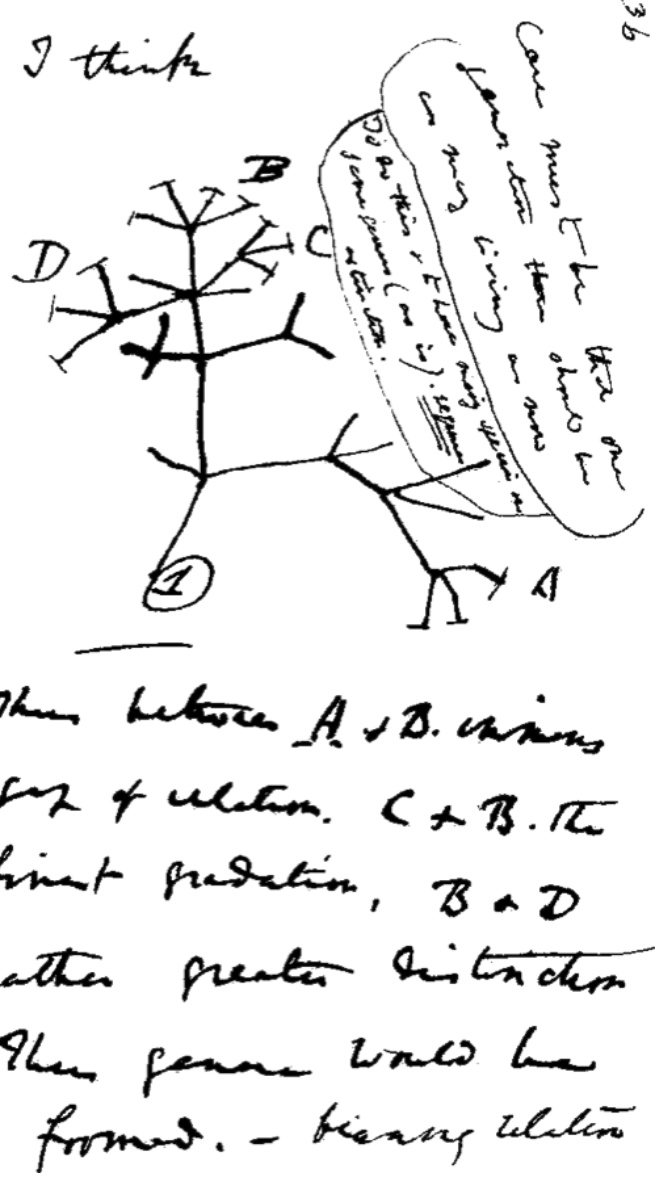
Functional Genomics

- Genomic differences can underpin phenotypic (morphological or physiological) differences.
- Where phenotypes/other organism-level properties are known, comparison of genomes can give mechanistic or functional insight into differences (e.g. GWAS).
- Genomic changes reveal evolutionary processes and constraints.



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Types of comparison

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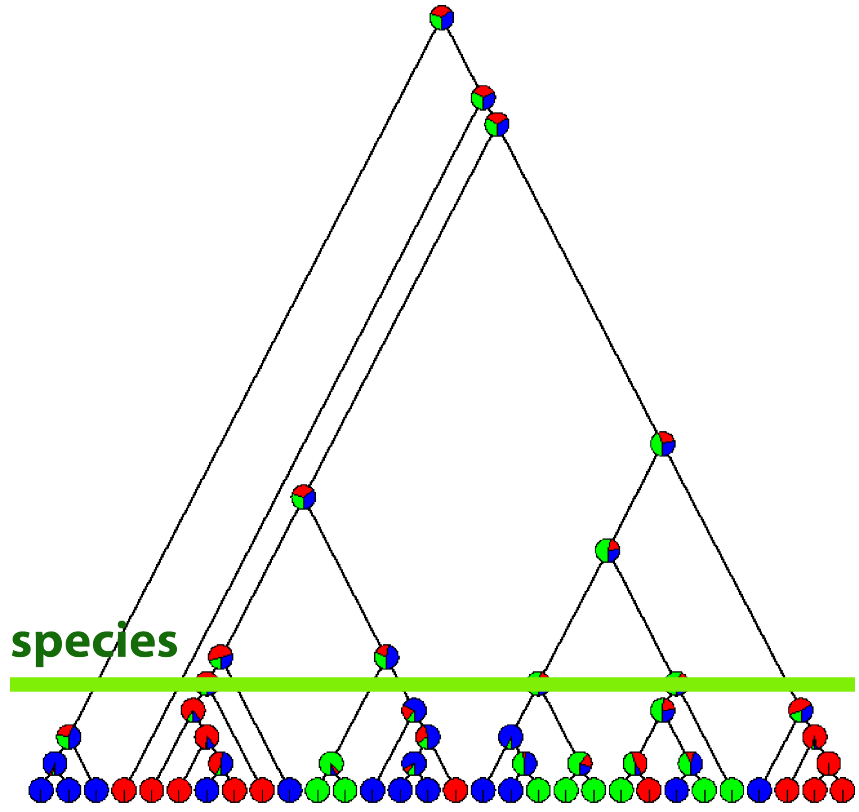
Within species

- e.g. isolate-level (and even within individuals)
- which genome features may account for unique characteristics of organisms/cell-types (e.g. tumours)?
- what epigenetic changes occur in an individual?



Types of comparison

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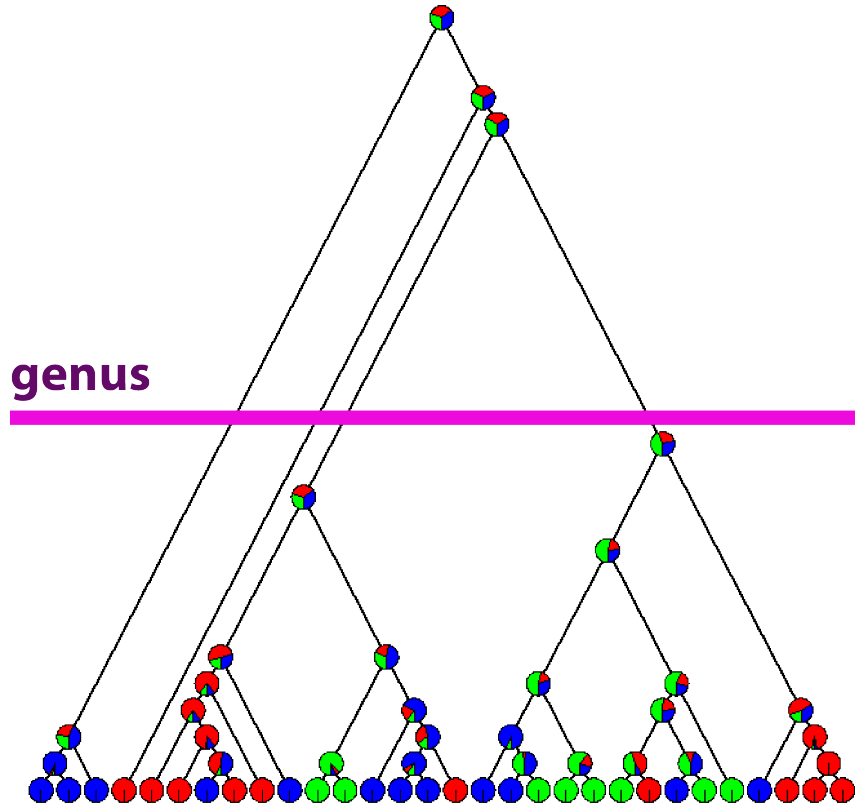
Within genera/between species

- what genome features show evidence of selective pressure?
- which species are under selective pressure for which functions?



Types of comparison

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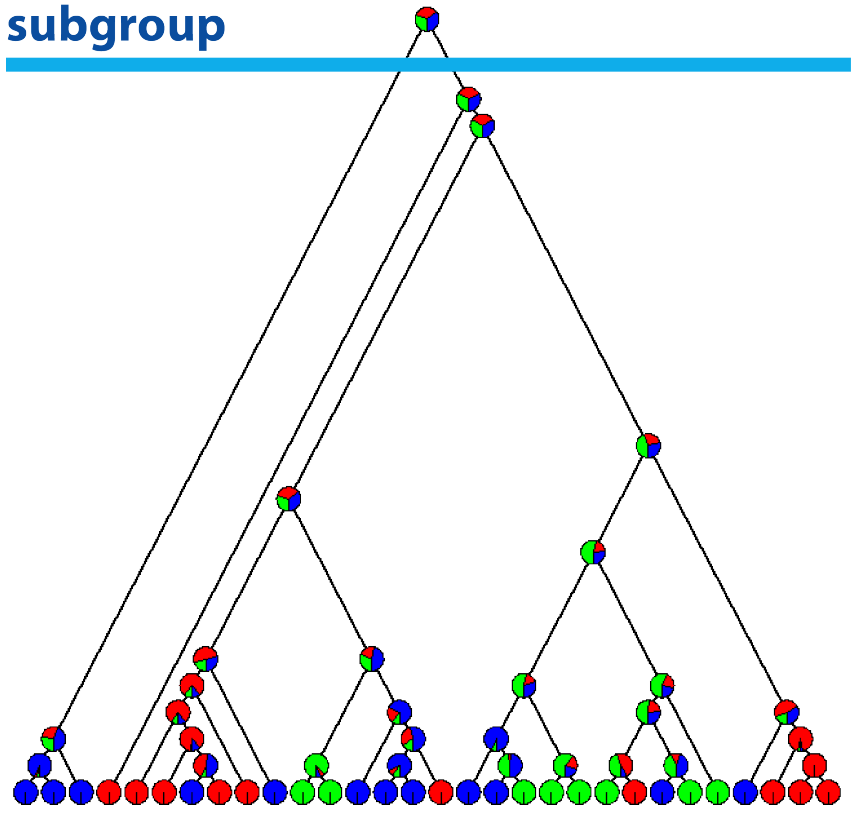
Between subgroups

- what are the core set of genome features that define a subgroup or genus?
- what functions are present/absent between groups?



E. coli LTEE [a] [b] [c]

[a] Jeong *et al.* (2009) *J. Mol. Biol.* doi:10.1016/j.jmb.2009.09.052

[b] Barrick *et al.* (2009) *Nature* doi:10.1038/nature08480

[c] Wiser *et al.* (2013) *Science* doi:10.1126/science.1243357

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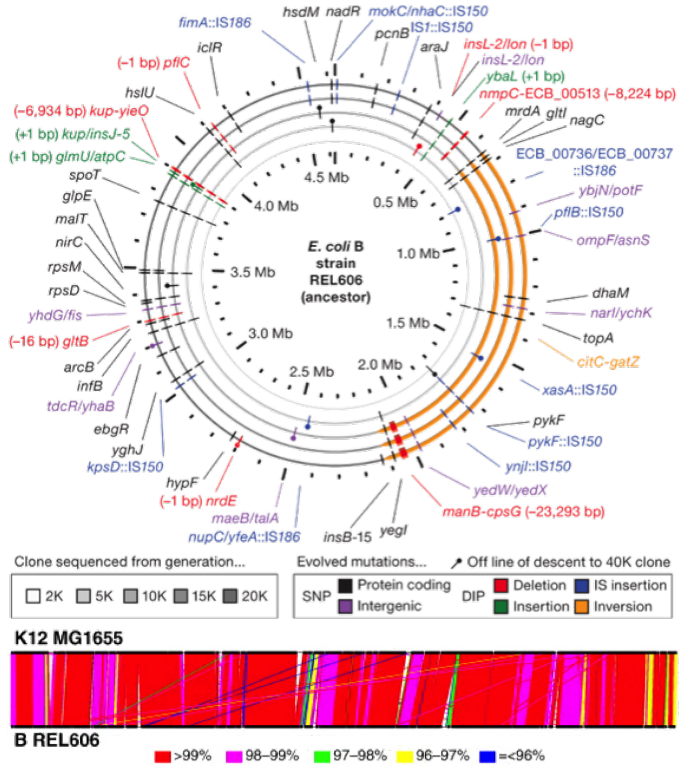
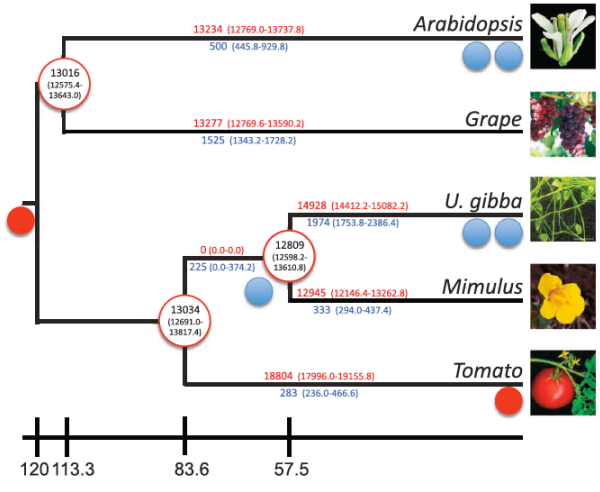
- Run by the Lenski lab, Michigan State University since 1988 (http://myxo.css.msu.edu/ecoli/)
- 12 flasks, citrate usage selection
- >50,000 generations of *E coli*!
  - Cultures propagated every day
  - Every 500 generations (75 days), mixed-population samples stored
  - Mean fitness estimated at 500 generation intervals



Comparative genomics in the news [a] [b] [c]

[a] Washington Post 23/2/2015
[b] Ibarra-Laclette *et al.* (2013) *Nature* doi:10.1038/nature12132
[c] Carretero-Paulet *et al.* (2015) *Mol. Biol. Evol.* doi:10.1093/molbev/msv020

- *Utricularia gibba*: carnivorous bladderwort
- Genome: 82Mbp, 17,324 genes (wheat: 17bn bases, ≈94-96k genes)
- Intergenic region contraction (3% repeat elements; most plants: 10-60% repeat elements)
- Genomic context for flowering plants does not require "hidden regulators" (cf. ENCODE)



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Levels of comparison

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Bulk Properties

- chromosome/plasmid counts and sizes, nucleotide content, etc.

Whole Genome Sequence

- sequence similarity
- organisation of genomic regions (synteny), etc.

Genome Features/Functional Components

- numbers and types of features (genes, ncRNA, regulatory elements, etc.)
- organisation of features (synteny, operons, regulons, etc.)
- complements of features
- selection pressure, etc.

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