Comparative Genomics

Isheng Jason Tsai

Week5 [2020 version]

Lecture outline

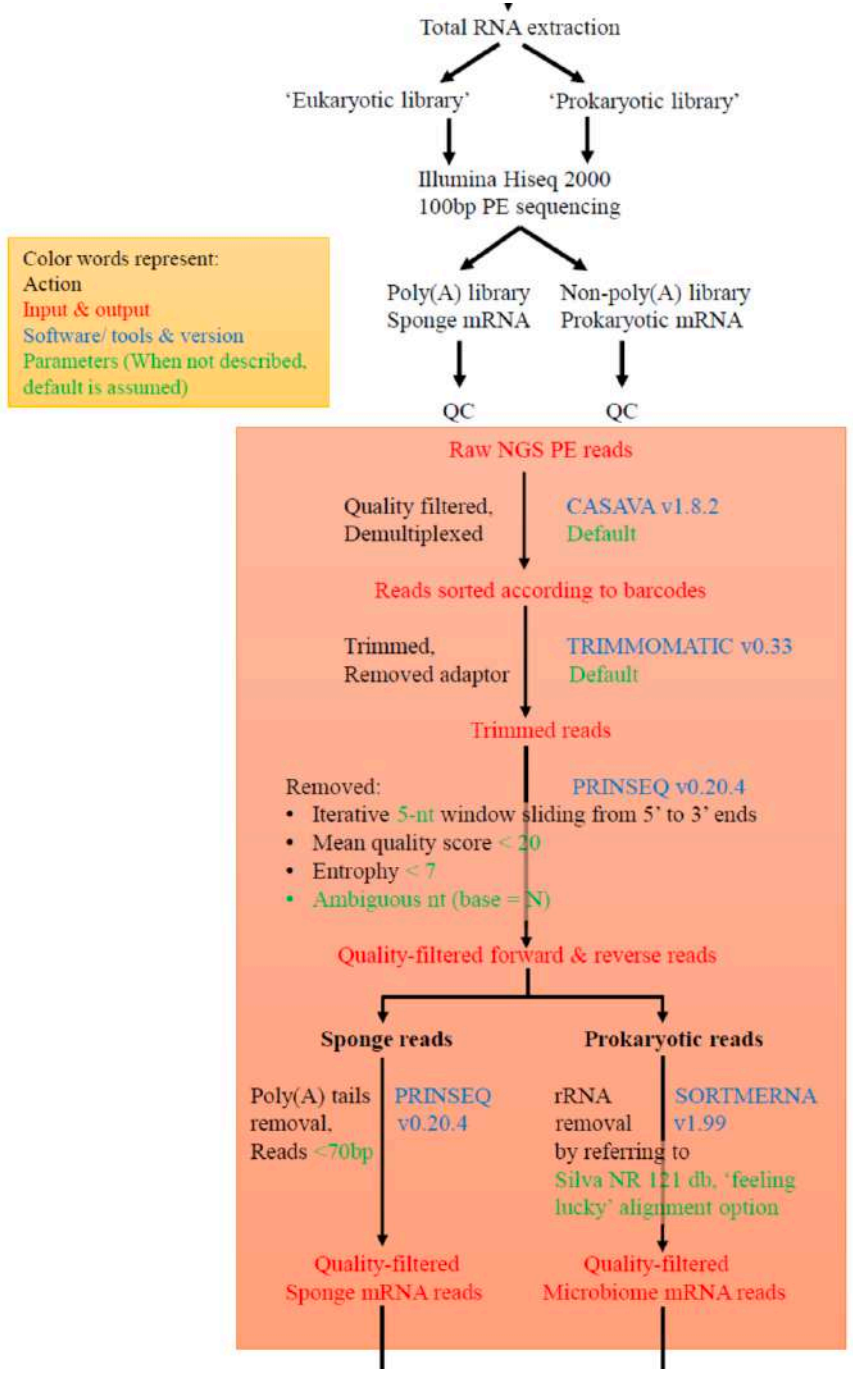
Announcements

1. Concept of homology
2. Inferring homology
    1. Orthology prediction methods
    2. Caveats
3. Inferring synteny
4. Visualisation

5. Applications
    1. Phylogenomics
    2. Genome duplications
    3. Case studies

Assignment update: I: protocols

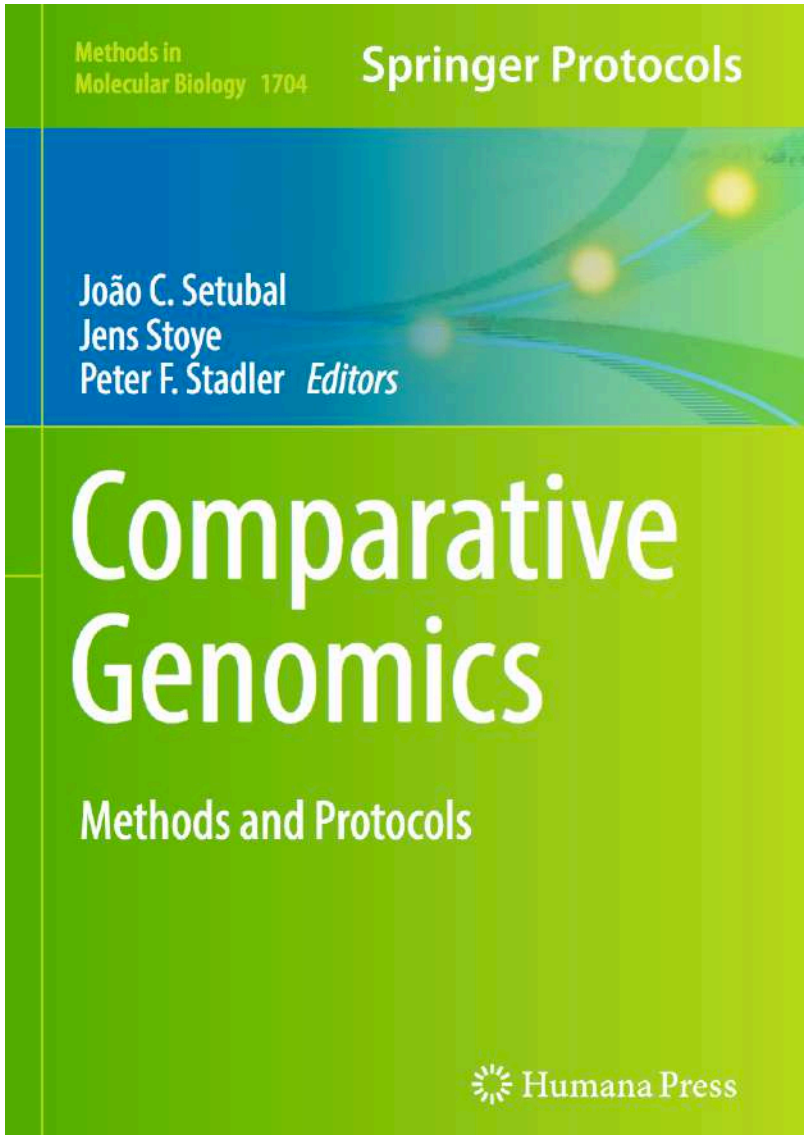
RNA-seq			
Procedure	**Description**	**Input/sample**	**Output/product**
1. RNA extraction	RNA was isolated from cell pellets using Qiagen RNeasy Kit and homogenized with	iPSC lines derived from 4 non-disease	Purified RNA



I look for good understanding of the methods, with cle versioning, input and output. And any strengths and weaknesess

Week	Date	Topic
~~Week 1~~	~~3/4~~	~~Introductory lecture (Jason)~~
~~Week 2~~	~~3/11~~	~~Linux and R; basic usage (Jason)~~
~~Week 3~~	~~3/18~~	~~*Practical I: Statistics in R (Jason)~~
~~Week 4~~	~~3/25~~	~~Mapping and Case studies (Jason)~~
~~Week 5~~	~~4/1~~	~~Genome Assembly (Jason)~~
Week 6	4/8	Comparative Genomics (Jason) <- this week
Week 7	4/15	Transcriptomes (Jason)
Week 8	4/22	Alignment to phylogenies (Professor Jia-Ming Chang)
Week 9	4/29	Amplicon / Metagenomic (Jason)
Week 10	5/6	Population Genomics (Dr. John Wang)
Week 11	5/13	*Study week (no class; Protocol assignment due)
Week 12	5/20	*Midterm exam (Students)
Week 13	5/27	*Final presentation I (Students)
Week 14	6/3	*Final presentation II (Students)
Week 15	6/10	*Practical I: Statistics in R (Jason)
Week 16	6/17	*Practical II: RNAseq analysis in R (Jason)
Week 17	6/24	Experiences in NGS library preparation and construction (Dr. Meiyeh Lu)
Week 18	7/1	*Study week (no class; R assignment due)

Recommended book



https://link.springer.com/book/10.1007%2F978-1-4939-7463-4

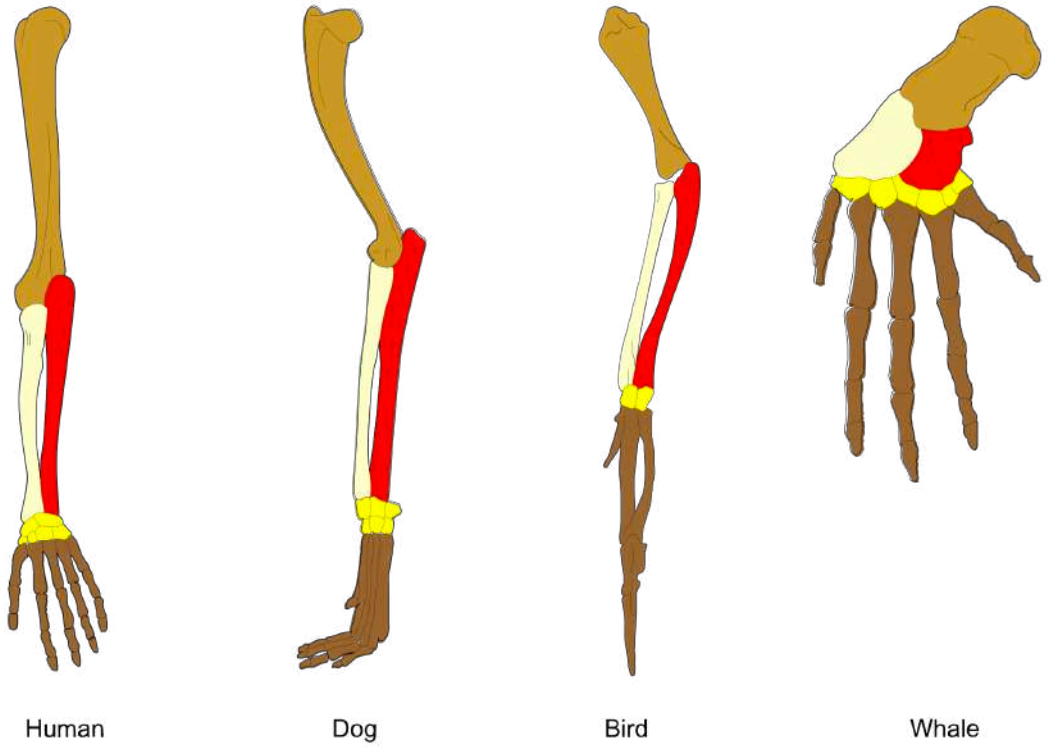
Homology

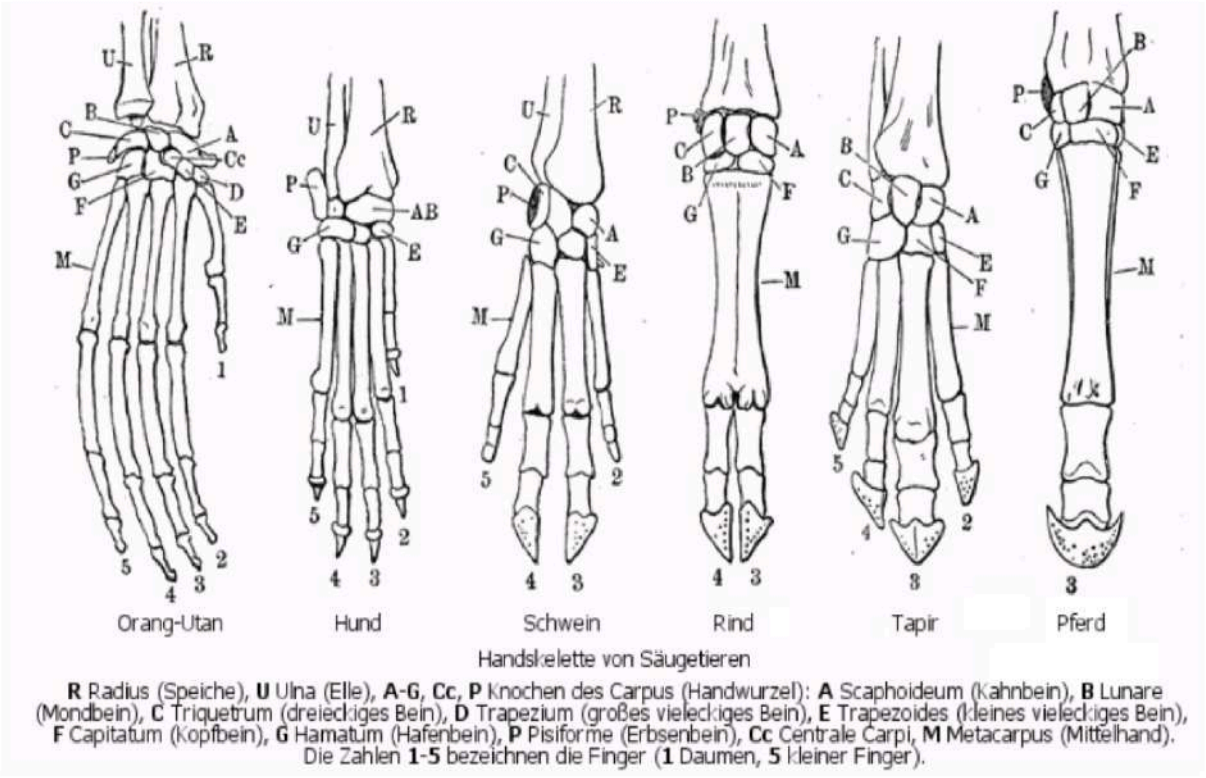
Termed before Darwin's time!

Sir Richard Owen KCB FRS (20 July 1804 – 18 December 1892) was an English biologist, comparative anatomist and paleontologist.

Wiki

Homology



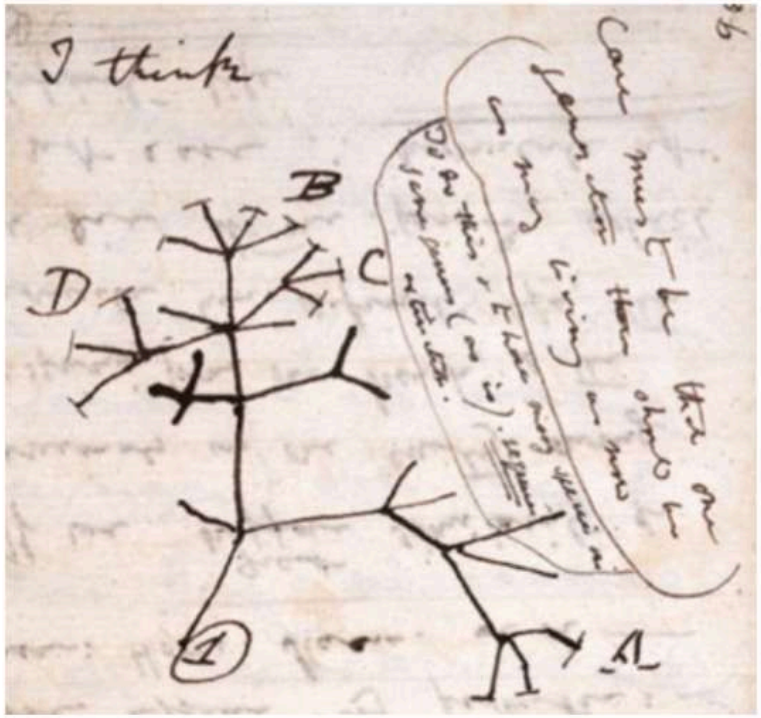


“the same organ in different animals under every variety of form and function” – Richard Owen

Owen 1843, p.379

https://en.wikipedia.org/wiki/Homology_(biology)

Darwin later reformulated homology as a result of **“descent with modification”**



CHAPTER VI.

DIFFICULTIES ON THEORY.

CHAPTER XIII.

MUTUAL AFFINITIES OF ORGANIC BEINGS: MORPHOLOGY: EMBRYOLOGY: RUDIMENTARY ORGANS.

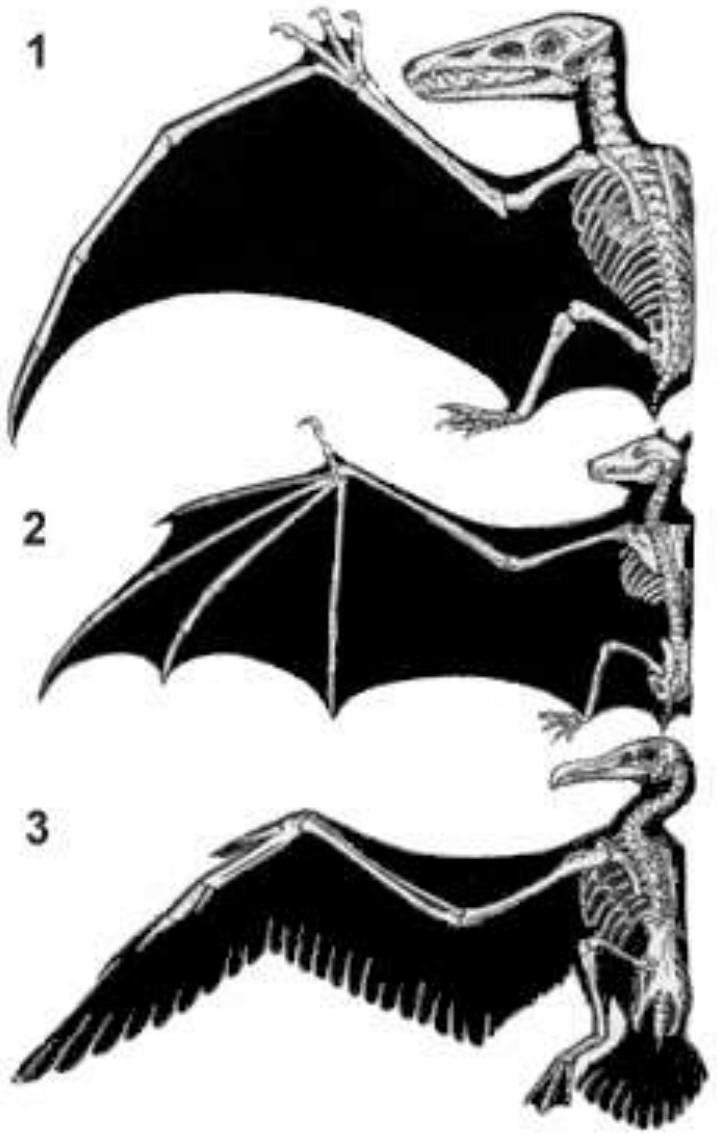
CLASSIFICATION, groups subordinate to groups—Natural system—Rules and difficulties in classification, explained on the theory of descent with modification—Classi-

http://darwin-online.org.uk/

Homology

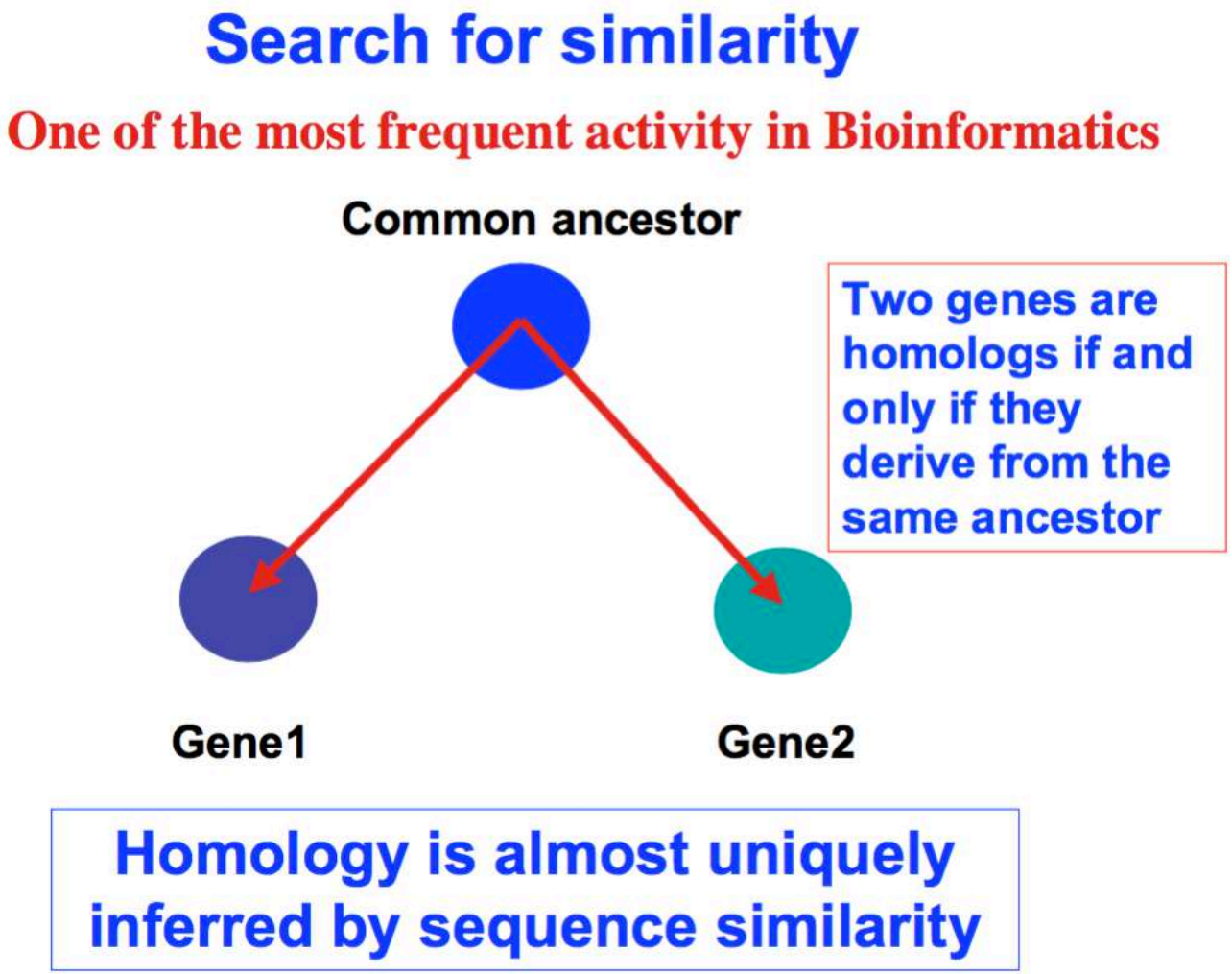
The wings of pterosaus (1), bats(2) and birds (3) are **analogous** as wings, but **homologous** as forelimbs.

Homologs (any features: genes, trait, morphology) share **ancestry**



https://en.wikipedia.org/wiki/Homology_(biology)

Search for similarity , collinearity, conservation of morphological characters



Slide of Fred Tekaia

Beware ; why?

~~Significant homology~~

~~Weak homology~~

If you think about the meaning of homology, **then it really makes no sense**

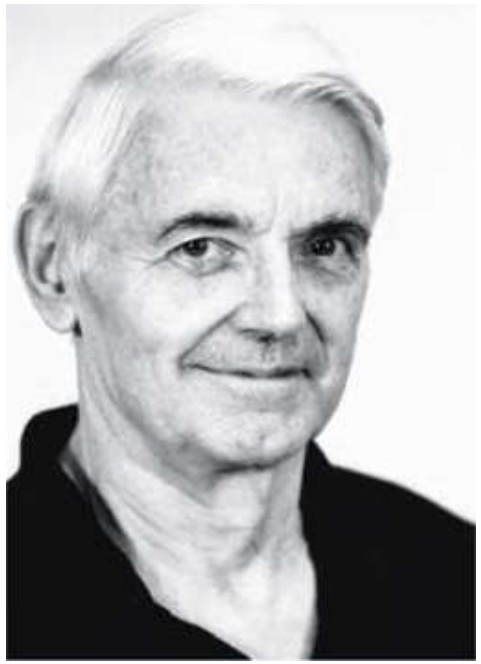
Significant similarity

Weak similarity

55% married?
45% grandmom?

DISTINGUISHING HOMOLOGOUS FROM ANALOGOUS PROTEINS (1970)

WALTER M. FITCH



1929 - 2011

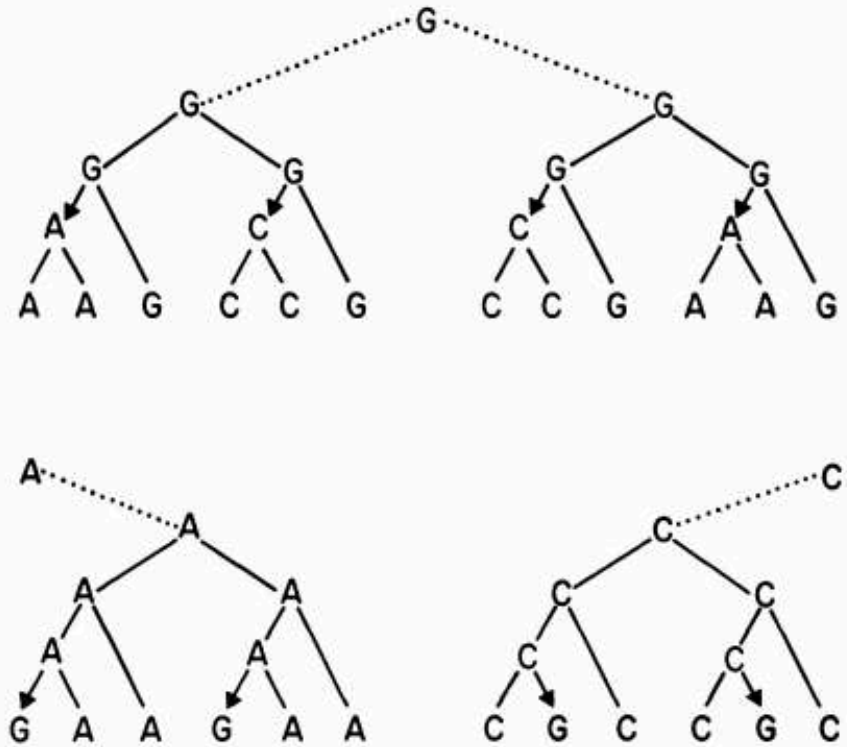
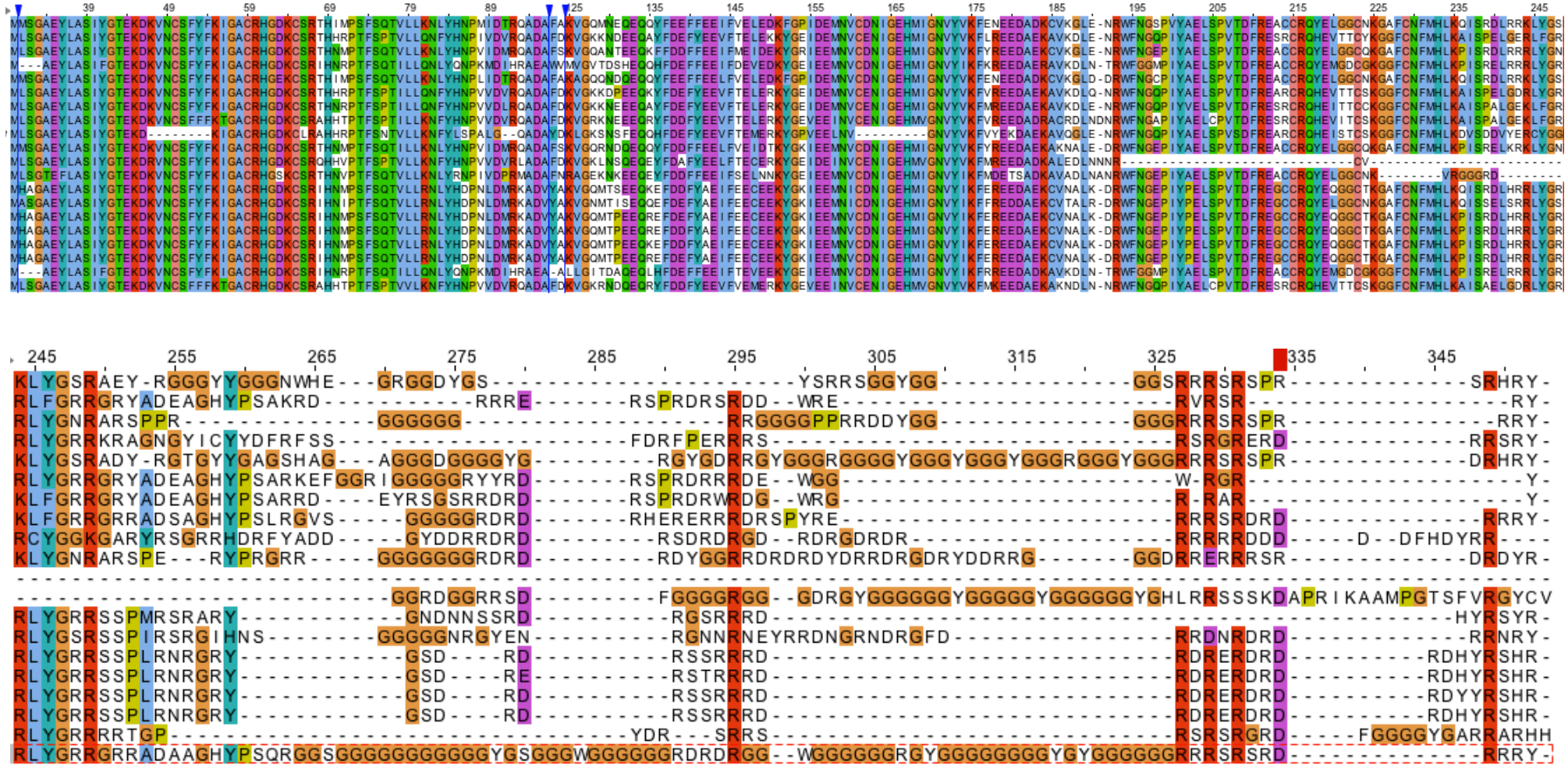


FIG. 1.—Distinguishing convergent from divergent types of nucleotide replacement patterns. Given are two groups of species (related within each group as shown by the solid lines) together with the nucleotide present at a specific position of the gene for each member species as shown at the branch tips. Given also the requirement that the ancestral nucleotide must permit the descendant nucleotides to be obtained in the minimum number of replacements, the ancestral nucleotide of the upper two groups must be set as G, with the required replacements indicated by the arrows. Were one to postulate a common ancestor for the two groups, no new mutations would need to be assumed; hence, this kind of pattern is called the divergent types. The lower two groups are identical except for rearranging the nucleotides at the branch tips, but now, in order to account for descendants in only four nucleotide replacements, the ancestral nucleotide of the lower two groups must be A and C. To postulate a common ancestor for these two groups would require, unlike the upper pair, an additional mutation. This situation shows different ancestral characters apparently converging toward the same descendant character, and hence is called the convergent type. One can calculate the frequency with which one might expect each type to be found in examining a large number of such nucleotide positions and compare that value to what is in fact found for a particular set of proteins. An abnormally large number of either type is evidence favoring that type of relation between the two groups examined.

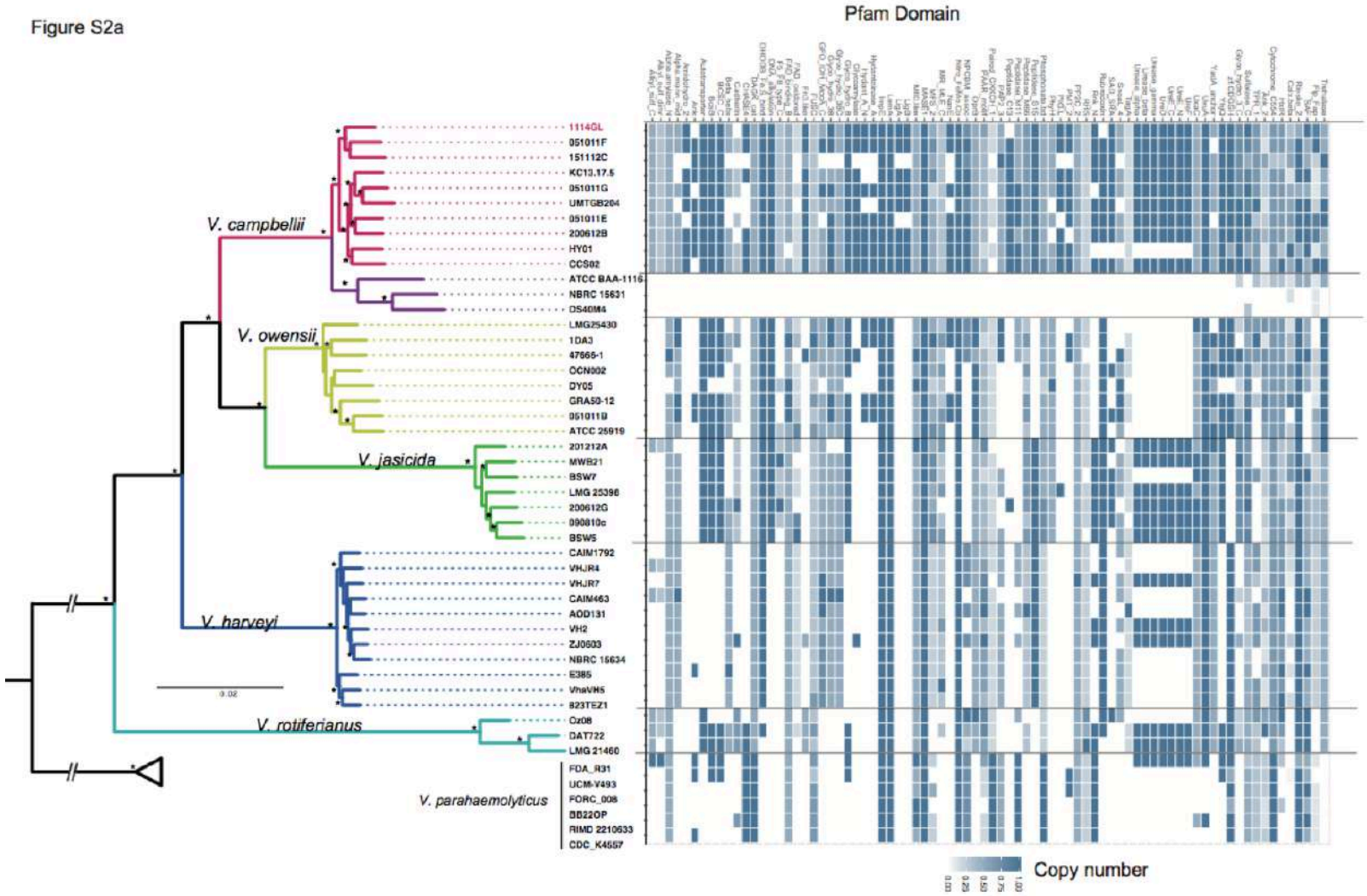
Extension of homology to sequences

Two sequences are homologous if they share the same a common ancestor



Extension of homology to genomes / species

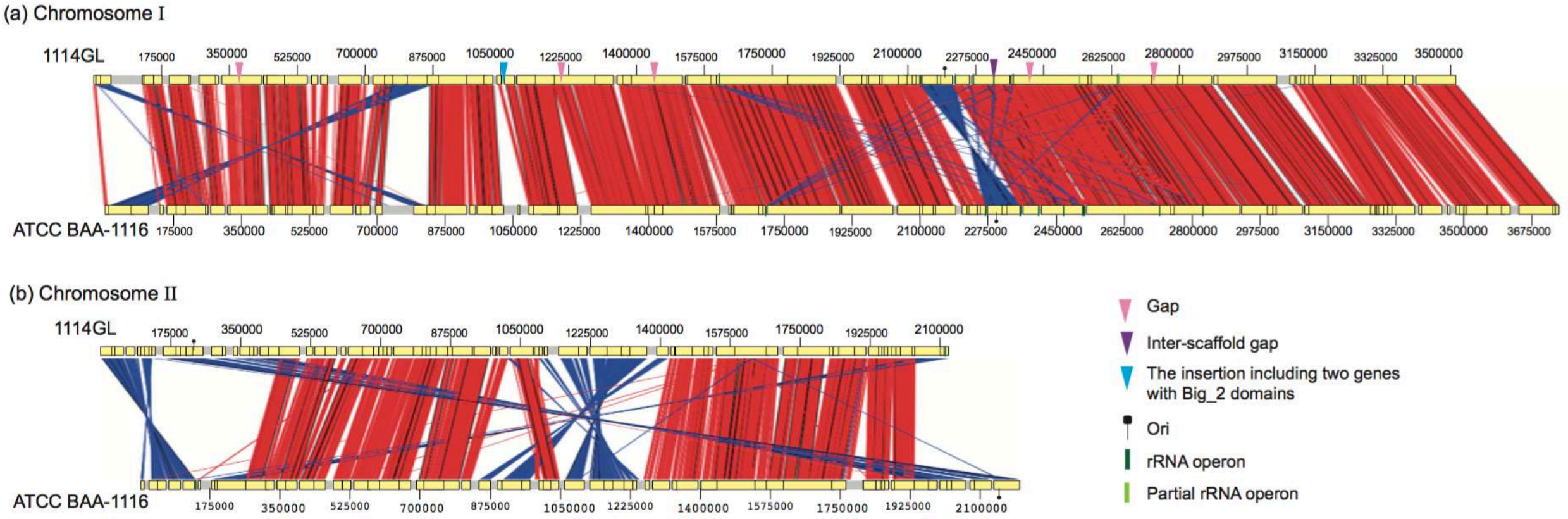
Similarity of individual sequences at different levels (sequence similarity ; domain combinations)



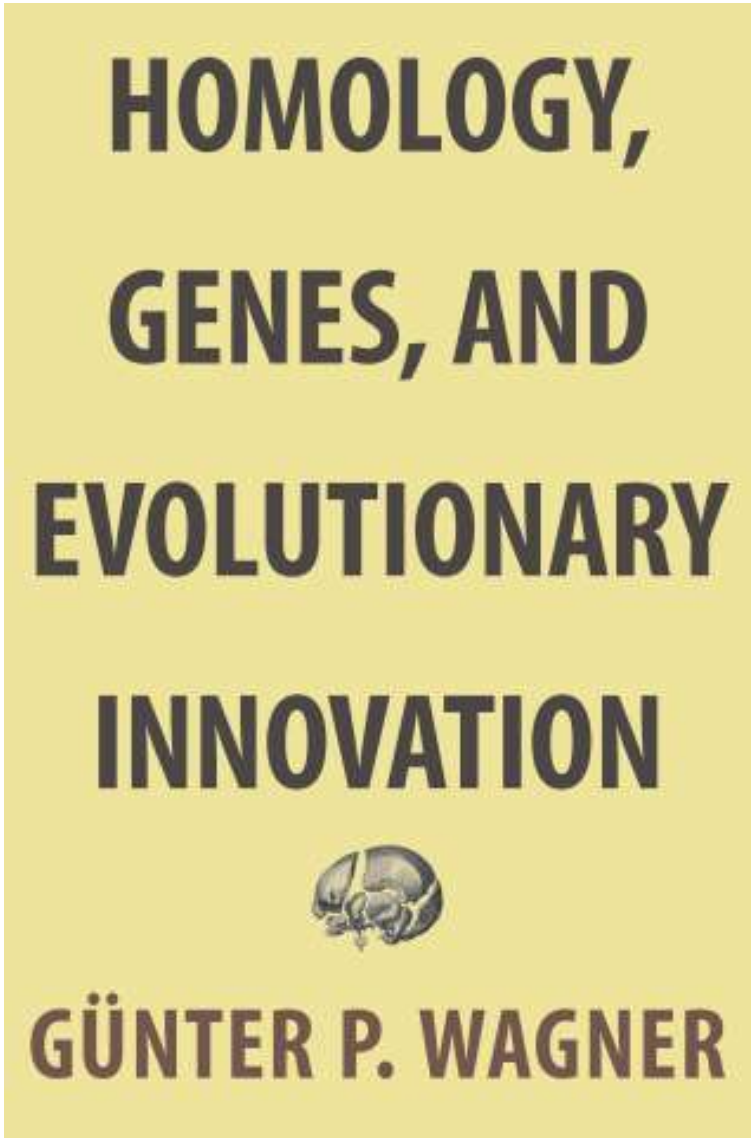
Hueimien Ke

Extension of homology to genomes / species

Similarity of individual features (ordering and rearrangement)



Hueimien Ke



Günter Wagner has thought long and hard about homology in relation to character identity, and in his new book he goes into great detail about why we should use **character identity as the basis for the homology of morphological characters.** For readers of *Systematic Biology*, the book is also a reminder that every **morphological character used in a phylogenetic analysis is a hypothesis of homology, and that great care is needed when deciding whether morphological characters in different organisms are likely to be homologs.**

…He also writes that "This book, although ostensibly about homology, is really a book on evolutionary developmental biology" (p. 3). Wagner argues that "the origin of novel characters and novel body plans is one of the most important but least researched questions in evolutionary biology" (p. 3)….

https://academic.oup.com/sysbio/article/64/2/365/1633524

Why comparative genomics? – A summary

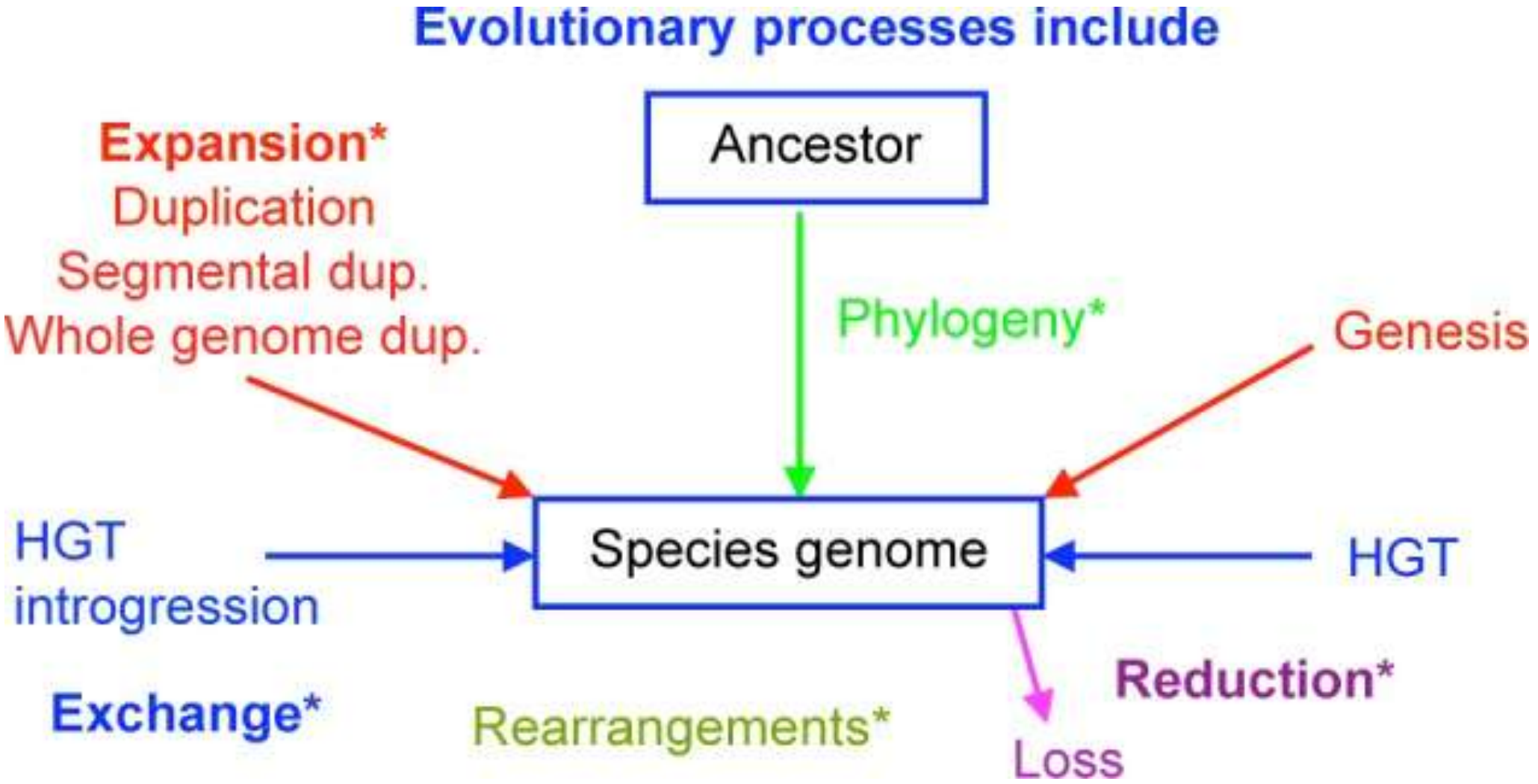
Compare multiple genomes now a norm

Similarity and differences between genomes

Use genomes to study evolution of these species:

- At various resolution (whole genome, chromosomes, regions, genes, base pairs)
- Identify the genomic basis of key phenotypes

Evolution process of a genome

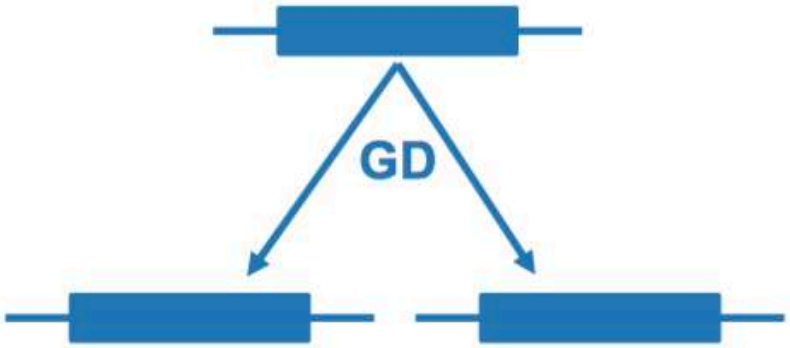


Tekaia (2016)

Sources of gene innovation
(Intuitive as genome gain genes of new functions)

Gene duplication (GD)

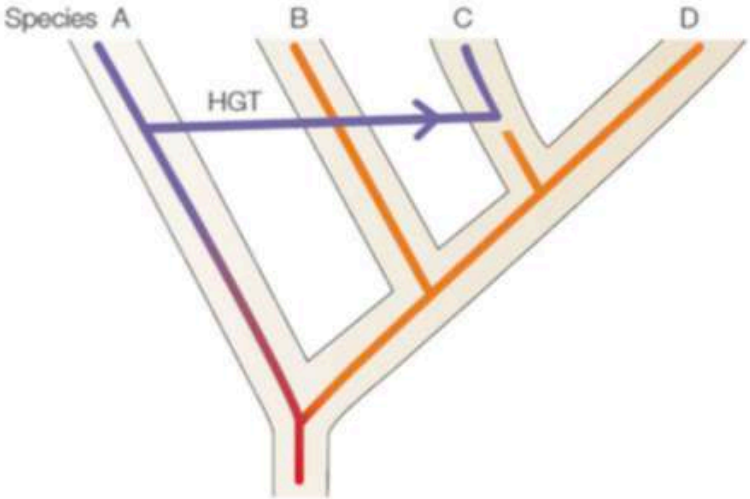
Any duplication of a region of DNA that contains a gene



- Plant organic material decay
- Starch catabolism
- Degradation of host tissues
- Toxin production

Horizontal gene transfer (HGT)

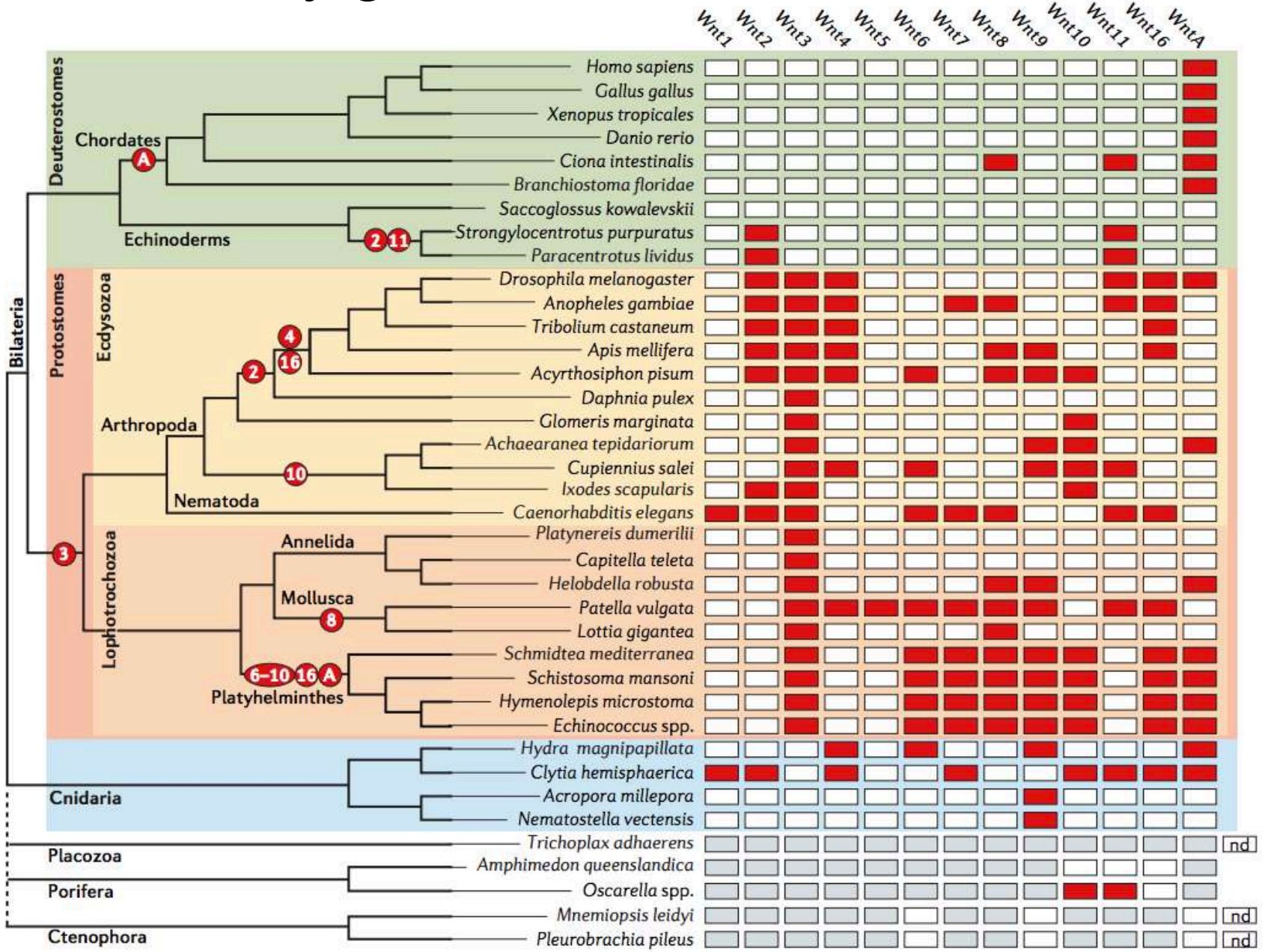
Exchange of genes between organisms other than through reproduction

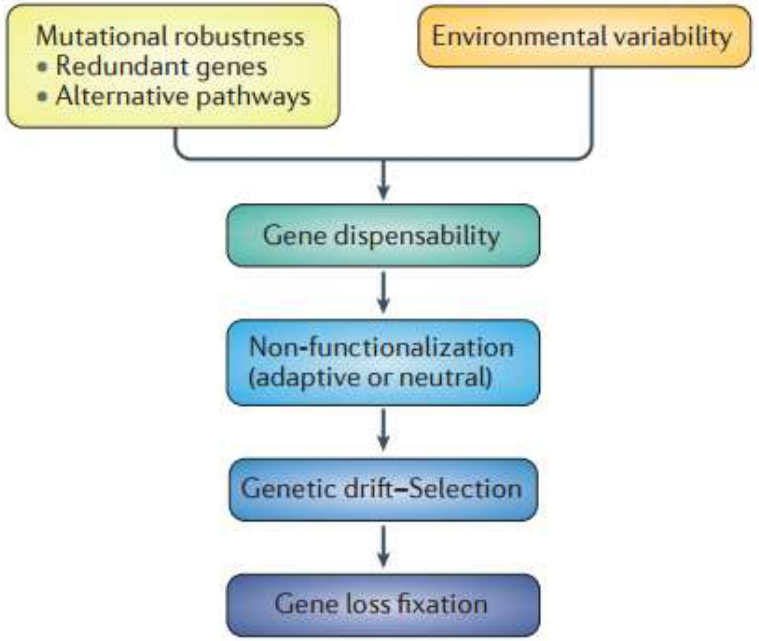


- Xenobiotic catabolism
- Toxin production
- Degradation of plant cell walls
- Wine fermentation

Slides of Antonis Rokas

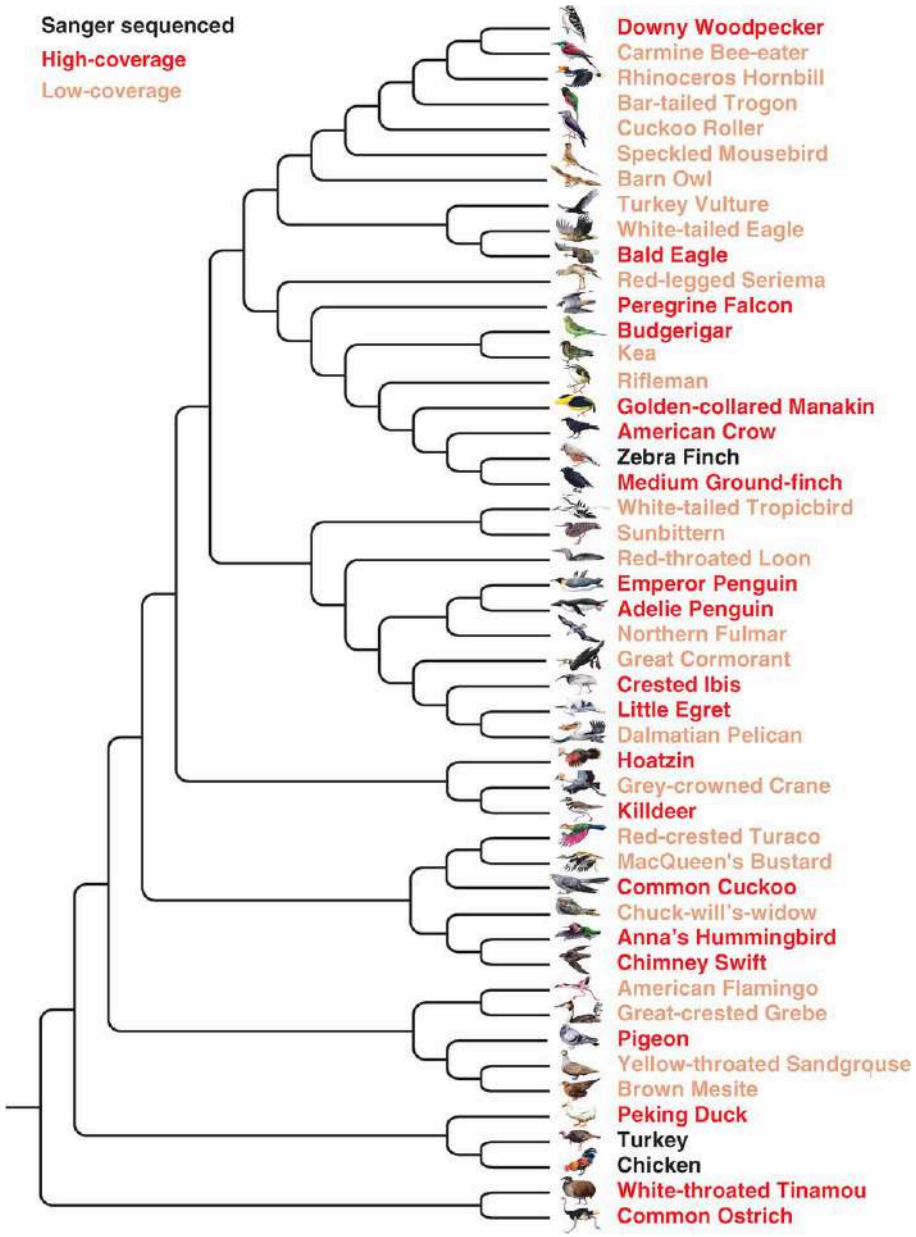
Evolution by gene loss

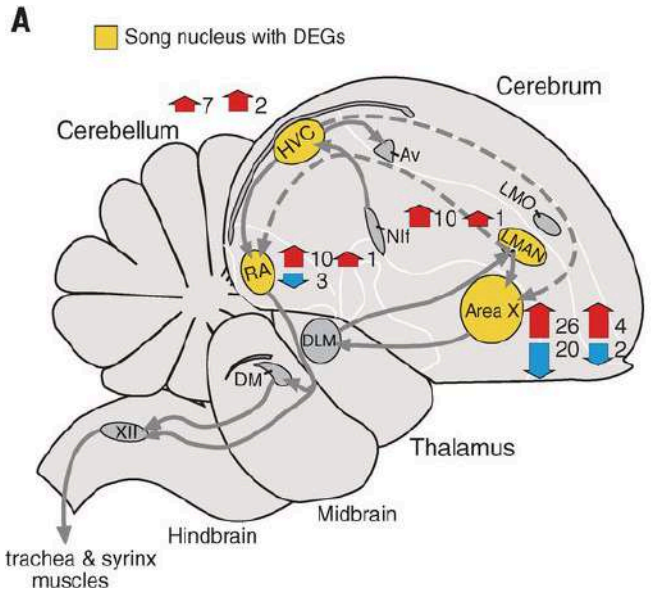


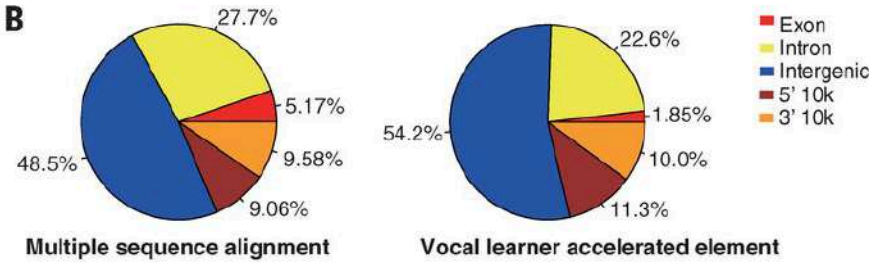


Albalat and Cañestro (2016)

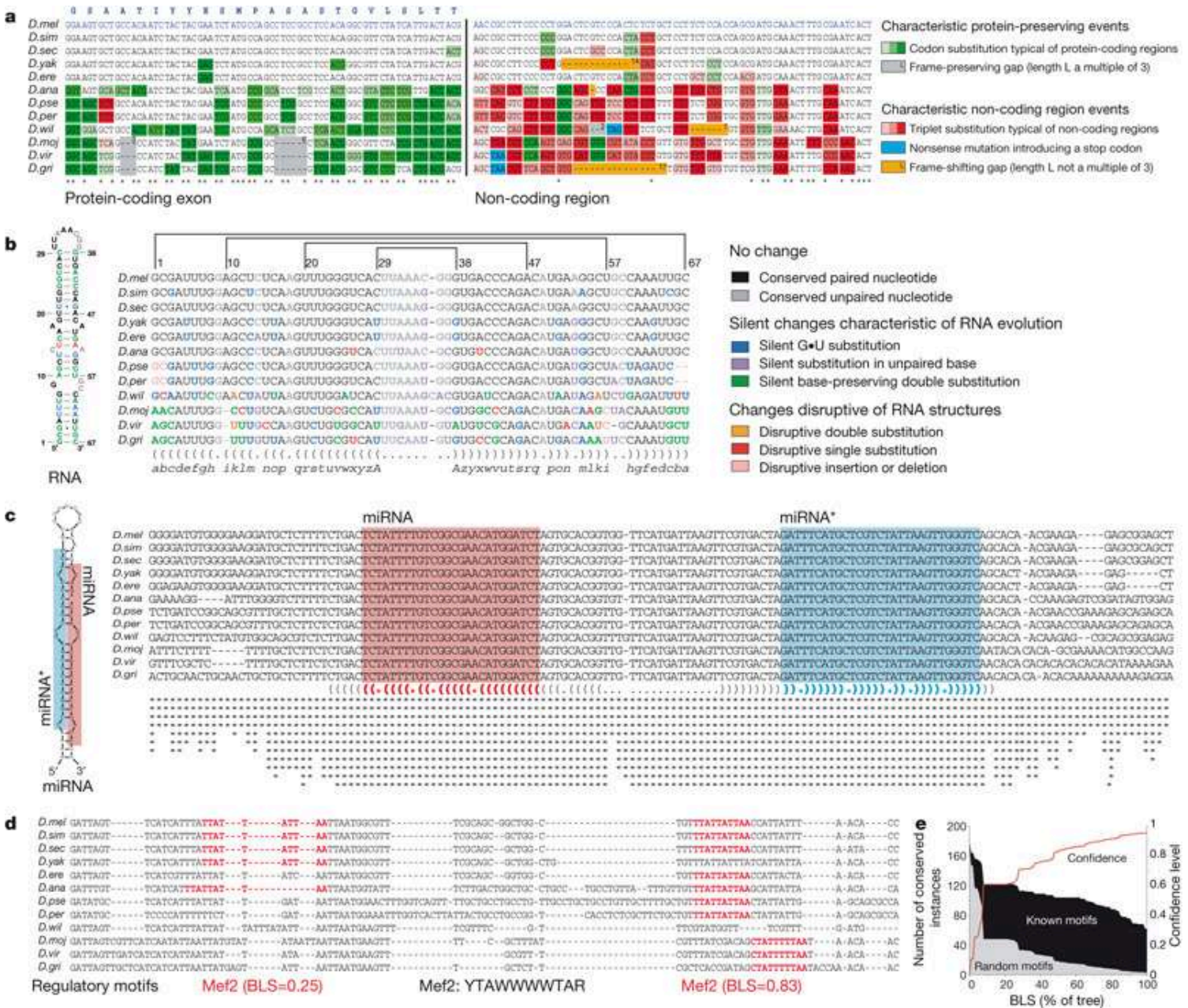
Reveal the evolutionary relationships among species







Link evolutionary processes with function

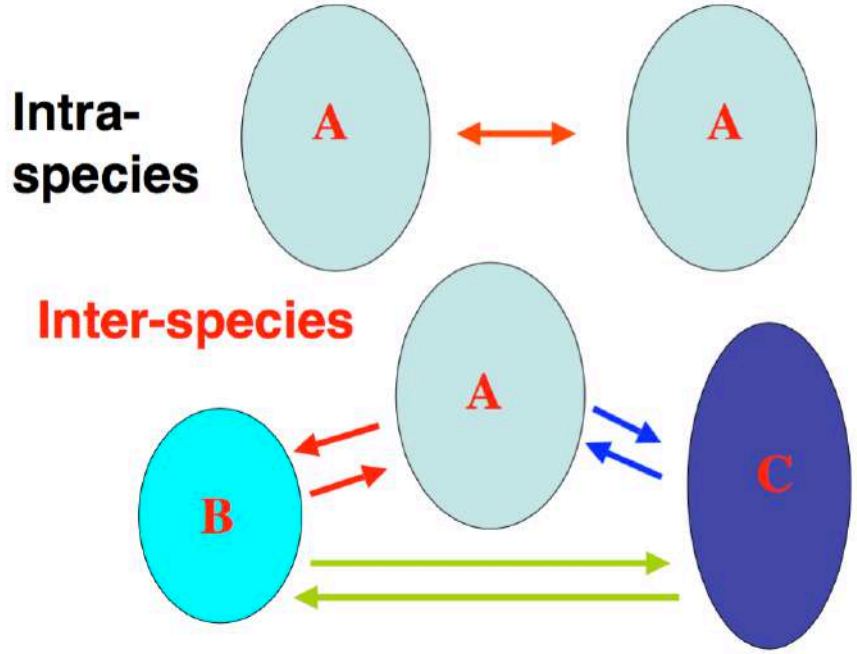


Clark et al (2007)

Comparing genomes

- Alignment of homologous regions
  - Inter-genomic: aligning genomic sequences from different species
  - Intra-genomic aligning genomic sequences from the same species

- Different levels of resolution
  - Comparative mapping (markers)
  - Synteny (~ gene content)
  - Colinearity (gene content + order conservation)
  - DNA-based alignments (base-to-base mapping)



Orthology

From homology to orthology

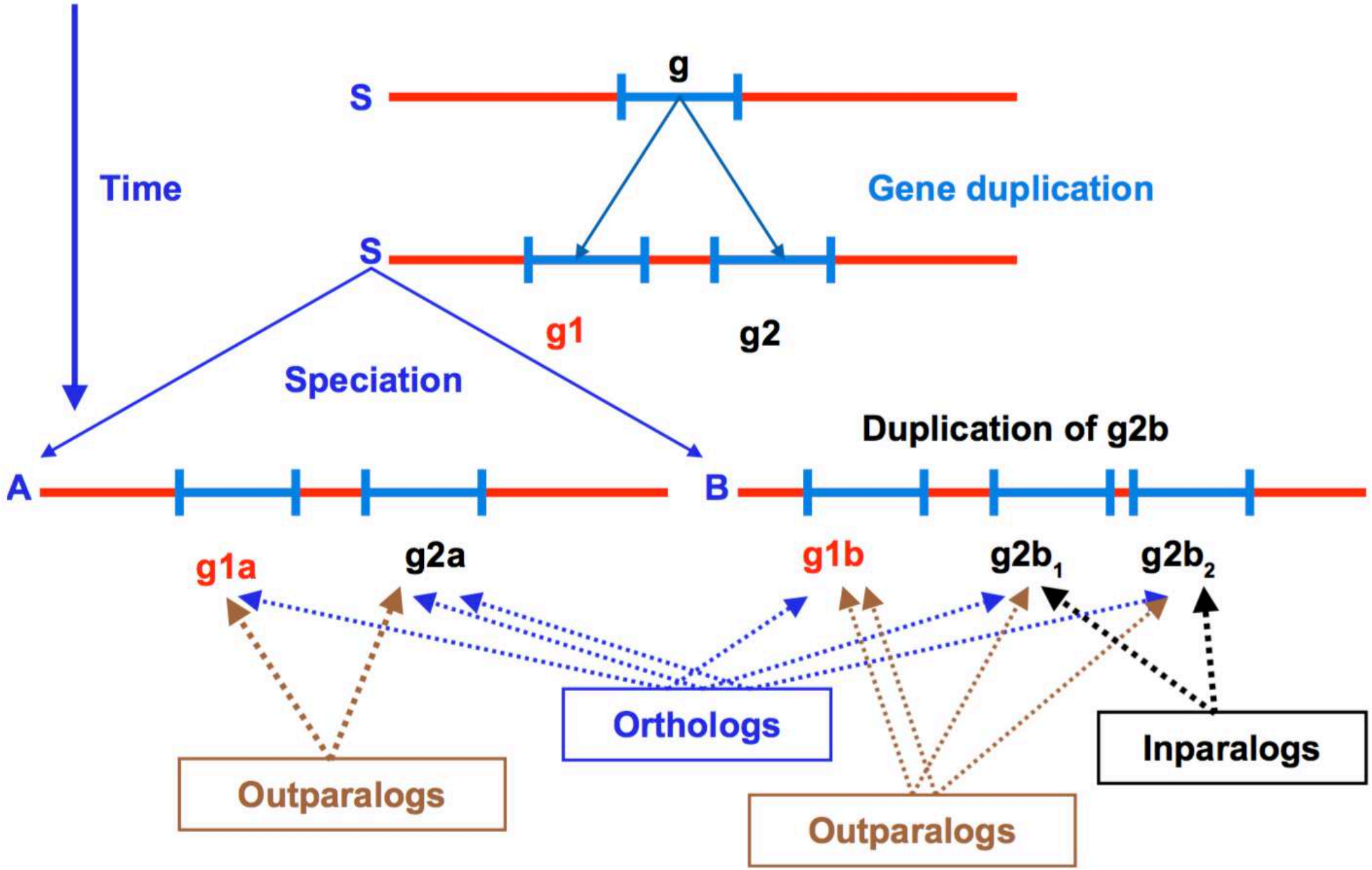
Homologues are sequences derived from a common ancestor...

- What are then orthologues? and paralogues?

Original definition of orthology and paralogy by Walter Fitch (1970, Systematic Zoology 19:99-113):

*"Where the homology is **the result of gene duplication** so that both copies have descended side by side during the history of an organism, (for example, alpha and beta hemoglobin) the genes should be called **paralogous** (para = in parallel).*

*Where the homology is **the result of speciation** so that the history of the gene reflects the history of the species (for example alpha hemoglobin in man and mouse) the genes should be called **orthologous** (ortho = exact)."*


Time
S
g
Gene duplication
S
g1
g2
Speciation
Duplication of g2b
A
B
g1a
g2a
g1b
g2b1
g2b2
Orthologs
Outparalogs
Outparalogs
Inparalogs

Tekaia (2016)

Why is orthology important?

Orthologs detection is of fundamental importance in:

- Reconstruction of the evolution of species and their genomes (Phylogenomics);

- Evolutionary studies of biological systems;

- Annotation of newly sequenced organisms;

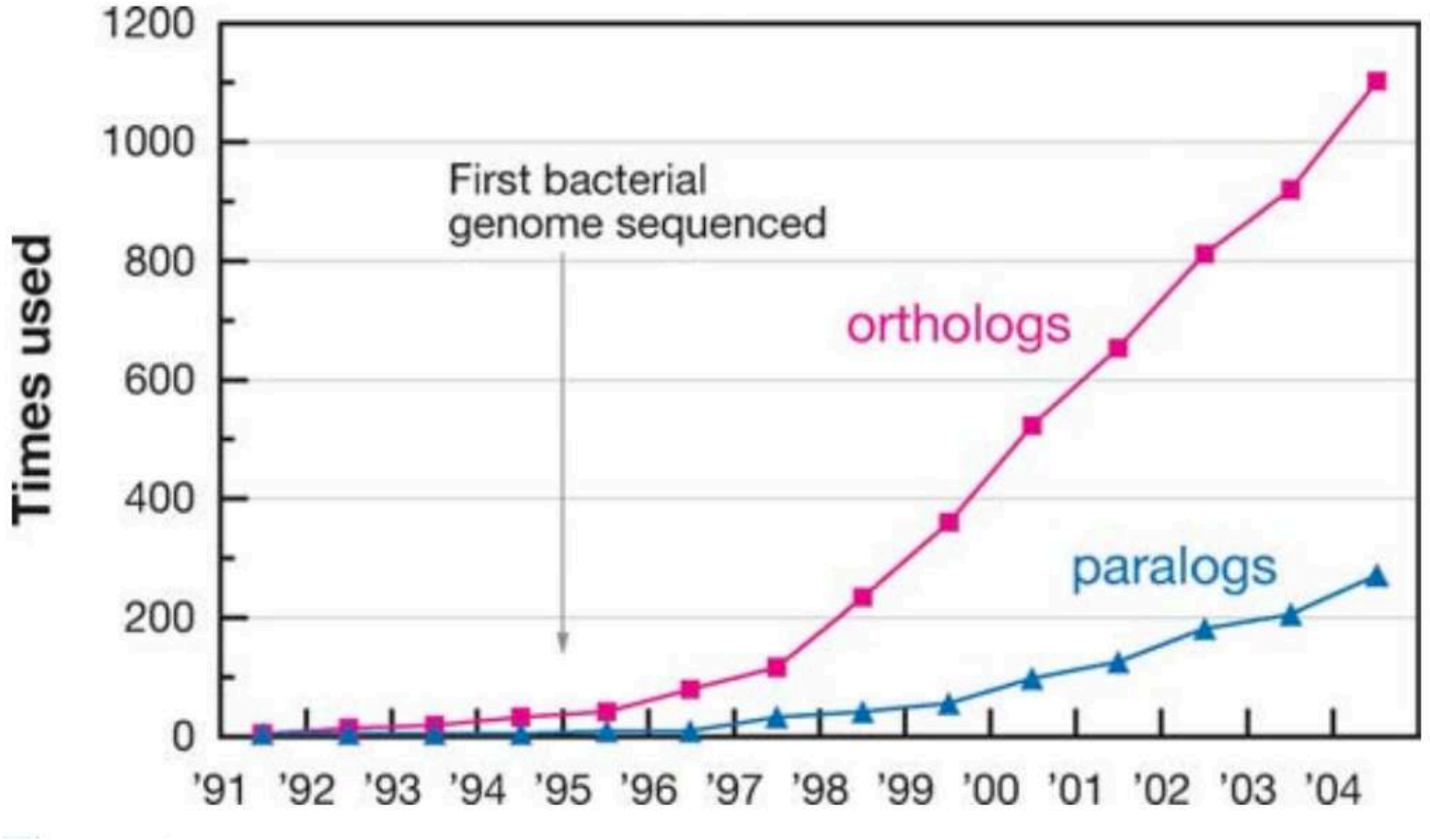
- Functional genomics (transfer of functional annotation predicted on "orthology-function conjecture");

- Gene organization in a given species.

Accurate determination of evolutionary relationships between orthologous gene families is of utmost importance for such goals.

Slide of Fred Tekaia

Usage of “ortholog” and ”paralog”



Koonin (2005)

Corollary

- Orthology definition is purely on evolutionary terms (not functional, not synteny…)
- There is no limit on the number of orthologs or paralogs that a given gene can have (when more than one ortholog exist, there is nothing such as "*the true ortholog*")
- Many-to-Many orthology relationships do exist (co-orthology)
- No limit on how ancient/recent is the ancestral relationship of orthologs and paralogs
- Orthology is non-transitive (as opposed to homology)

More precise definitions

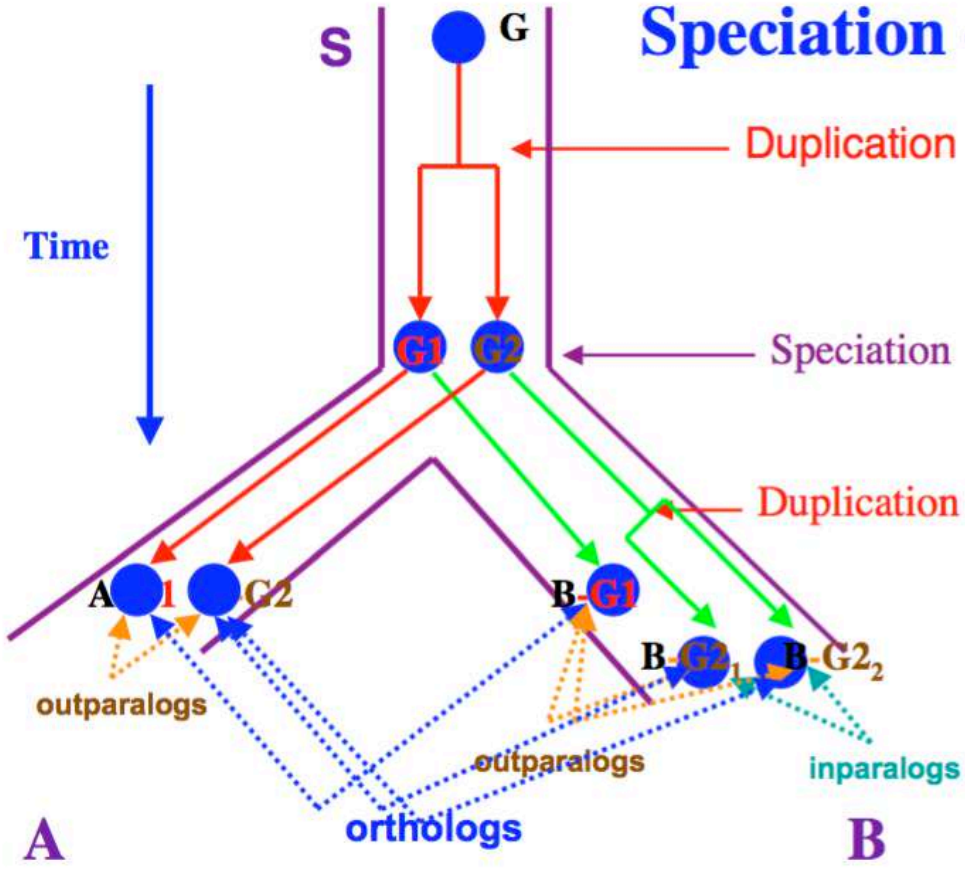


Table 1 Homology: terms and definitions

Homologs	**Genes sharing a common origin**
Orthologs	Genes originating from a single ancestral gene in the last common ancestor of the compared genomes.
Pseudoorthologs	Genes that actually are paralogs but appear to be orthologous due to differential, lineage-specific gene loss.
Xenologs	Homologous genes acquired via XGD by one or both of the compared species but appearing to be orthologous in pairwise genome comparisons.
Co-orthologs	Two or more genes in one lineage that are, collectively, orthologous to one or more genes in another lineage due to a lineage-specific duplication(s). Members of a co-orthologous gene set are inparalogs relative to the respective speciation event.
Paralogs	**Genes related by duplication**
Inparalogs (symparalogs)	Paralogous genes resulting from a lineage-specific duplication(s) subsequent to a given speciation event (defined only relative to a speciation event, no absolute meaning).
Outparalogs (alloparalogs)	Paralogous genes resulting from a duplication(s) preceding a given speciation event (defined only relative to a speciation event, no absolute meaning).
Pseudoparalogs	Homologous genes that come out as paralogs in a single-genome analysis but actually ended up in the given genome as a result of a combination of vertical inheritance and HGT.

Importance of assigning correct orthology

Important implications for phylogeny: only sets of orthologous genes are expected to reflect the underlying species evolution (although there are many exceptions)

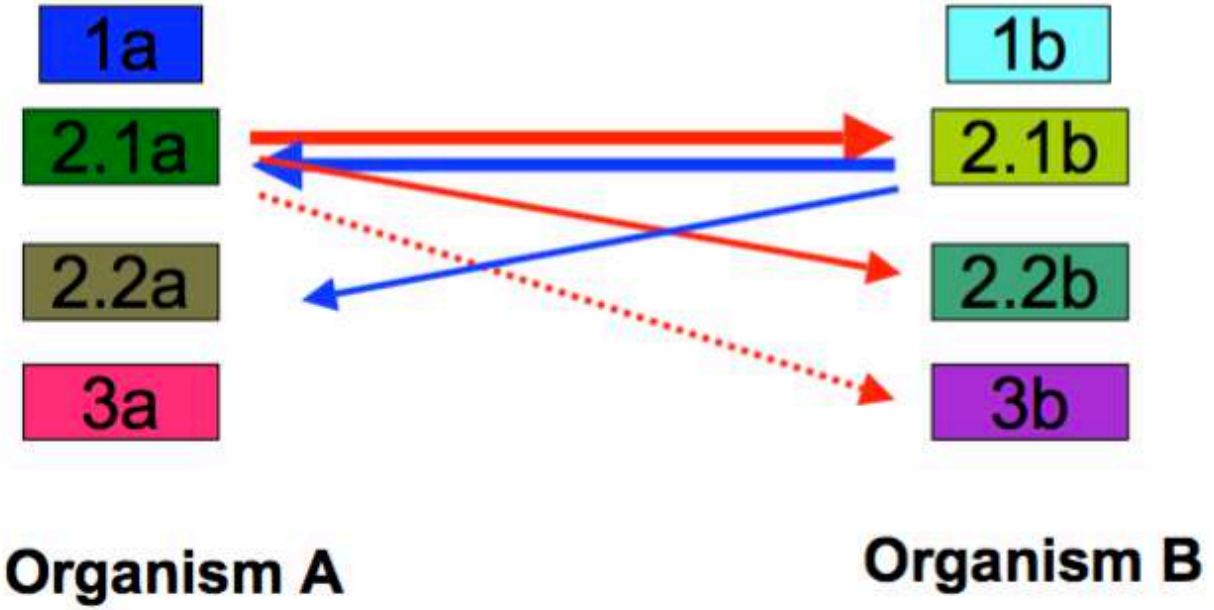
The most exact way of **comparing two (or more) genomes** in terms of their gene content. Necessary to uncover how genomes evolve.

Implications for **functional inference**: orthologs, as compared to paralogs, are more likely to share the same function

Ortholog inference methods

How to detect orthologous genes?

- The most intuitive way: **Best Reciprocal Hit (RBH)**

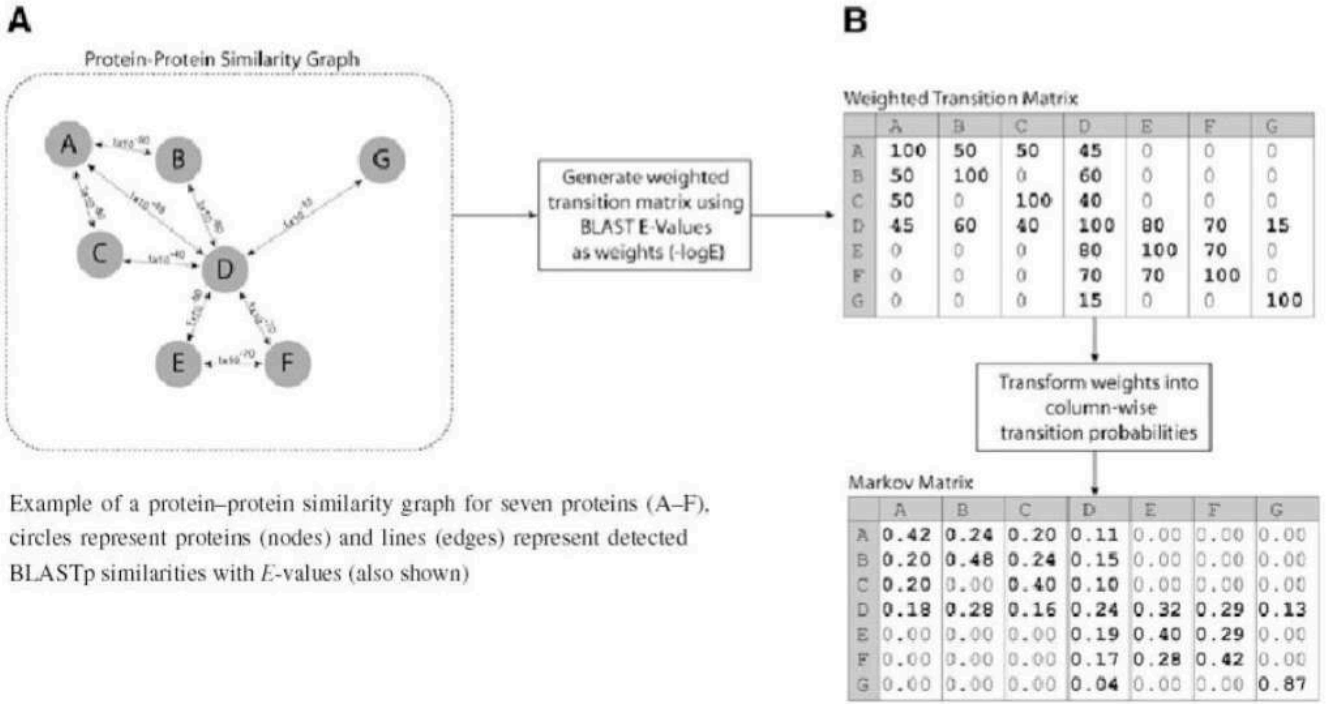


Slide of Fred Tekaia

Sequence by clustering

mcl: The Markov Cluster Algorithm

http://micans.org/mcl/ (Stijn Van Dongen)



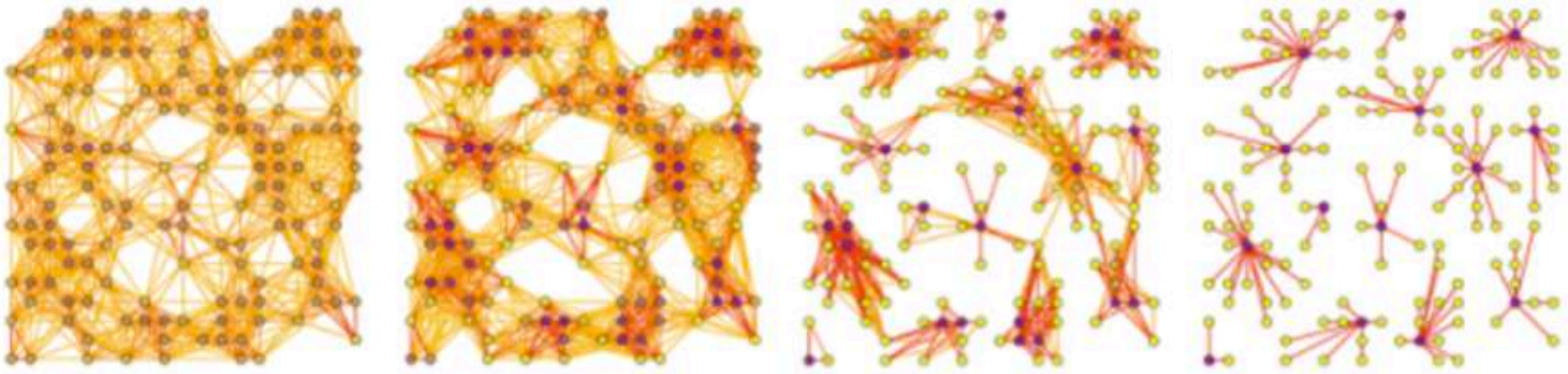
Weighted Transition Matrix	A	B	C	D	E	F	G
A	100	50	50	45	0	0	0
B	50	100	0	60	0	0	0
C	50	0	100	40	0	0	0
D	45	60	40	100	80	70	15
E	0	0	0	80	100	70	0
F	0	0	0	70	70	100	0
G	0	0	0	15	0	0	100

Markov Matrix	A	B	C	D	E	F	G
A	0.42	0.24	0.20	0.11	0.00	0.00	0.00
B	0.20	0.48	0.24	0.15	0.00	0.00	0.00
C	0.20	0.00	0.40	0.10	0.00	0.00	0.00
D	0.18	0.28	0.16	0.24	0.32	0.29	0.13
E	0.00	0.00	0.00	0.19	0.40	0.29	0.00
F	0.00	0.00	0.00	0.17	0.28	0.42	0.00
G	0.00	0.00	0.00	0.04	0.00	0.00	0.87

Example of a protein–protein similarity graph for seven proteins (A–F), circles represent proteins (nodes) and lines (edges) represent detected BLASTp similarities with *E*-values (also shown)

Weighted transition matrix and associated column stochastic Markov matrix for the seven proteins shown in (A).

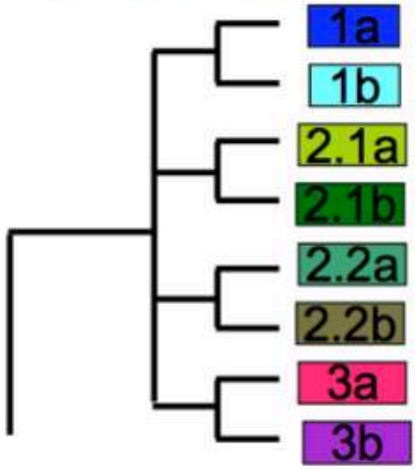
Produce clusters (gene families) using different inflation parameter



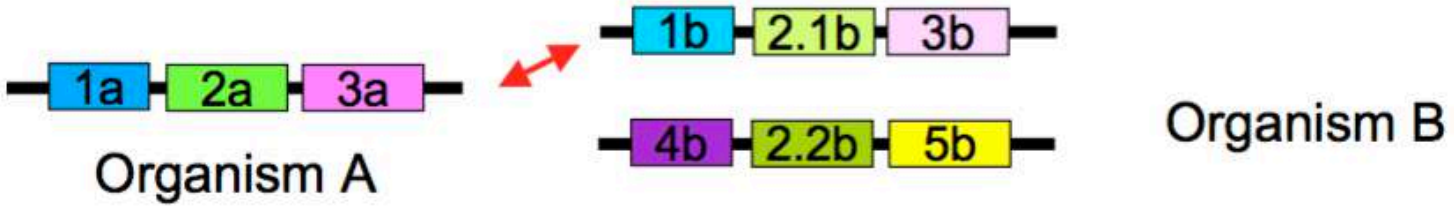
Slide of Fred Tekaia

How to detect orthologous genes?

- more rigorous: make a phylogenetic tree of the gene family



- more rigorous: look at synteny conservation



--> In fact inferring orthology is much more complicated particularly when considering more than 2 genomes!

Slide of Fred Tekaia

Tree reconciliation

Detection of speciation and duplication events using a species tree and gene family tree

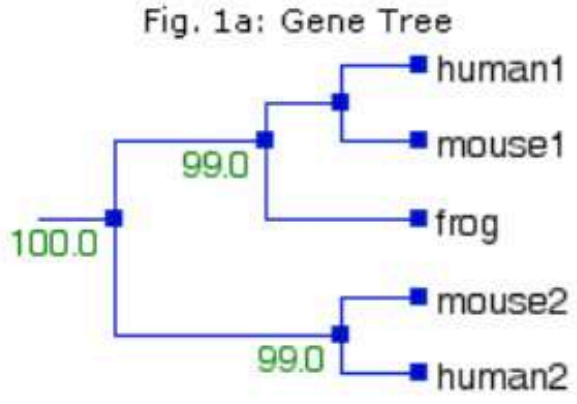


Fig. 1a: Gene Tree

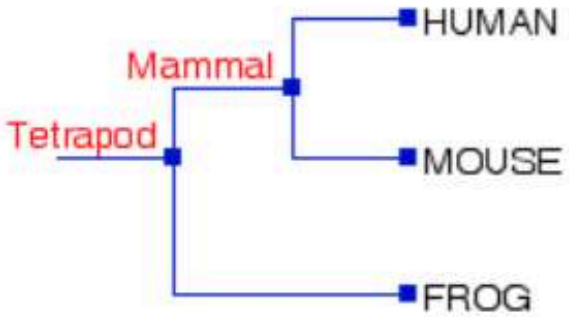


Fig. 1b: Species Tree

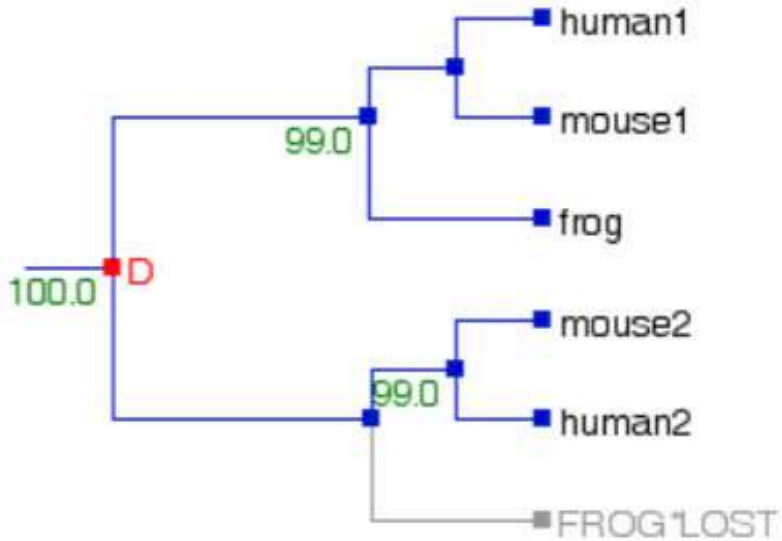
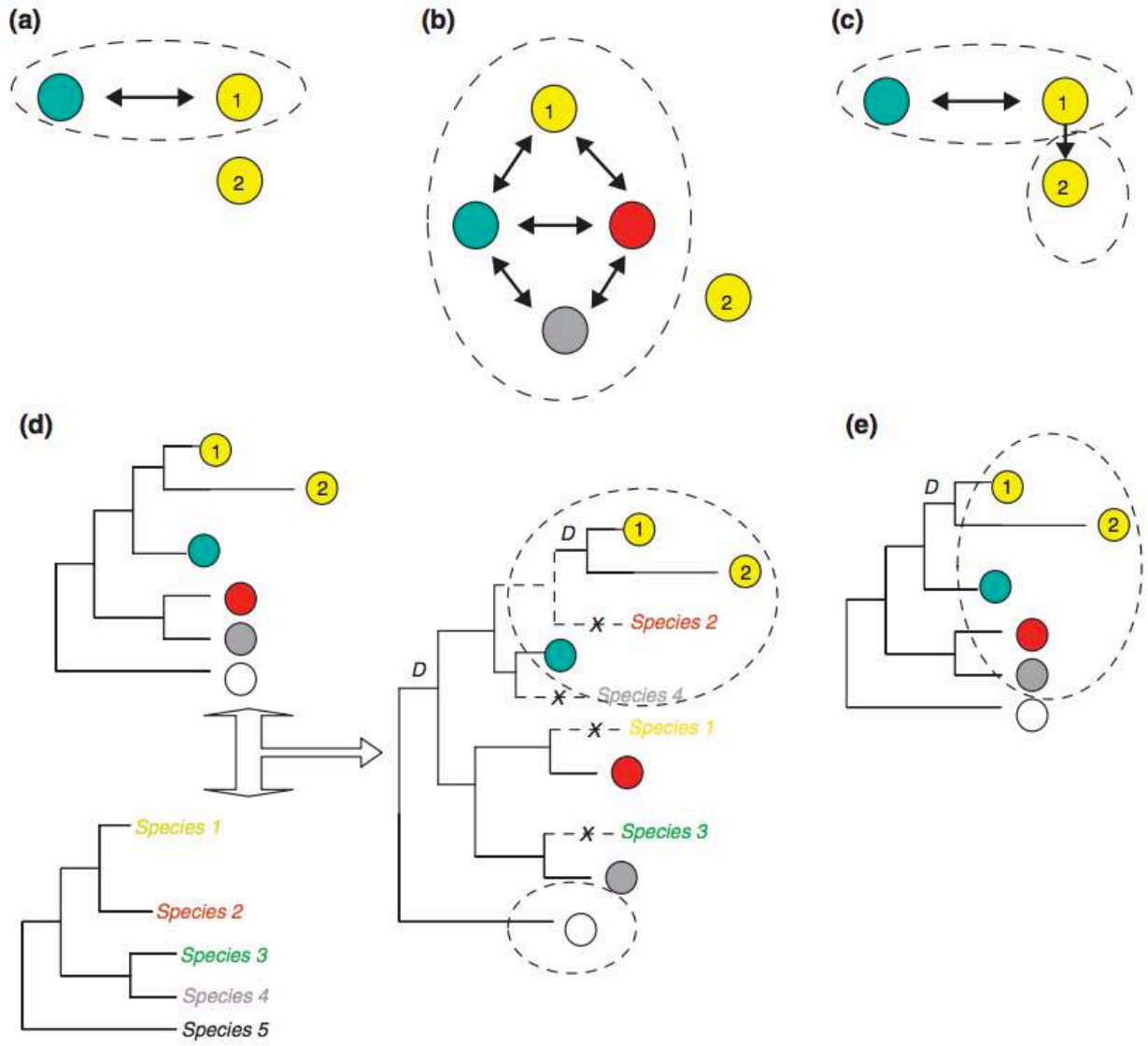


Fig. 1c: Reconciled Gene Tree

Stolzer et al (2012)

Orthology prediction methods



a) Best bidirectional hits
b) COG, MCL-clustering approach
c) InParanoid
d) Tree reconciliation
e) Species-overlap (PhylomeDB)

Gebaldon (2008)

Methods

Similarity

Rely on genome comparisons and clustering of highly similar genes to identify orthologous groups **(suitable for large genome datasets)**

Phylogeny

use candidate gene families determined by similarity and then rely on the reconciliation of the phylogeny of these genes with their corresponding species phylogeny to determine the subset of orthologs

(Good and more interpretable for small set of genomes)

Others

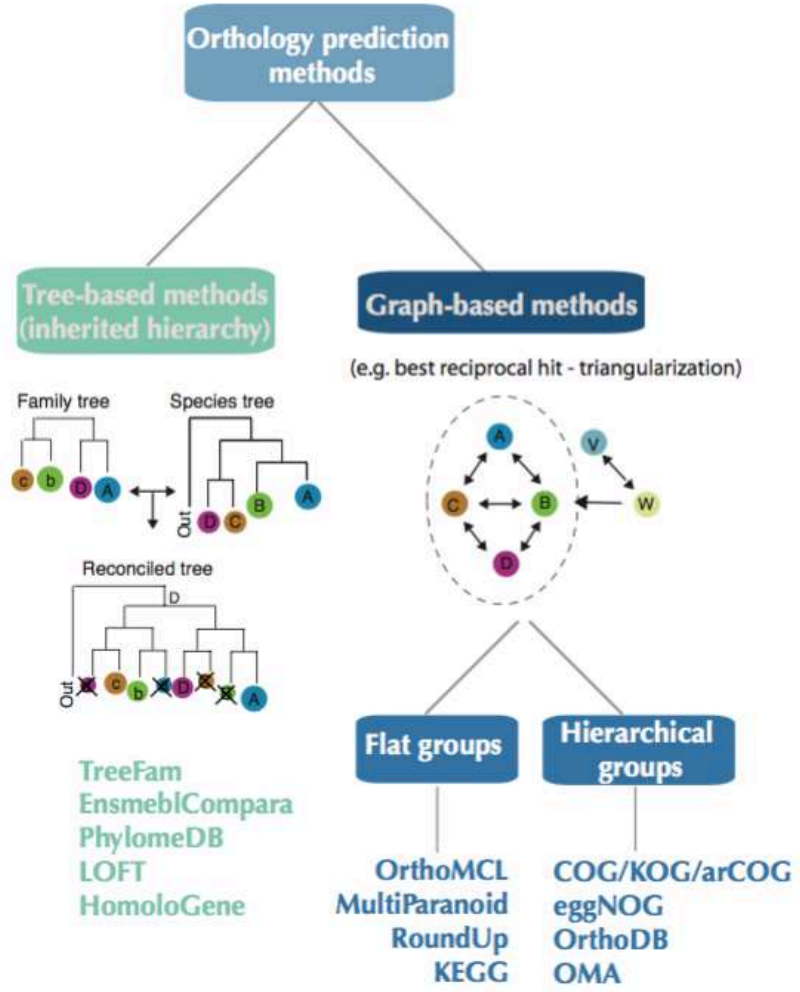
Combination of (1) and (2)

Some uses synteny

Tools

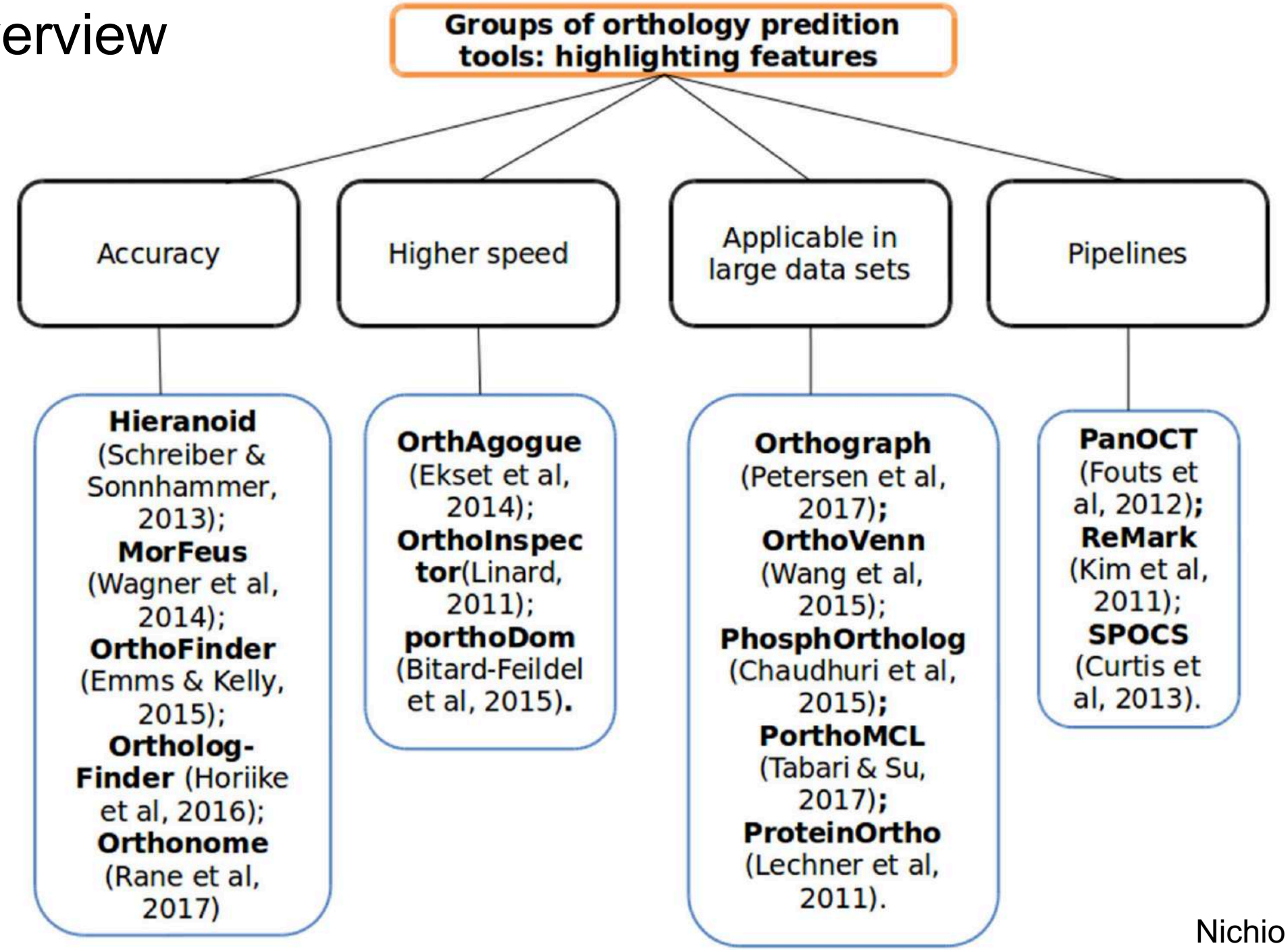
METHOD	ALGORITHM
COG[54]	Similarity—Single linkage clustering + Constraints
InParanoid/MultiParanoid[55]	Similarity (pair-wise species)/Extends to multiple species
OrthoMCL[56]	Similarity—MCL clustering algorithm
TribeMCL[57]	Similarity—MCL clustering algorithm
eggNOG[58]	Similarity—Detects false RBH due to gene fusion and protein domain shuffling
OrthoFocus[59]	Similarity—extended RBH to handle many-to-one and many-to-many relationships
OrthoInspector[60]	Smilarity
SPO[61]	Similarity (RBH)—Partition of orthologs includes Intra-species Partition and MCL clusteri
OrthoFinder[62]	Similarity—Clustering
Roundup[63]	Reciprocal Smallest Distance
RSD[64]	Reciprocal Smallest Distance (evolutionary distance = estimated number of amino acid s
OMA[65]	Similarity—Global sequence alignment
ME[66]	Minimum Evolution Method
MSOAR[67]	Similarity—Genome rearrangement—duplication
Orthostrapper[69]	Phylogeny—bootstrap
RIO[70]	Similarity (HMMER)—bootstrap—Phylogeny
PhIGs[71]	Similarity—Multiple sequence alignments—Phylogenetic trees
PhyOP[72]	Similarity (overlapping limits)—phylogeny based on d_s (synonymous substitution rates)
TreeFam[73]	Infer orthologs—paralog from the phylogenetic tree
LOFT[74]	Assigns hierarchical orthology numbers to genes based on a phylogenetic tree
EnsemblCompara GeneTrees[75]	Clustering—multiple alignment—tree generation based on TreeBeST method
SYNERGY[76]	Sequence similarity—species phylogeny—reconstruction of underlying gene evolutionary histories
PHOG[77]	Precomputed phylogenic trees followed by identification of orthologs as sequences from different species that are each others reciprocal nearest neighbors
COCO-CL[78]	Similarity—Correlation between sequences—single linkage clustering

Note: This table shows some orthology inference methods with corresponding reference and a short description of their underlying algorithm.



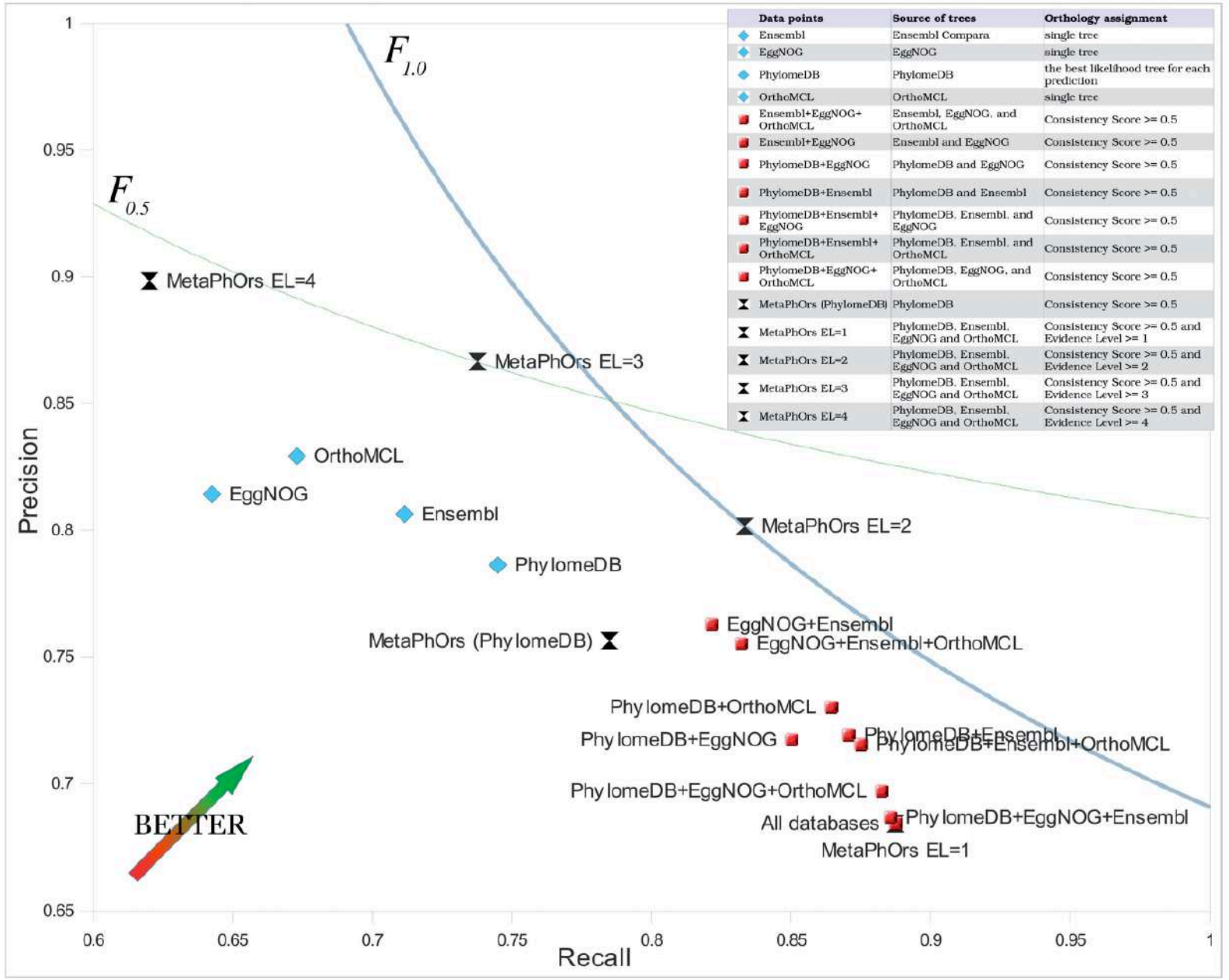
Tekaia (2016)

Tools overview



Nichio *et al* (2017)

Every tool kind of disagrees…



Pryszcz et al (2011)

Caveats

Evolution of multi-domain proteins

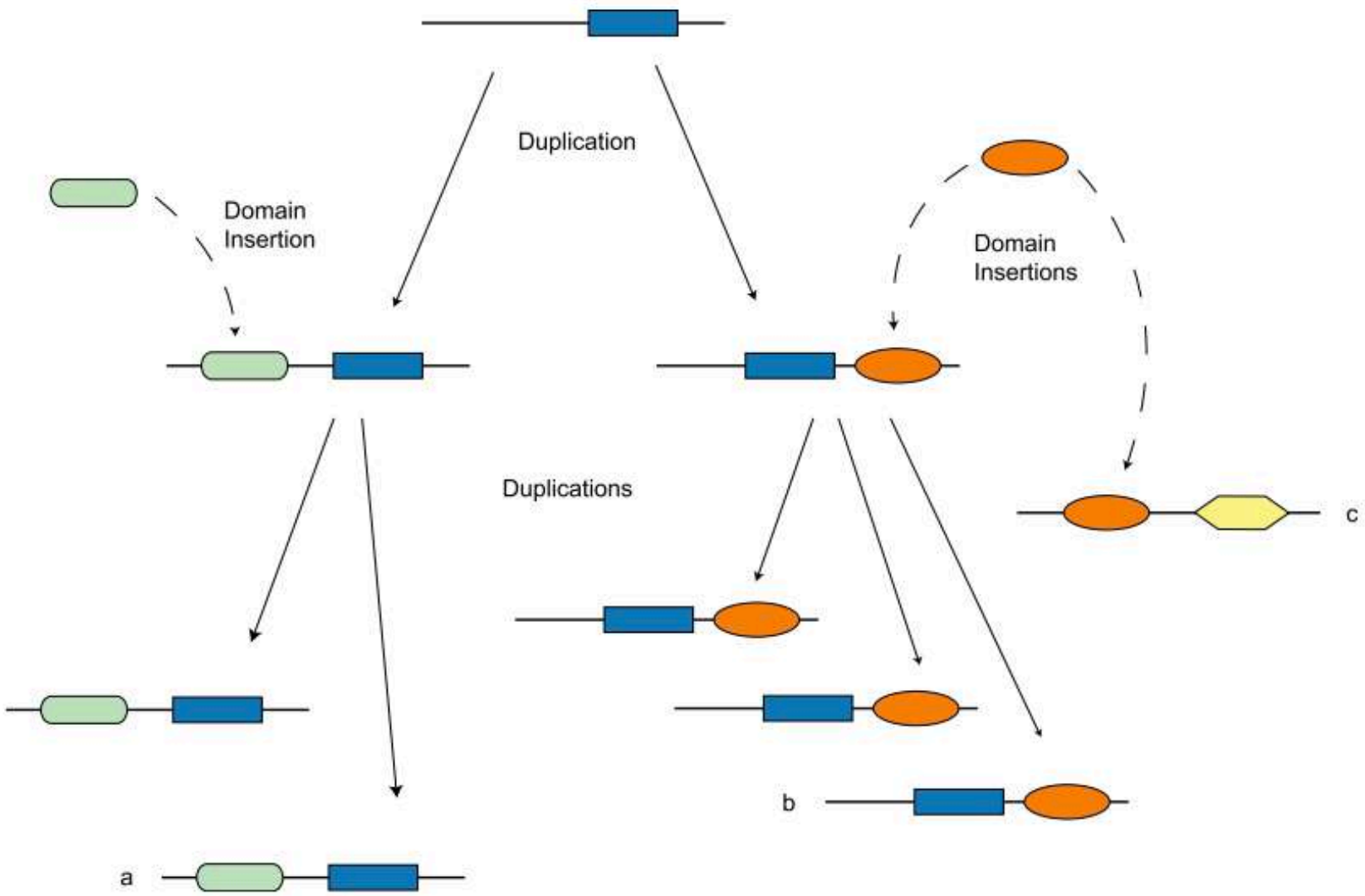
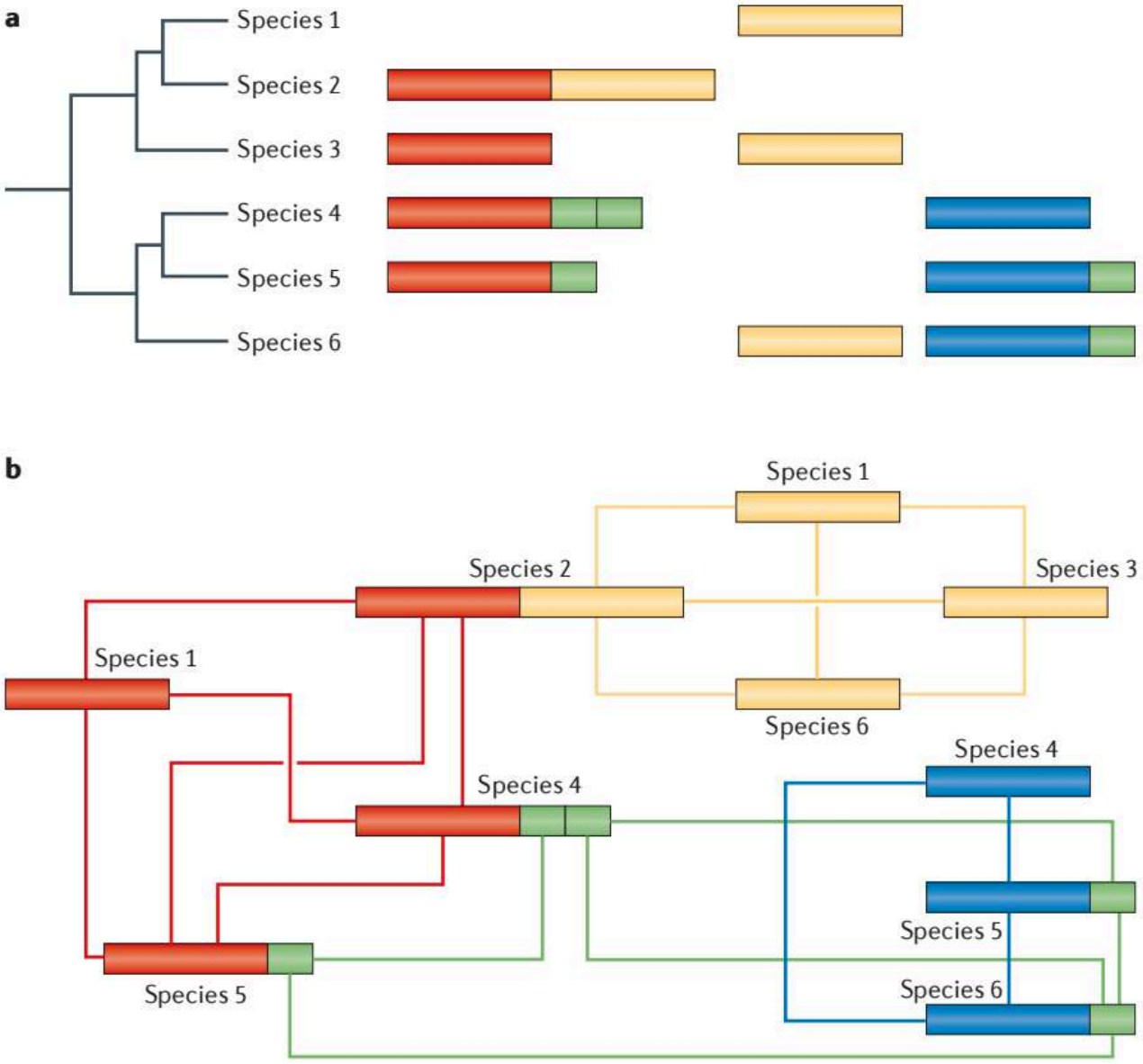


Figure 1. The evolution of a hypothetical multidomain family by gene duplication and domain insertion. Genes in the *a* and *b* subfamilies share a common ancestor but do not have identical domain composition. Gene *c* shares a homologous domain with genes in the *b* subfamily, but there is no gene that is ancestral to both *b* and *c*.
doi:10.1371/journal.pcbi.1000063.g001

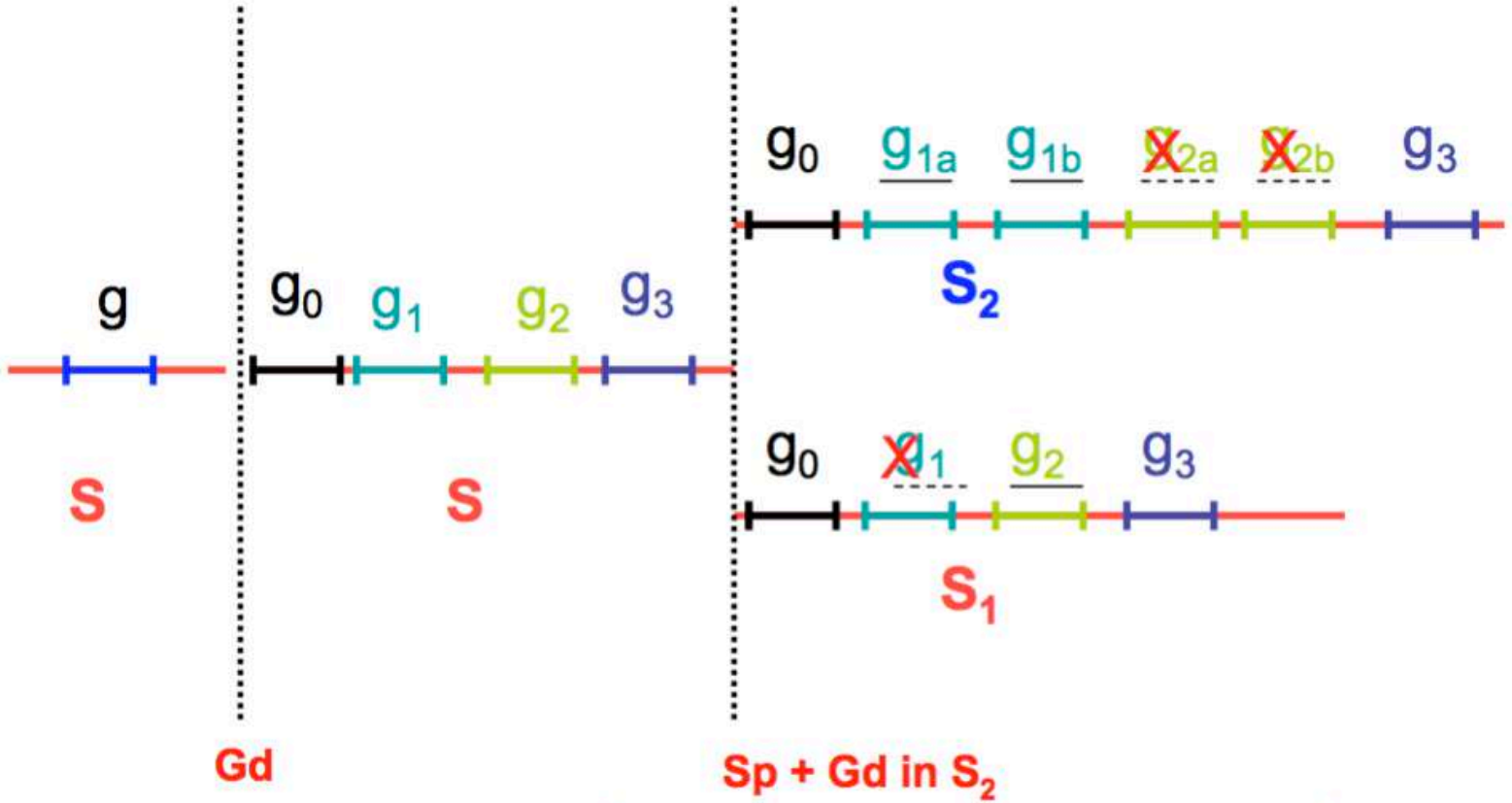
Song et al (2008)

Problem of clustering to assign gene families when comes to different domain combinations



Gabaldon and Koonin (2013)

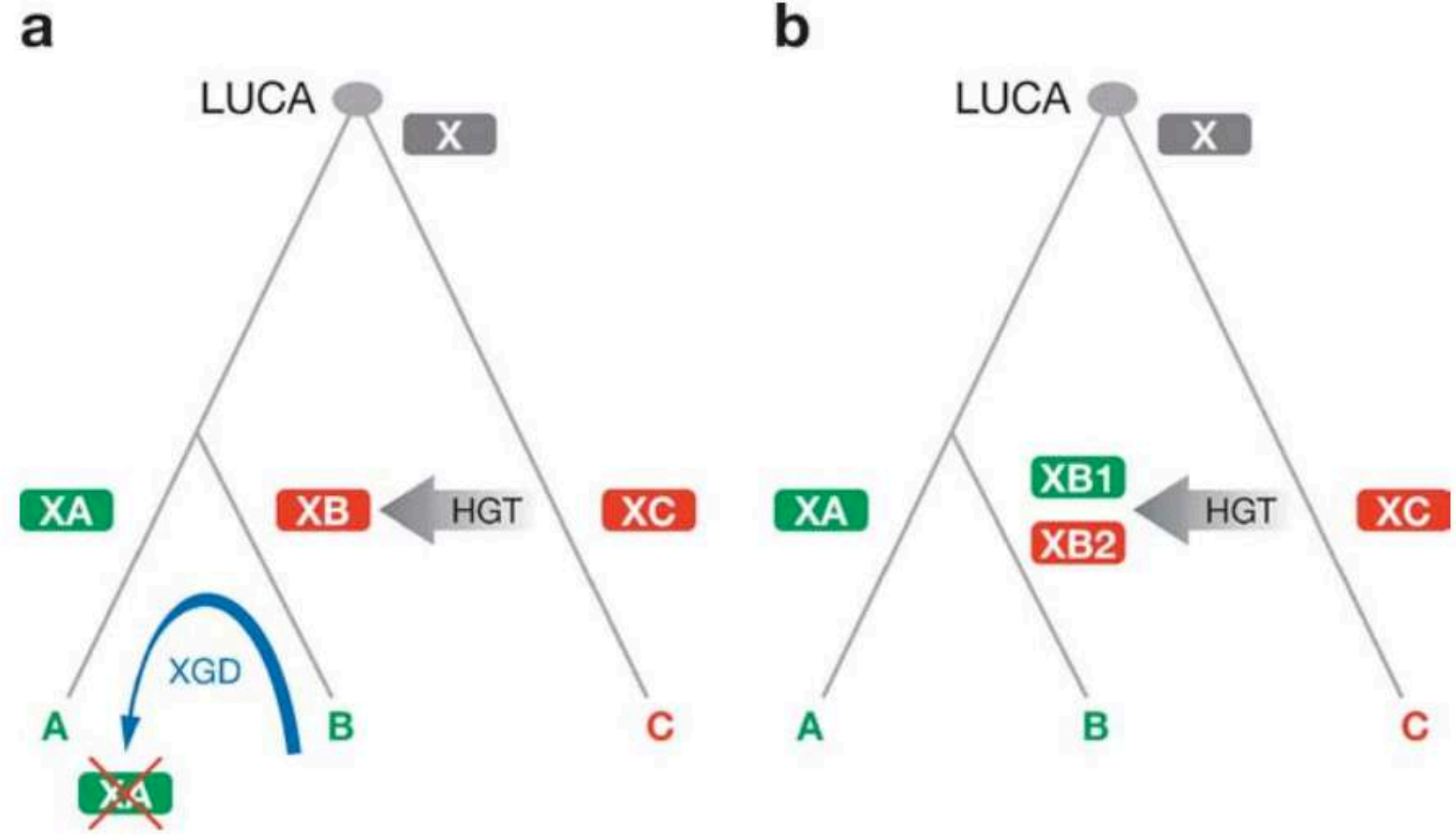
Detection can go wrong: Example of an orthology misleading situation



We assume that gene g_1 (in S_1) and genes g_{2a} and g_{2b} (in S_2) are lost, similarity and phylogenetic methods for orthology detection will assign erroneously orthology to g_2, g_{1a} and g_{1b}. Indeed these are not orthologous, because g_2, g_{1a} and g_{1b} do not result from the same ancestral gene after the speciation event.

In this case solely the environment conservation, will help in detecting the gene duplication and loss event, and hypothesise their non-orthology.

Effect of HGT on orthology and paralogy
(If orthology is simply inferred by gene content)



xenologous gene displacement

Figure 4

Effect of horizontal gene transfer on orthology and paralogy. (*a*) A hypothetical evolutionary scenario with HGT leading to xenology. (*b*) A hypothetical evolutionary scenario with HGT leading to pseudoparalogy. LUCA, Last Universal Common Ancestor (of all extant life forms).

Koonin (2005)

Caveat: Do orthologs, as compared to paralogs, are more likely to share the same function?

How confident can we be that orthologs are similar, but paralogs differ?

Romain A. Studer and Marc Robinson-Rechavi

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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

Some designs for the study of gene duplication.

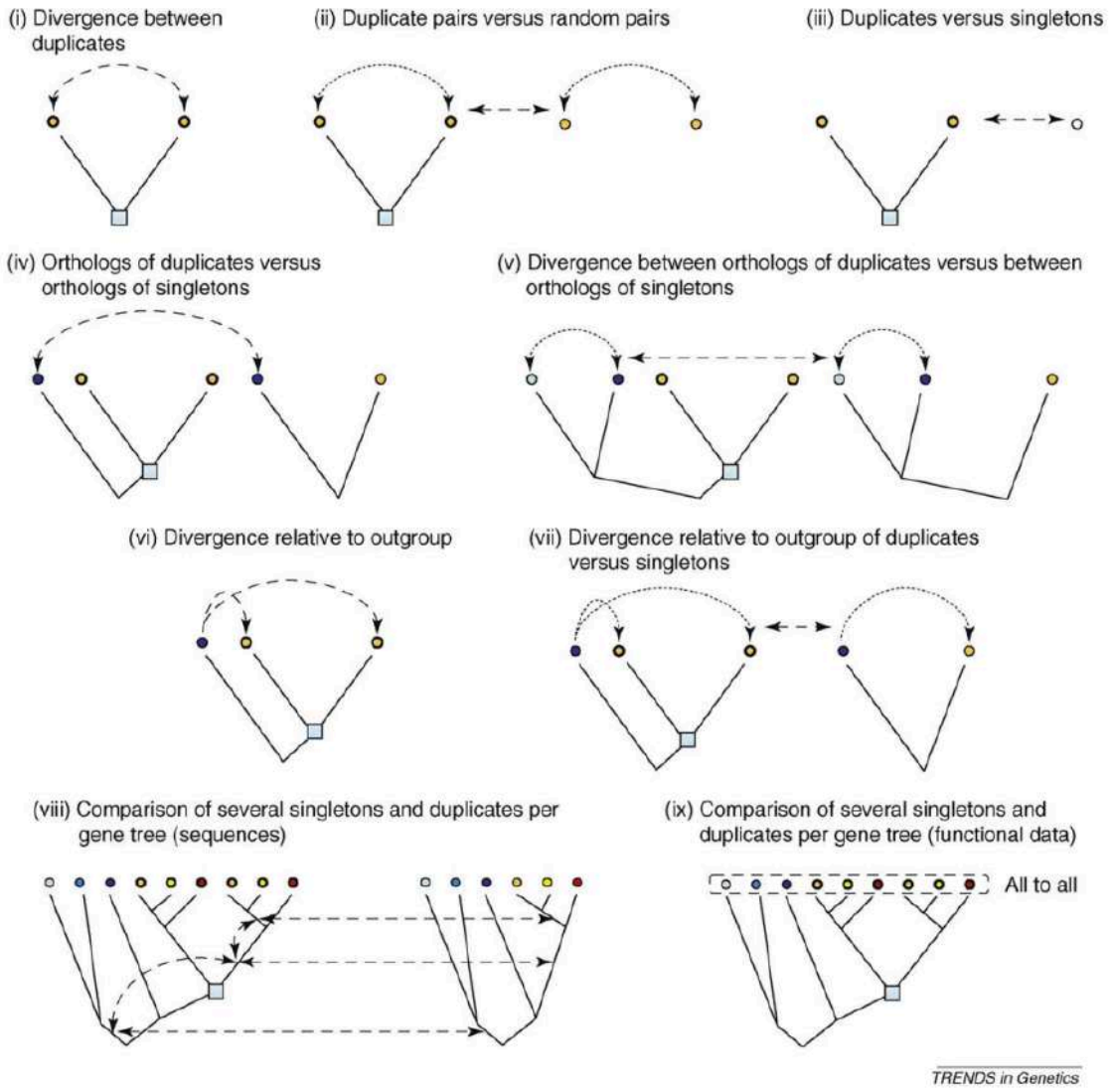

Table 1. The impact of study design on tests of evolution after duplication

Study design[a]	Data type[b]	Predictions under simple evolutionary models			Refs
		Preferential change after duplication		Function change after duplication or speciation	
		Subfunctionalization[c]	Neofunctionalization		
(i) Divergence between duplicates	Functional	Differences between paralogs			[19,20,55]
(ii) Duplicate pairs versus random pairs	Functional	Paralogs more similar than random pairs, but not identical			[11,19,54]
(iii) Duplicates versus singletons	Functional	Measure of retention bias, confused by evolution after duplication			[11,19,25]
(iv) Orthologs of duplicates versus orthologs of singletons	Functional	Measure of retention bias			[12]
(v) Divergence between orthologs of duplicates versus between orthologs of singletons	Sequence	Measure of retention bias			[12,53]
(vi) Divergence relative to outgroup	Sequence	No prediction relative to symmetry, relaxed purifying selection	Asymmetry between paralogs, positive selection[e]		[11,17,58]
	Functional	Two paralogs different, complementary to full outgroup function	One paralog similar to outgroup, one different		[18,21]
(vii) Divergence relative to outgroup of duplicates versus singletons	Sequence	Higher divergence of duplicates[d], confused by retention bias			[62]
	Functional	Two paralogs different, complementary to outgroup; singleton similar to outgroup	One paralog similar to outgroup, one different; singleton similar to outgroup	No specific prediction[f]	[18,24,25]
(viii) Comparison of several singletons and duplicates per gene tree	Sequence	Higher relaxation of purifying selection on branches after duplication	More positive selection on branches after duplication	Positive selection in various branches of the tree[g]	[13,43,48,56]
(ix) *idem*	Functional	Conservation of pattern among singletons; sub-patterns in duplicates	Conservation in most homologs; new patterns[h] in some duplicates	Variation in pattern among homologs, with gain of new patterns[h]	

Studer and Robinson-Rechavi (2009)

Testing duplication combining transcriptome dataset

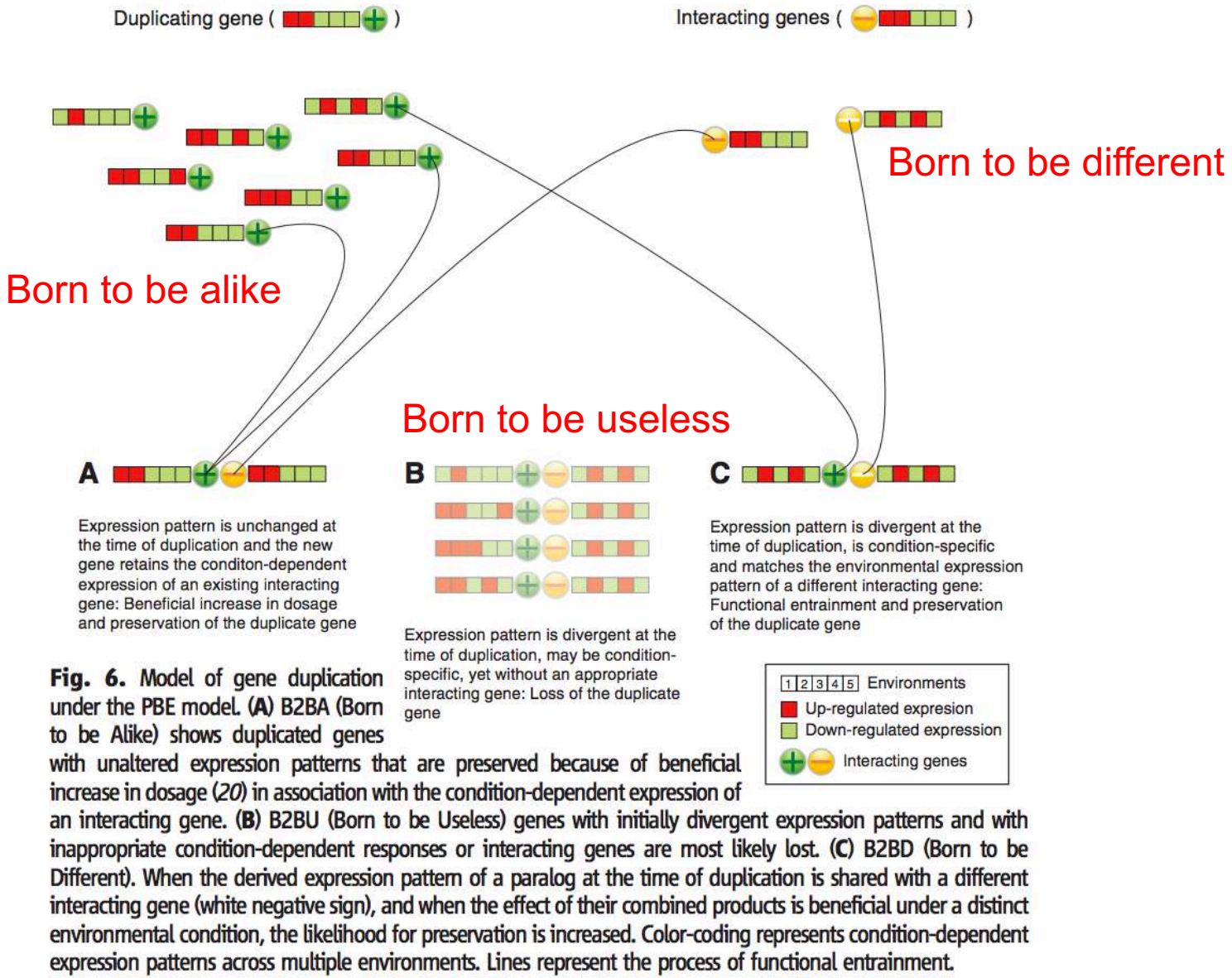

Fig. 6. Model of gene duplication under the PBE model. **(A)** B2BA (Born to be Alike) shows duplicated genes with unaltered expression patterns that are preserved because of beneficial increase in dosage (*20*) in association with the condition-dependent expression of an interacting gene. **(B)** B2BU (Born to be Useless) genes with initially divergent expression patterns and with inappropriate condition-dependent responses or interacting genes are most likely lost. **(C)** B2BD (Born to be Different). When the derived expression pattern of a paralog at the time of duplication is shared with a different interacting gene (white negative sign), and when the effect of their combined products is beneficial under a distinct environmental condition, the likelihood for preservation is increased. Color-coding represents condition-dependent expression patterns across multiple environments. Lines represent the process of functional entrainment.

Colbourne et al (2011)

Summary point

SUMMARY POINTS

1. Orthologs and paralogs are two types of homologous genes that evolved, respectively, by vertical descent from a single ancestral gene and by duplication.
2. Distinguishing between orthologs and paralogs is crucial for successful functional annotation of genomes and for reconstruction of genome evolution.
3. A finer classification of orthologs and paralogs has been developed to reflect the interplay between duplication and speciation events, and effects of gene loss and horizontal gene transfer on the observed homologous relationship.
4. Methods for identification of sets of orthologous and paralogous genes involve phylogenetic analysis and various procedures for sequence similarity–based clustering.
5. Analysis of clusters of orthologous and paralogous genes is instrumental in genome annotation and in delineation of trends in genome evolution.
6. Rearrangements of gene structure confound orthologous and paralogous relationships.
7. The gene-centered concepts of orthology and paralogy can be generalized downward, to the level of strings of nucleotides and even single base pairs, and upward, to multigene arrays.

Koonin (2005)

Comparing genomes beyond gene level

Extension of homology to genomes

Gene family gains and losses in previous lecture

Comparing genomes at **different resolution**

- Synteny (gene content on the same chromosome)
- Colinearity (gene content + order conservation)
- DNA-based alignments (base-to-base mapping)

Extension of homology to genomes: synteny

Synteny Conservation and Chromosome Rearrangements During Mammalian Evolution

Jason Ehrlich,*,[1] David Sankoff† and Joseph H. Nadeau*,[2]

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Manuscript received December 13, 1996
Accepted for publication June 4, 1997

MAPS of LINKAGE and SYNTENY HOMOLOGIES between MOUSE and MAN

JOSEPH H. NADEAU

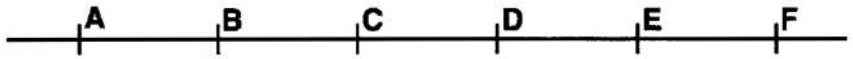
1989

Synteny refers to the occurrence of two or more genes on the same chromosome, whereas *conserved synteny* refers to two or more homologous genes that are syntenic in two or more species, regardless of gene order on each chromosome, *i.e.*, synteny but not necessarily gene order is conserved (Figure 2; see also NADEAU 1989). *Conserved linkage* pertains to the conservation of both synteny and order of homologous genes between species (Figure 2; see also NADEAU 1989). A *disrupted synteny* refers to circumstances where a pair of genes are located on the same chromosome in one species but their homologues are located on different chromosomes in another species, *i.e.*, the genes are syntenic in only one of the two species. Syntenic genes can be identified by examining published genetic maps and conserved segments can be identified by comparing

Synteny

conservation of gene content

A. Genetic map in reference species



Each unit is gene

Conserved synteny and linkage

Gene arrangement:

Definition: **Same gene order and similar genetic distances.**

Count:
One *conserved linkage* involving genes,
one conserved synteny. involving genes A,B,C,E,F.

Possible cause:
No inter-chromosomal rearrangement.
No intra-chromosomal rearrangement.

Conserved synteny, conserved linkage, disrupted linkage

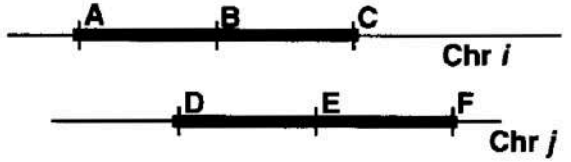
Gene arrangement:

Count:
One *conserved linkage* involving genes B,C,D;
One *conserved linkage* involving genes E,F.
One *disrupted linkage* involving genes B,C,D vs E,F vs A.
One *conserved synteny* involving genes A,B,C,D,E,F.

Possible causes:
An intra-chromosomal rearrangement,
such as a paracentric inversion.

Conserved synteny, disrupted synteny, conserved linkage, disrupted linkage

Gene arrangement:



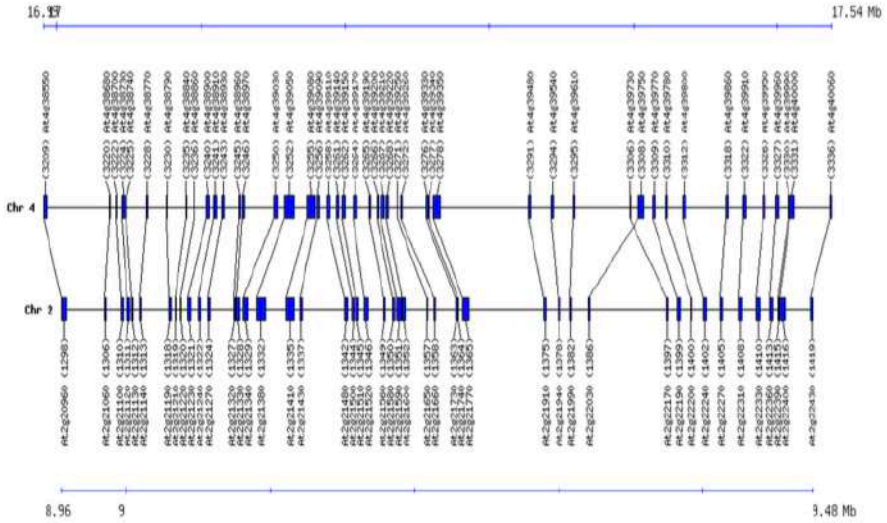
Count:
One *conserved linkage* involving genes A,B,C;
One *conserved linkage* involving genes D,E,F.
One *disrupted linkage* involving genes A,B,C vs D,E,F .
One *conserved synteny* involving genes A,B,C.
One *conserved synteny* involving genes D,E,F.
One *disrupted synteny* involving genes A,B,C vs D,E,F.

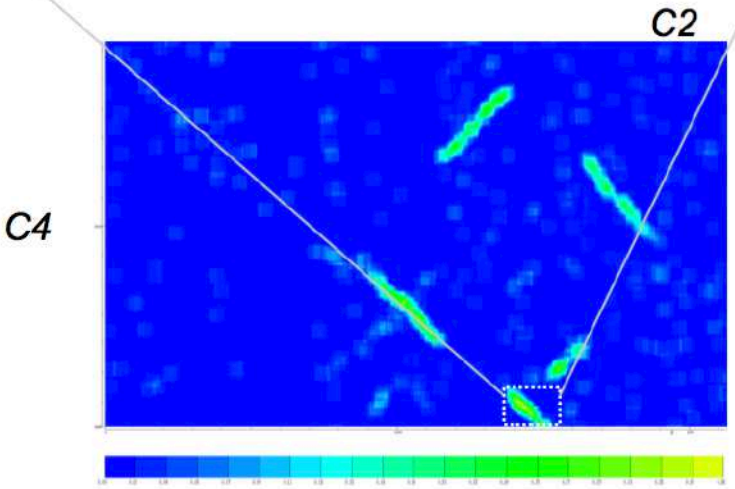
Possible causes:
An inter-chromosomal rearrangement,
such as a reciprocal translocation.

Ehrlich (1997)

Synteny and colinearity

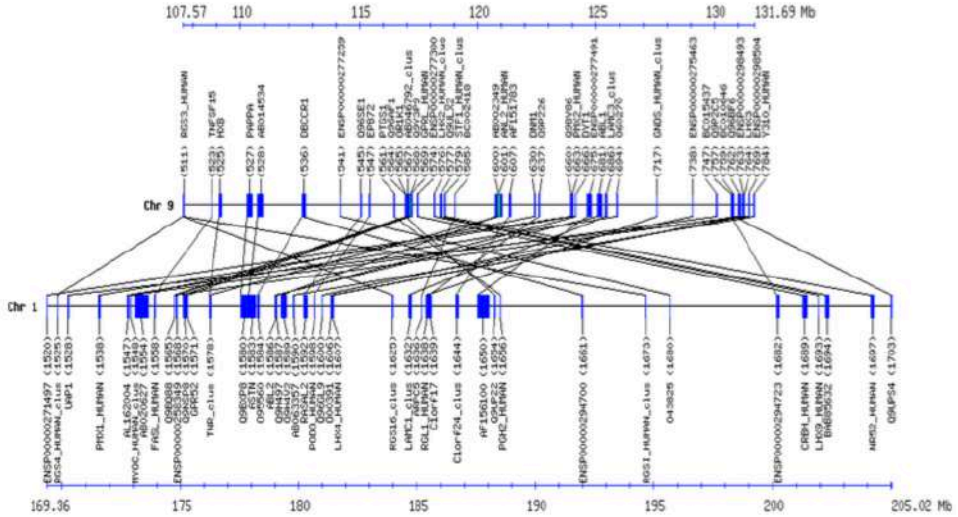
recent duplication

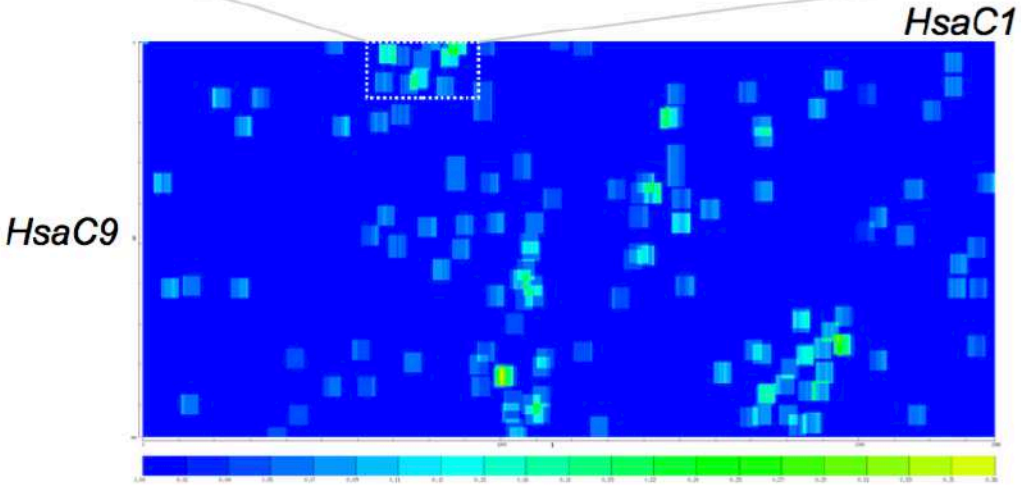




colinearity

ancient duplication

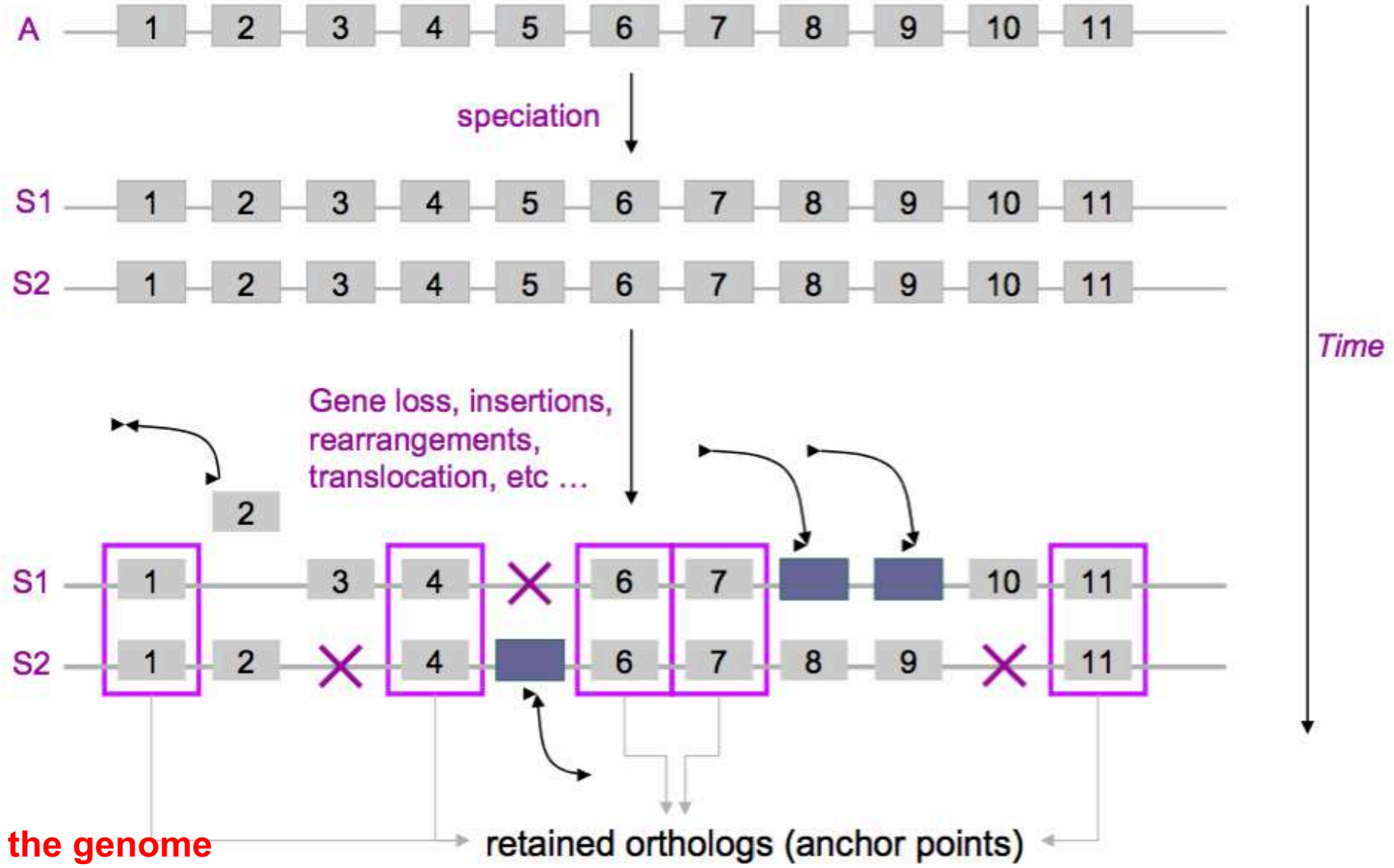




synteny

Slide by Klaas Vandepoele

Inferring gene collinearity



Correctly identify orthologs

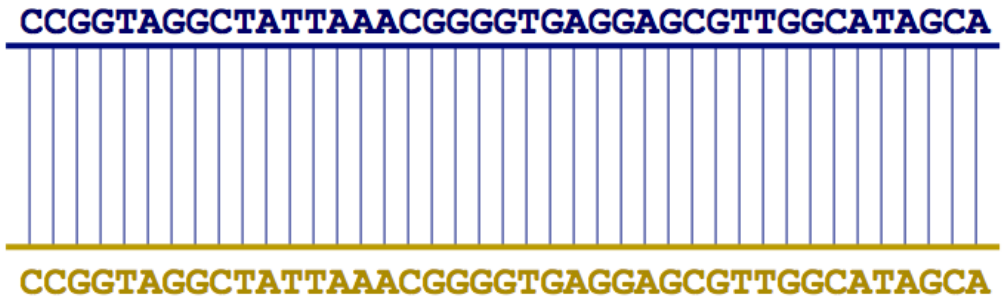
+

Determine their position on the genome

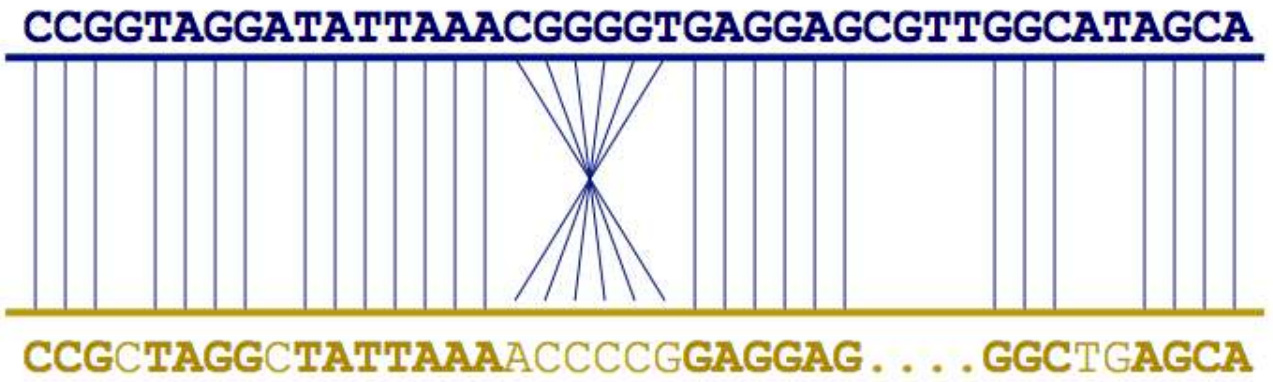
Slide by Klaas Vandepoele

Whole genome alignment

For two genomes, A and B, find a mapping from each position in A to its corresponding position in B

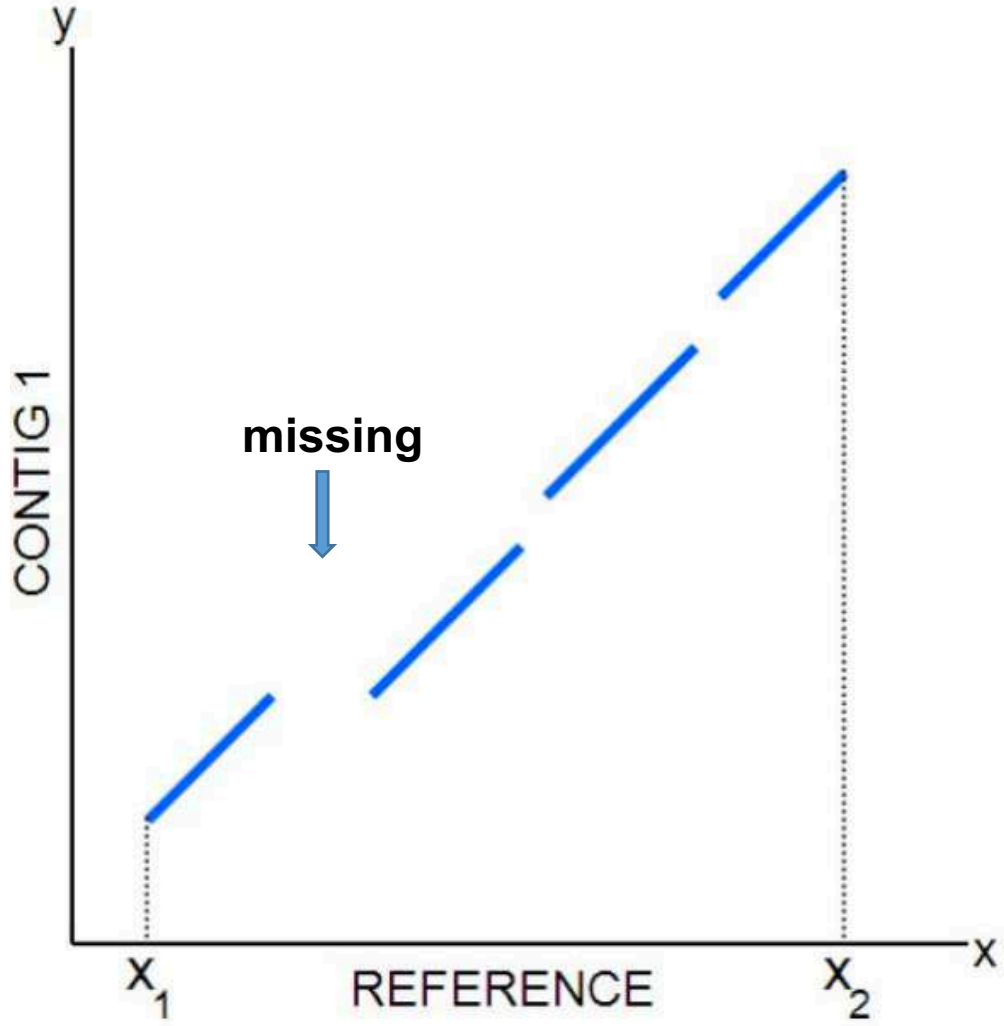


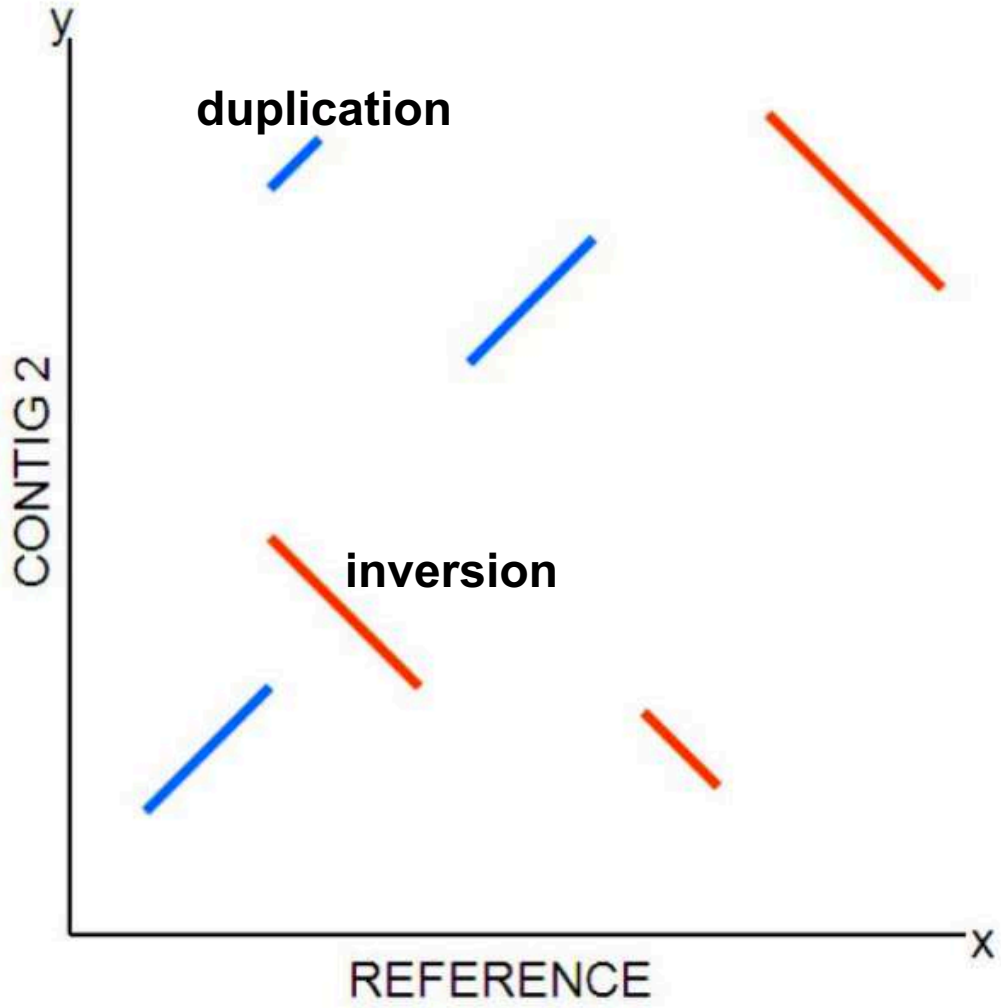
In reality, Genome A may have insertions, deletions, translocations, inversions, duplications or SNPs with respect to B (sometimes all of the above)



Slide of Mike Schatz

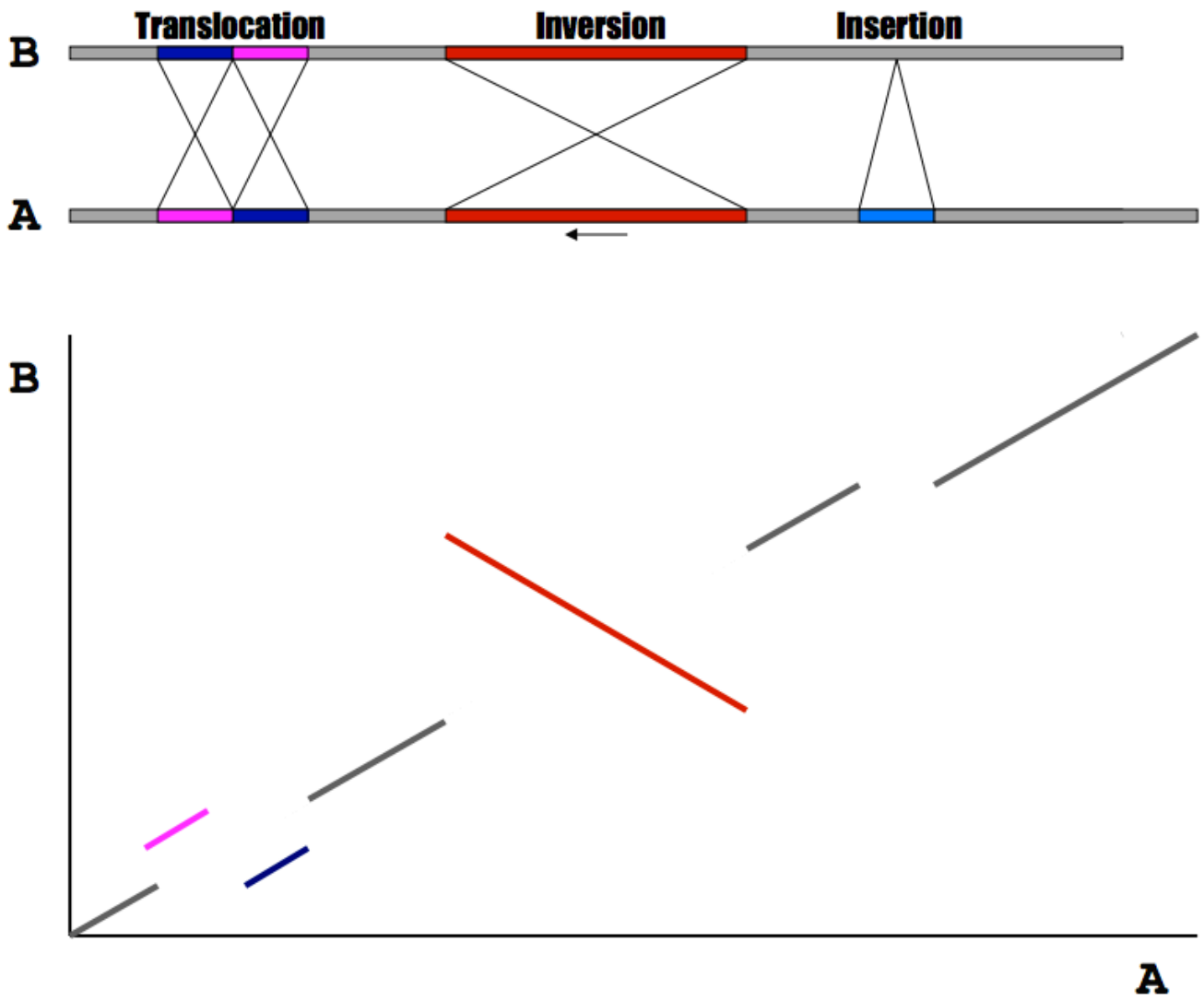
Aligning genome at nucleotide / amino acid level
Visualise through **dotplot**





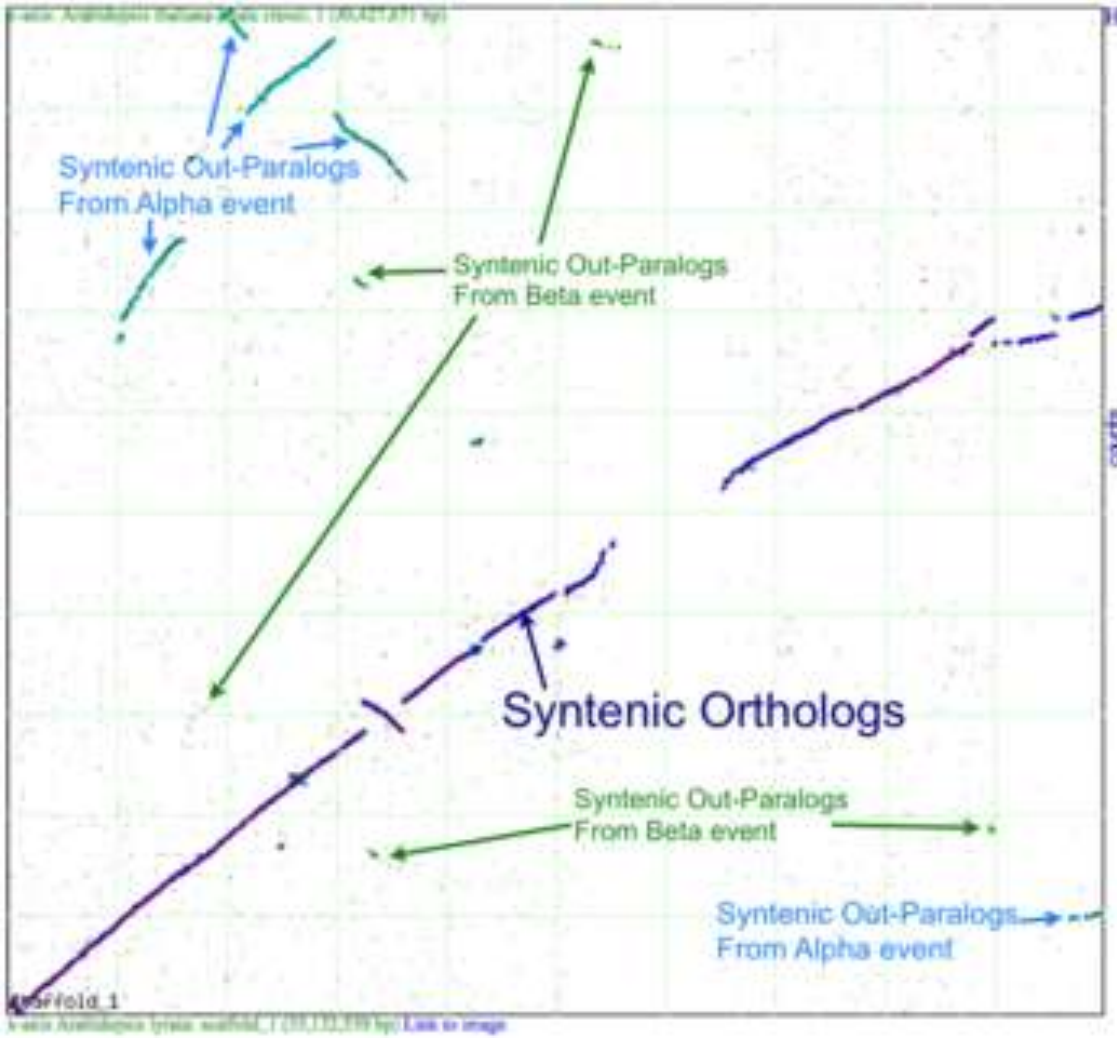
González and Liao (2008)

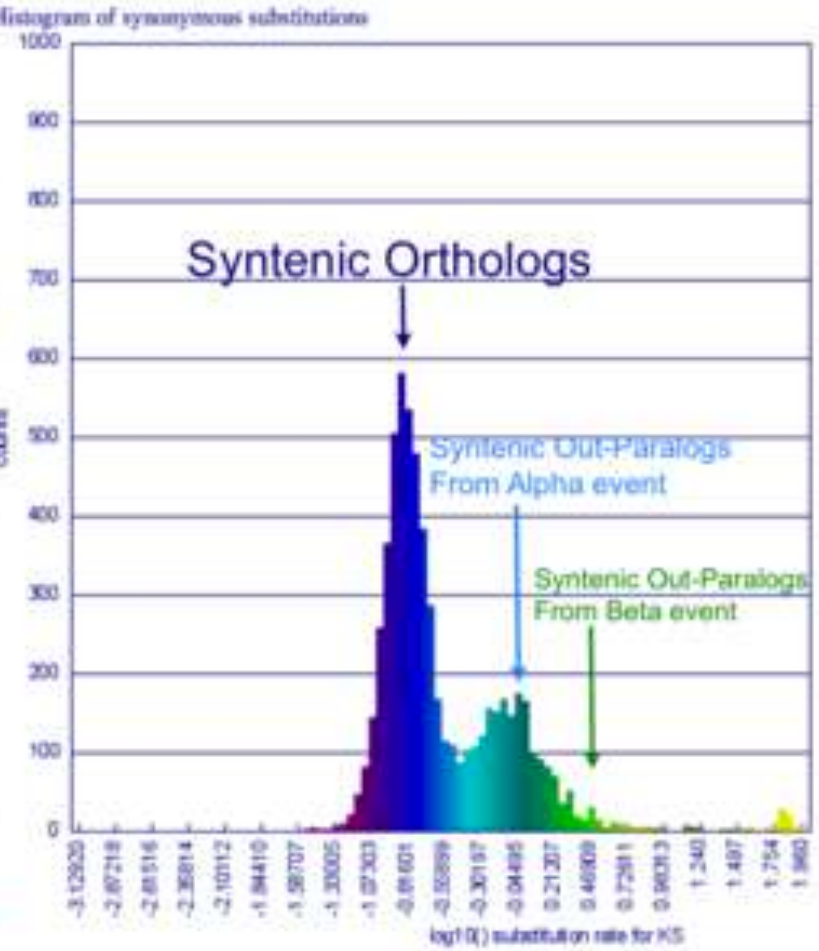
Aligning genome at nucleotide / amino acid level
Visualise through **dotplot**

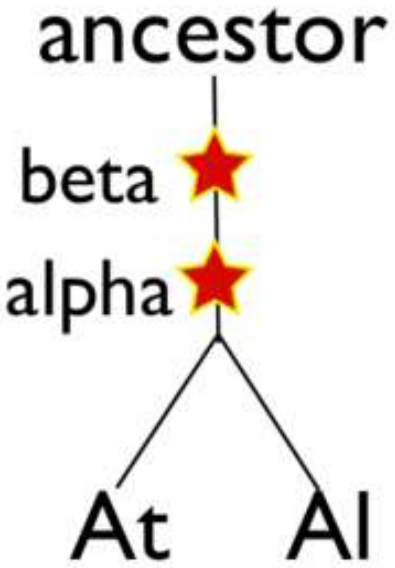


Slide of Mike Schatz

Relationship between genome synteny, syntenic orthologs and duplications

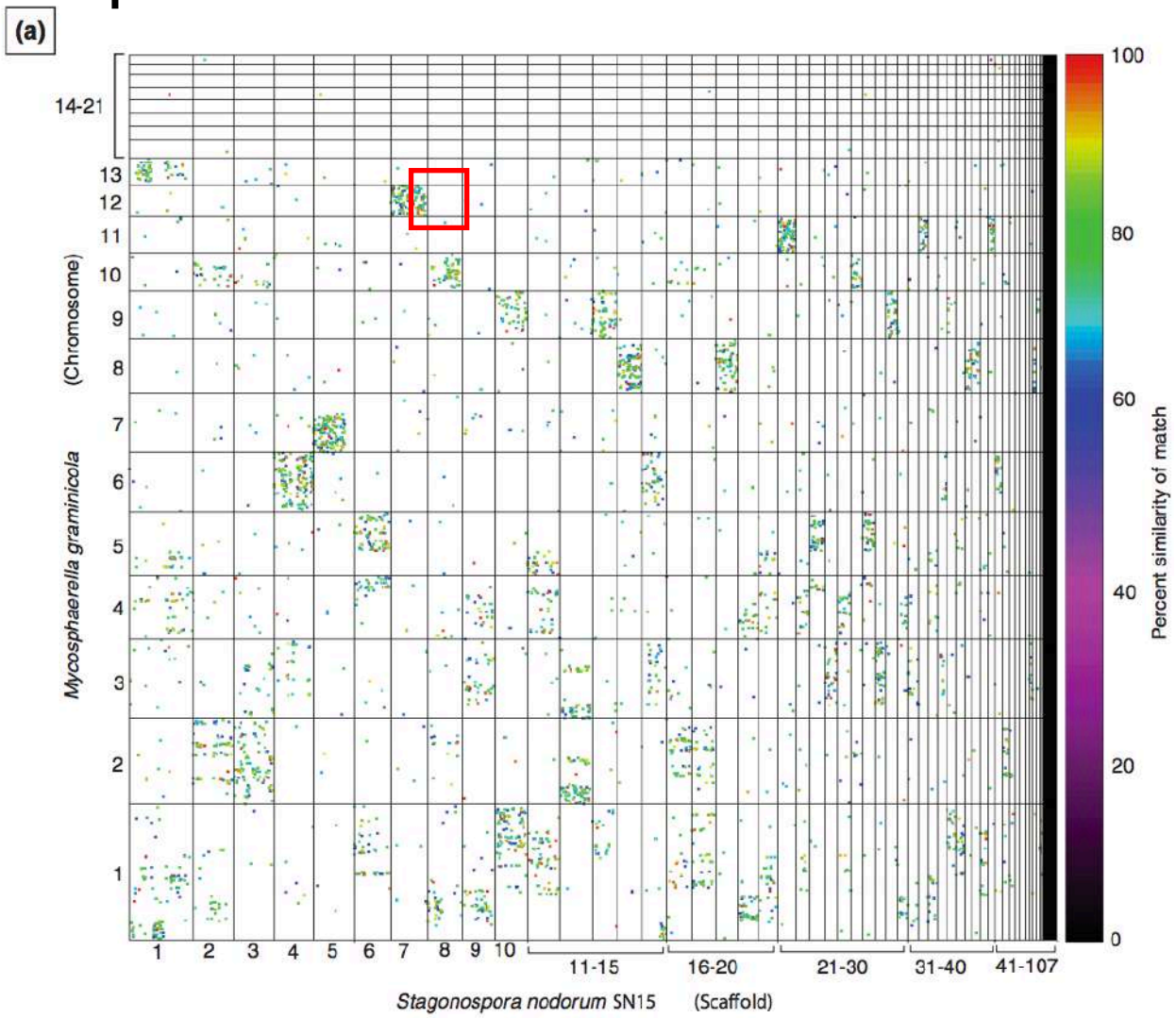


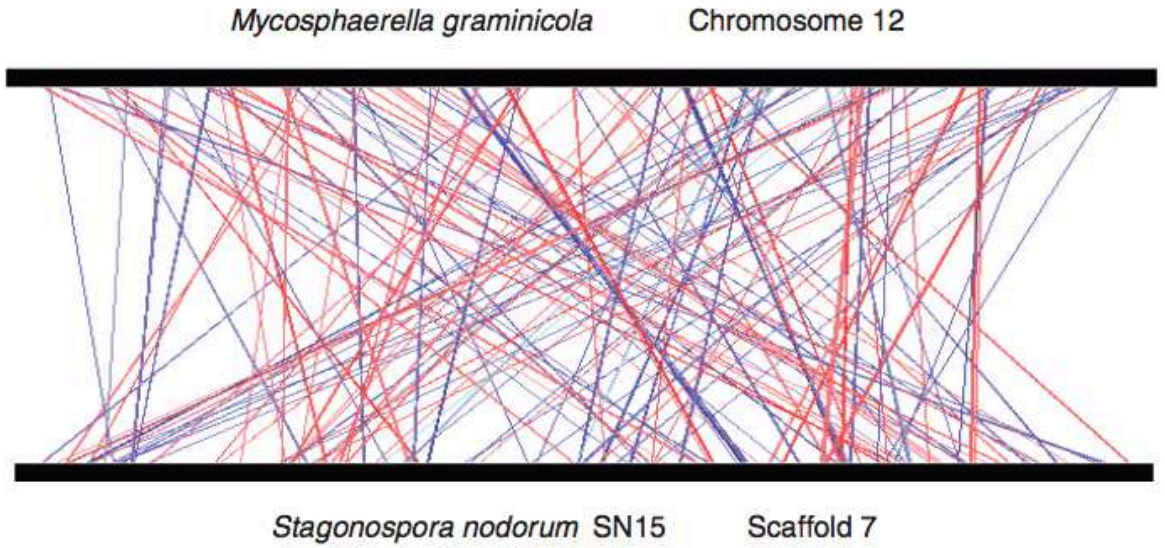




https://genomevolution.org/wiki/index.php/Syntenic_comparison_of_Arabidopsis_thaliana_and_Arabidopsis_lyrata

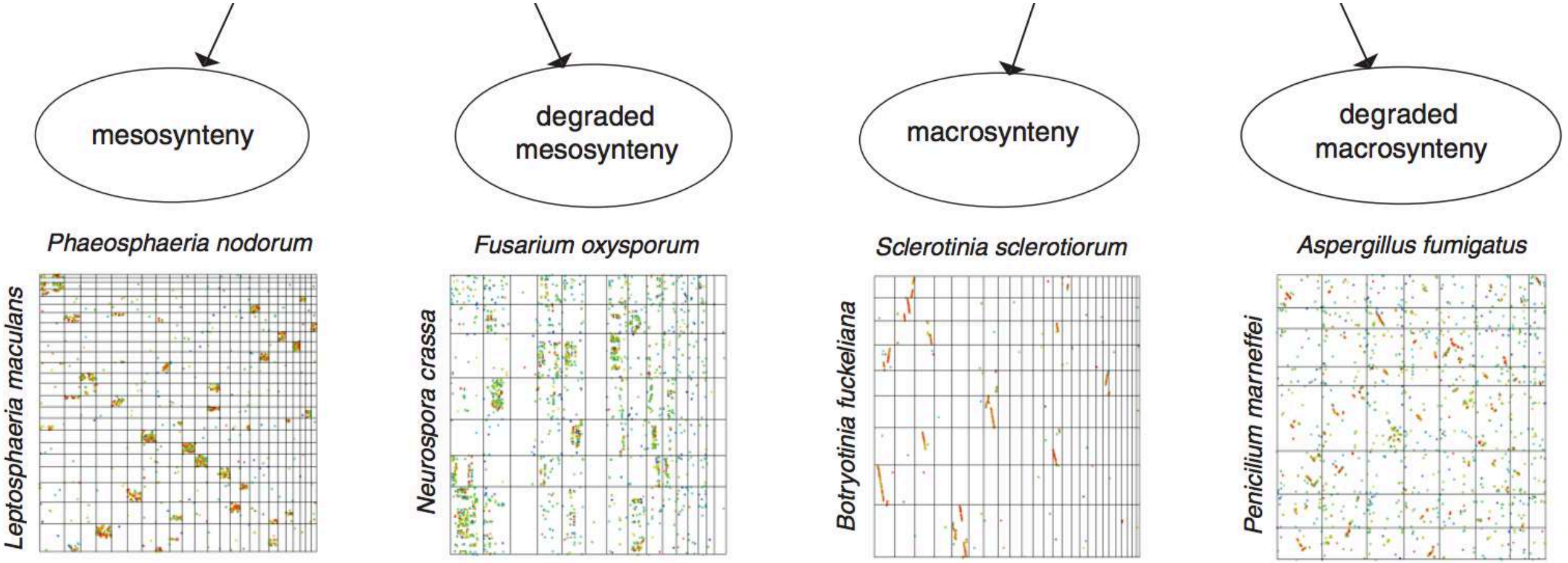
Relationship between genome synteny, syntenic orthologs and duplications





Hane et al (2011)

Different kinds of genome synteny



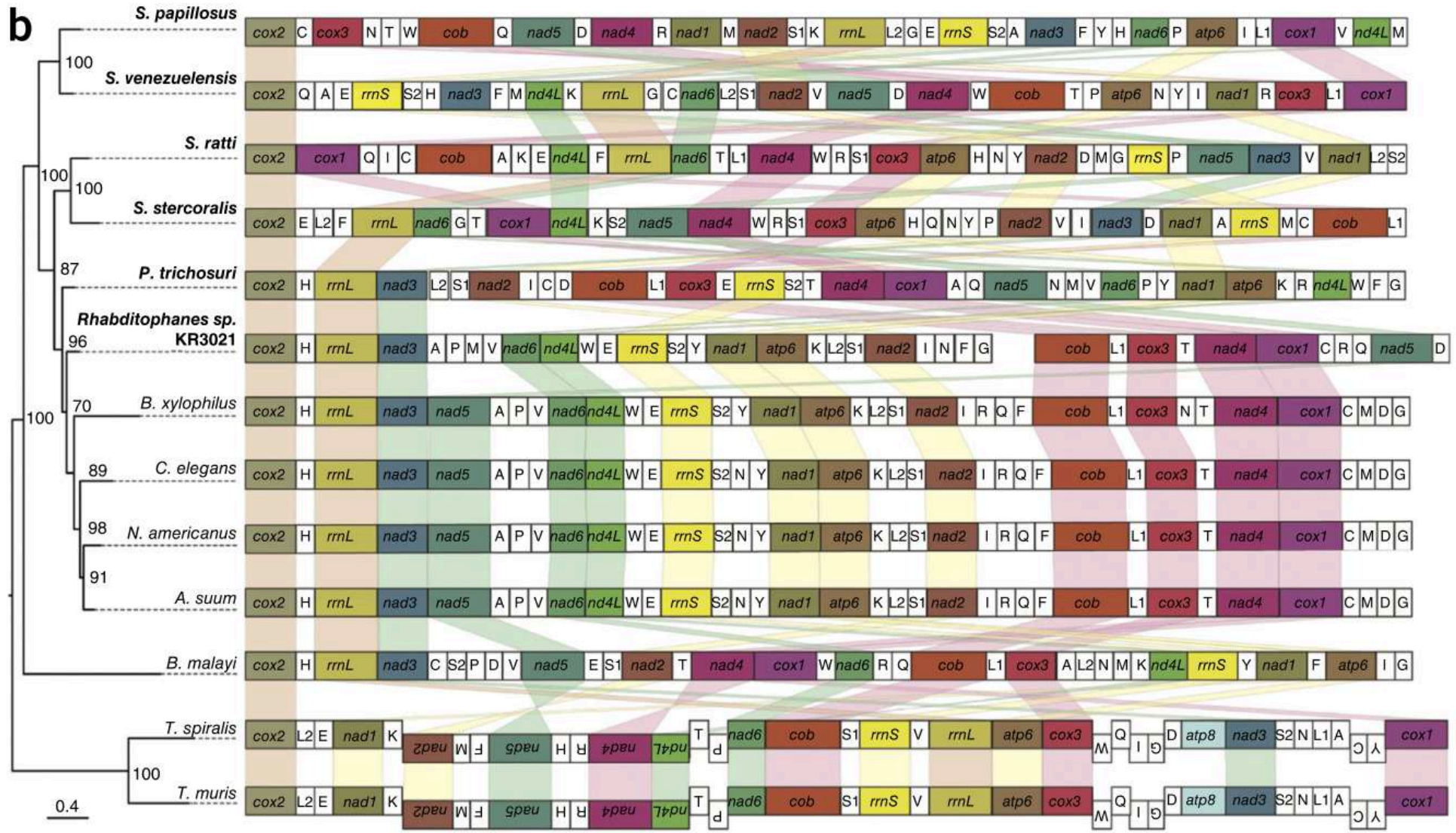
genes are conserved within homologous chromosomes, but with randomized orders and orientations

genes are conserved within homologous chromosomes, and with colinear gene regions

Hane et al (2011)

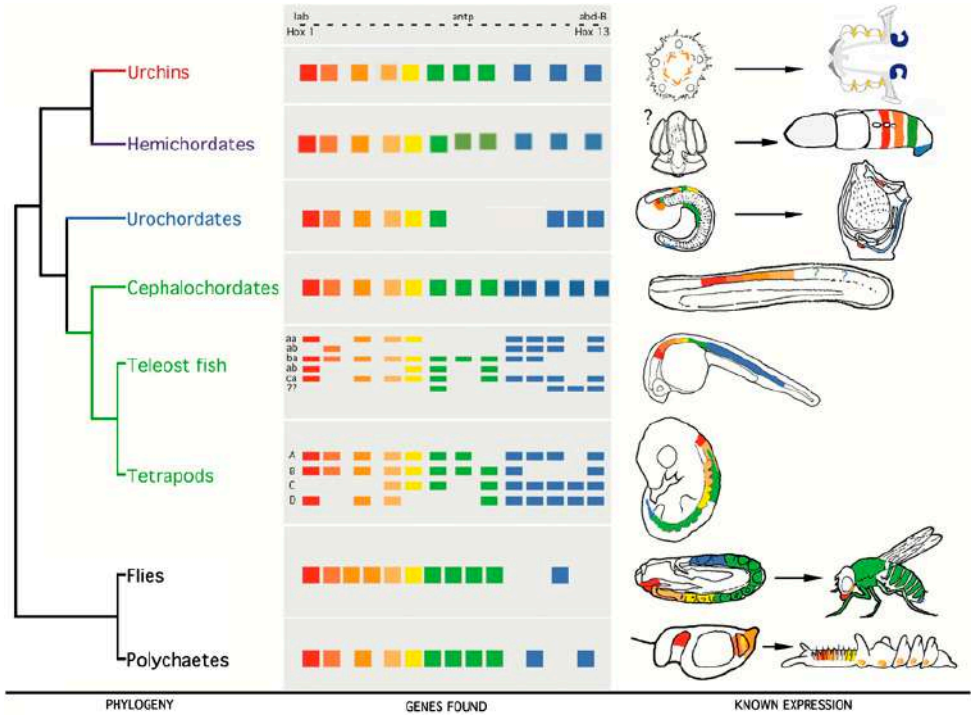
Why are we interested in synteny and collinearity?

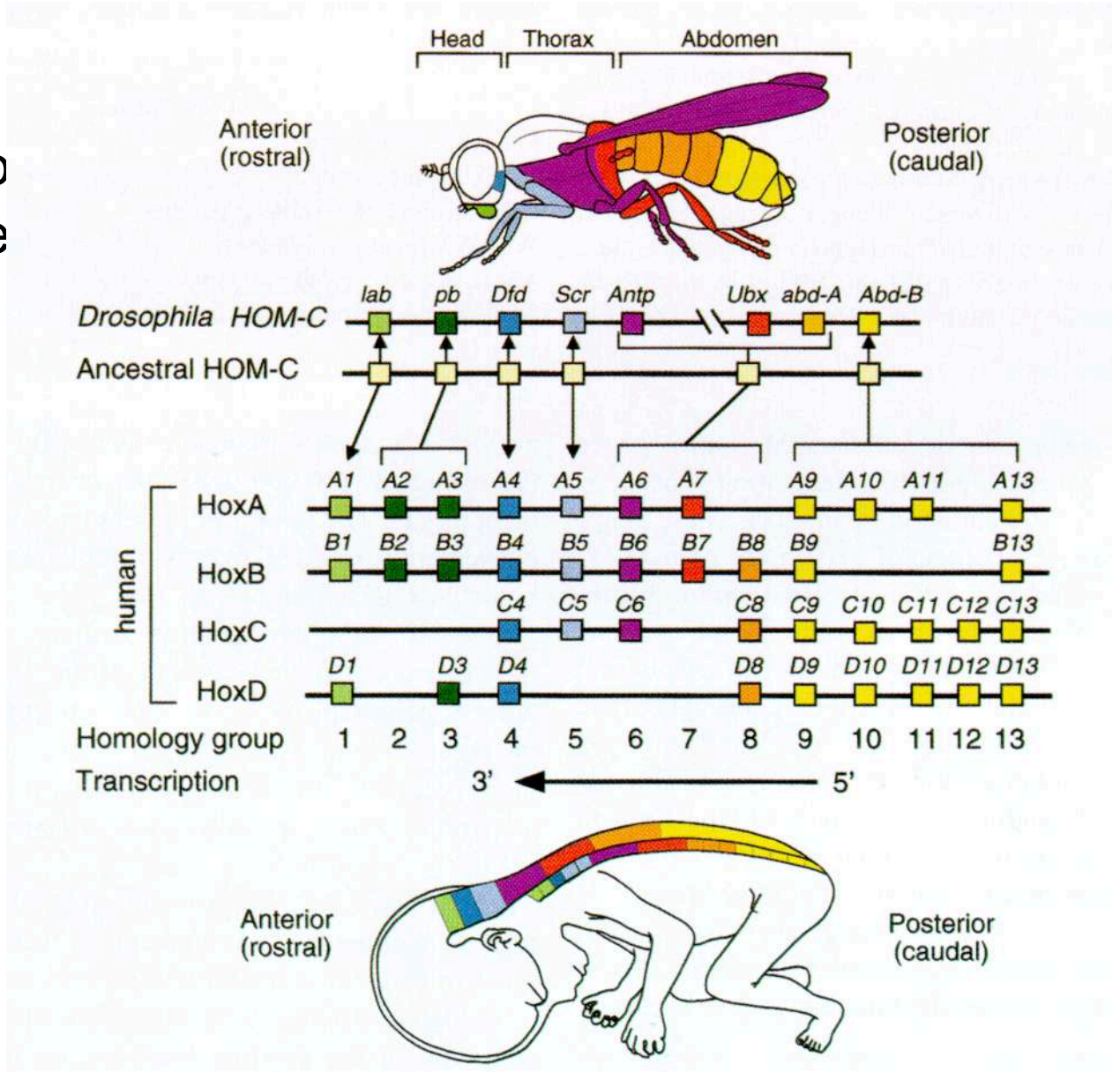
Establish relationship between species



Why are we interested in synteny and collinearity?

Evolutionary conserved features (orthologs, synteny, collinearity) are goo indicators of functionally important genome regions

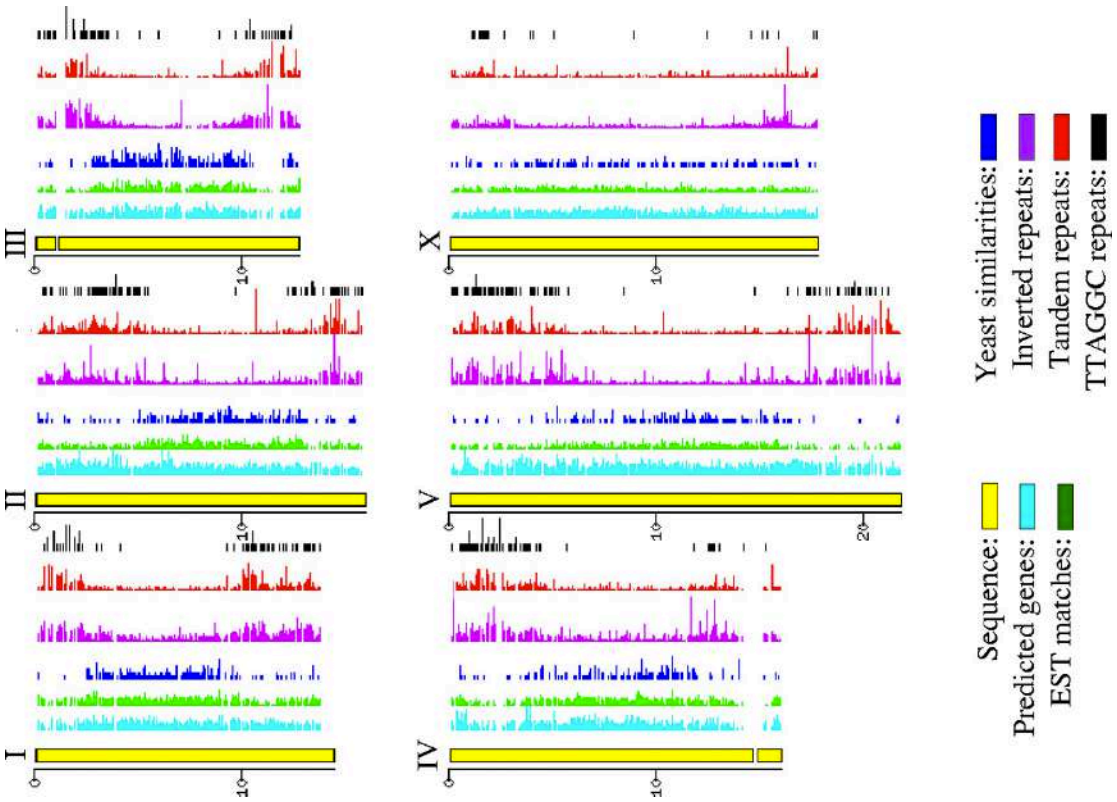


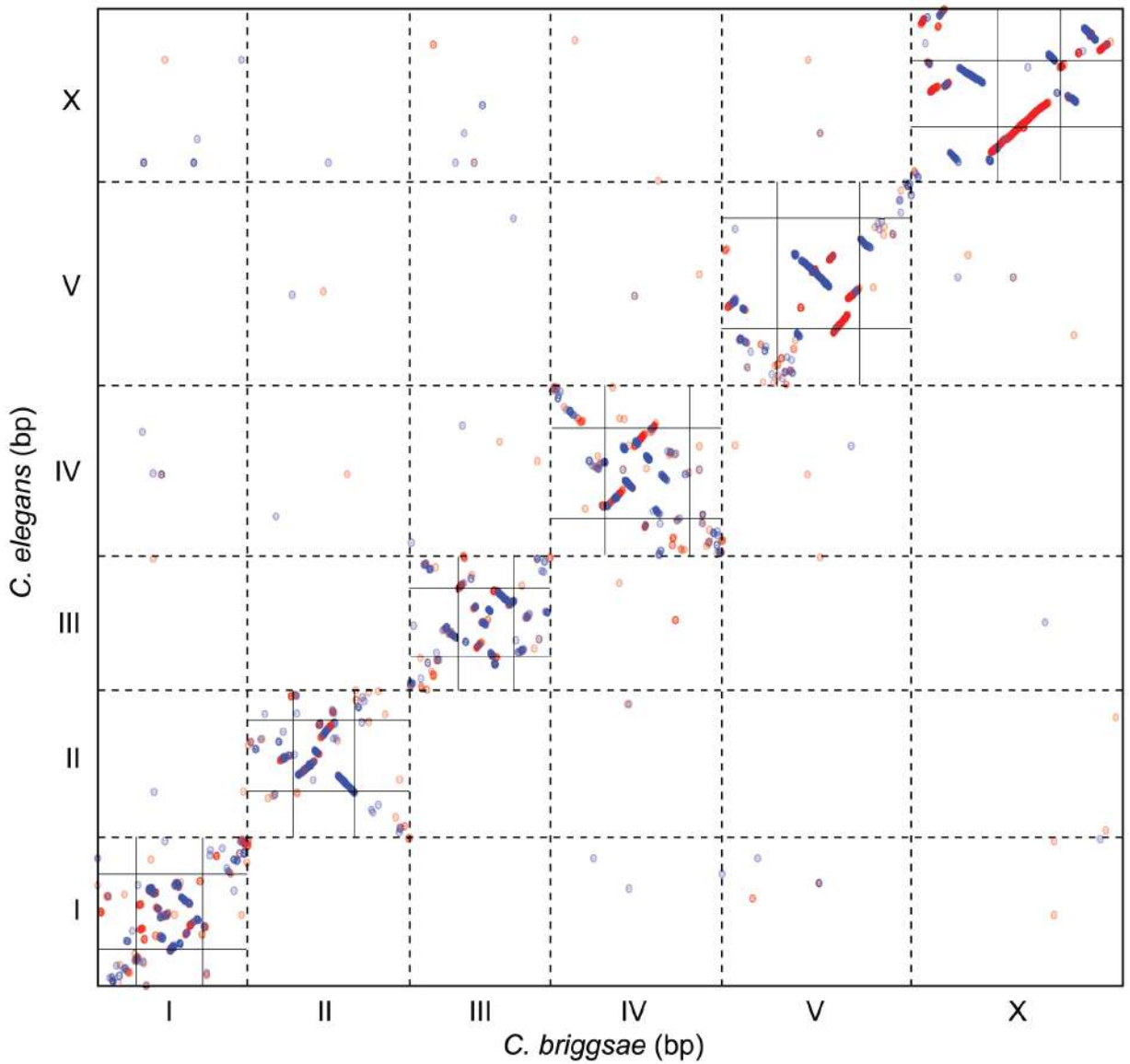


Swalla (2006) ; Mark et al (1997)

Why are we interested in synteny and collinearity?

Evolutionary conserved features (orthologs, synteny, collinearity) relate to genome biology



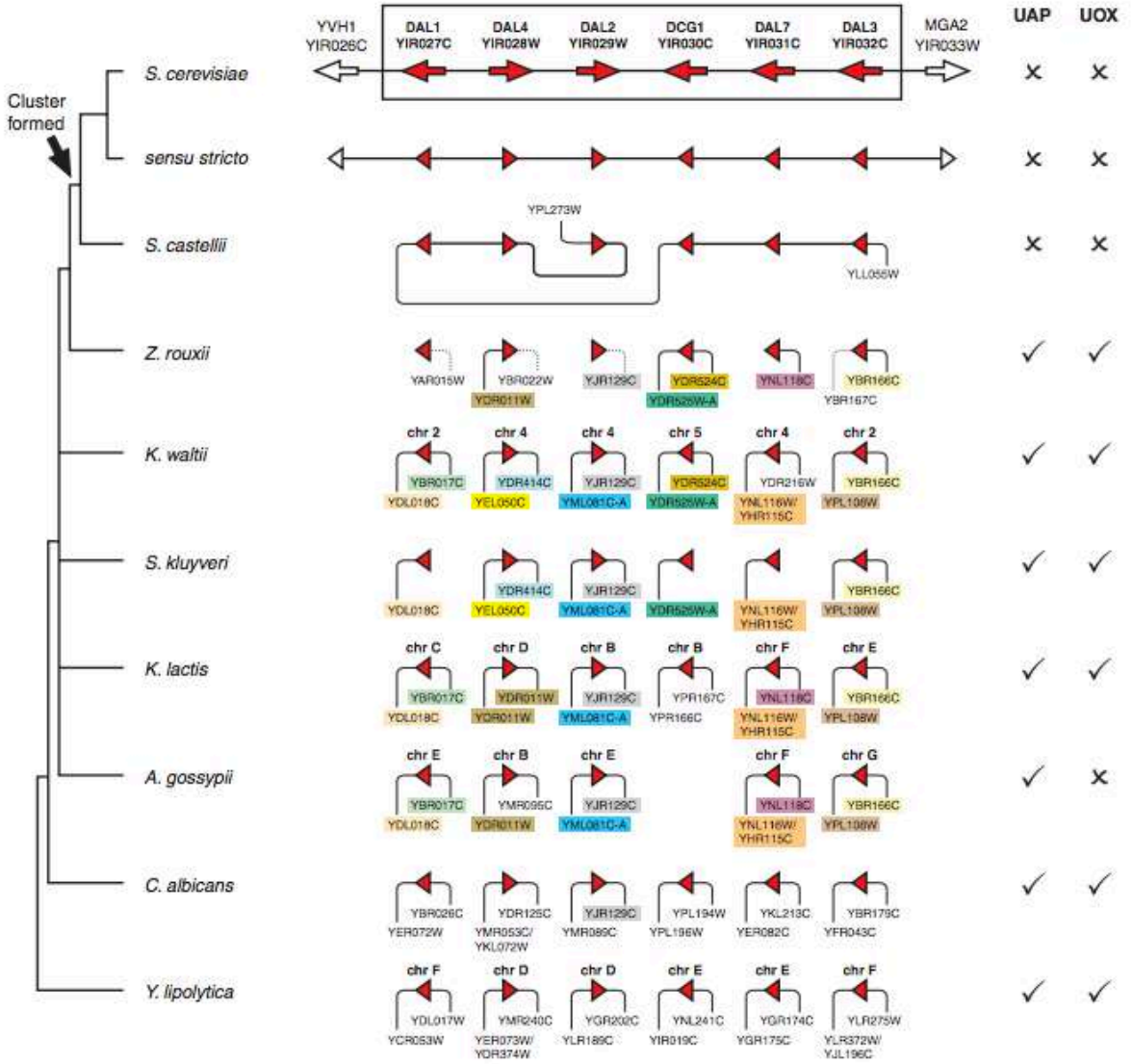


Stein *et al.*, PLOS Biology 2003

The *C. elegans* Sequencing Consortium Science 1998

Why are we interested in synteny and collinearity?

We can **reconstruct evolutionary histories of gene & gene families** and eventually lead to functioning of species

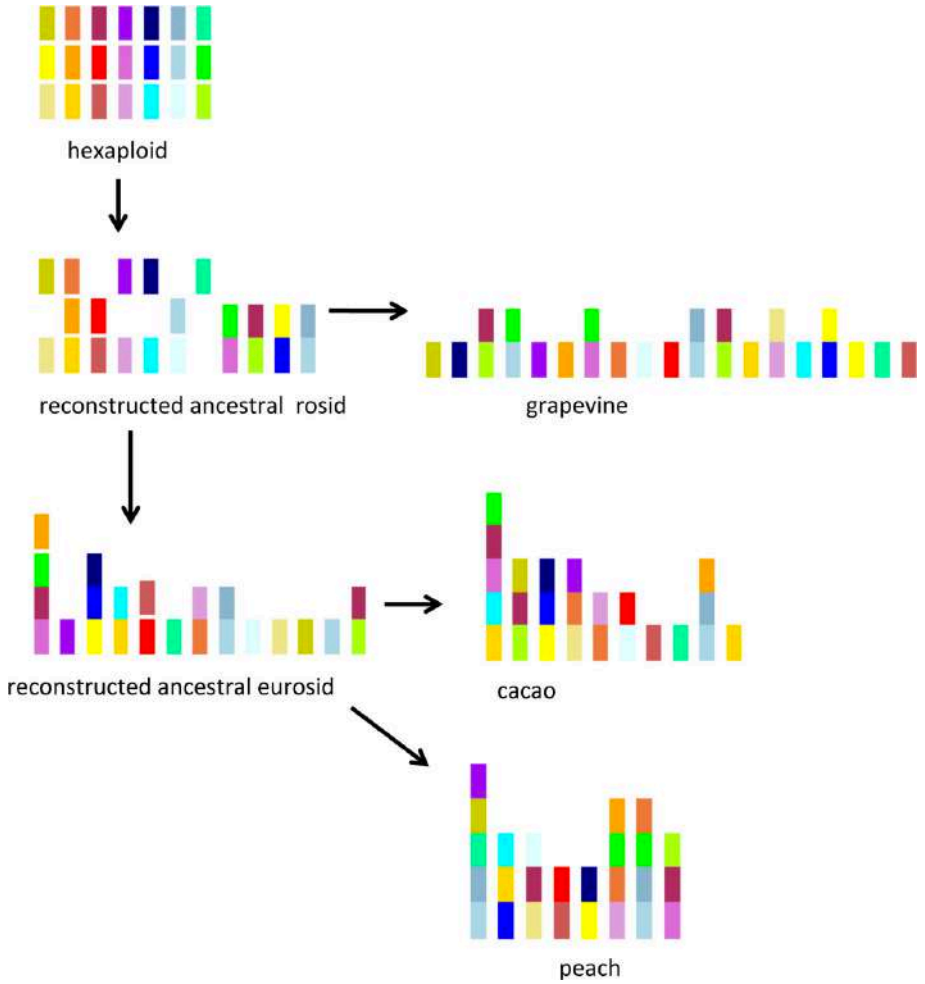


Birth of a metabolic gene cluster in yeast by adaptive gene relocation

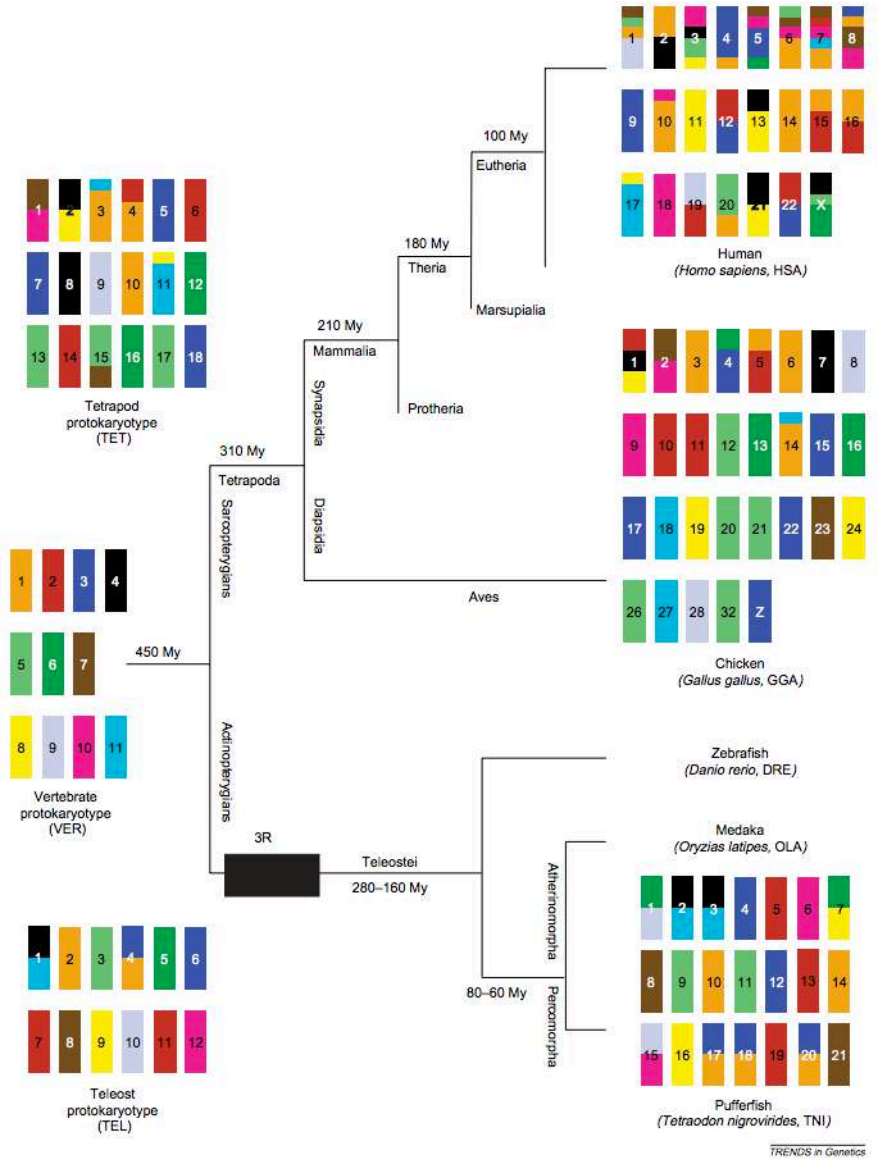
Simon Wong & Kenneth H Wolfe

Why are we interested in synteny and collinearity?

We can **reconstruct ancient karyotypes** that eventually lead to better understanding of evolution of species



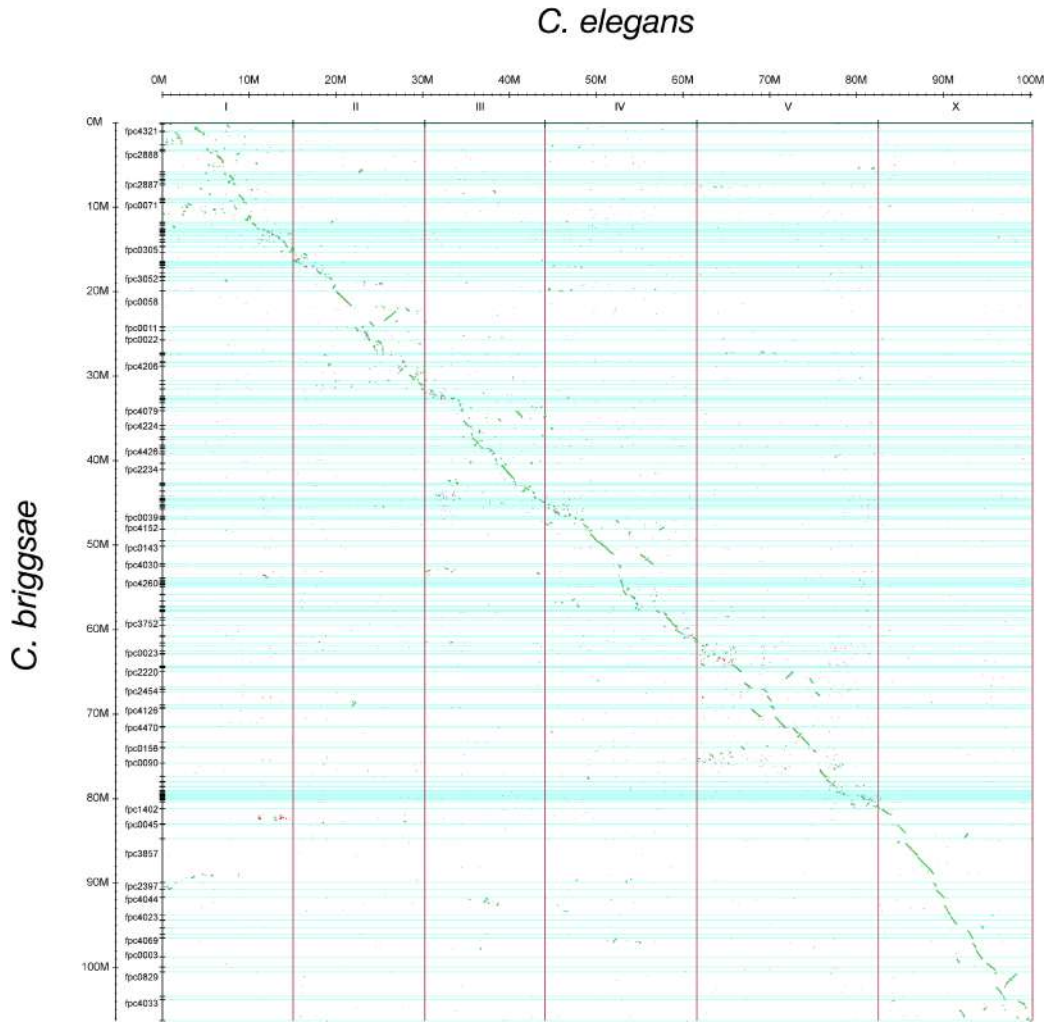
Zheng et al (2013)



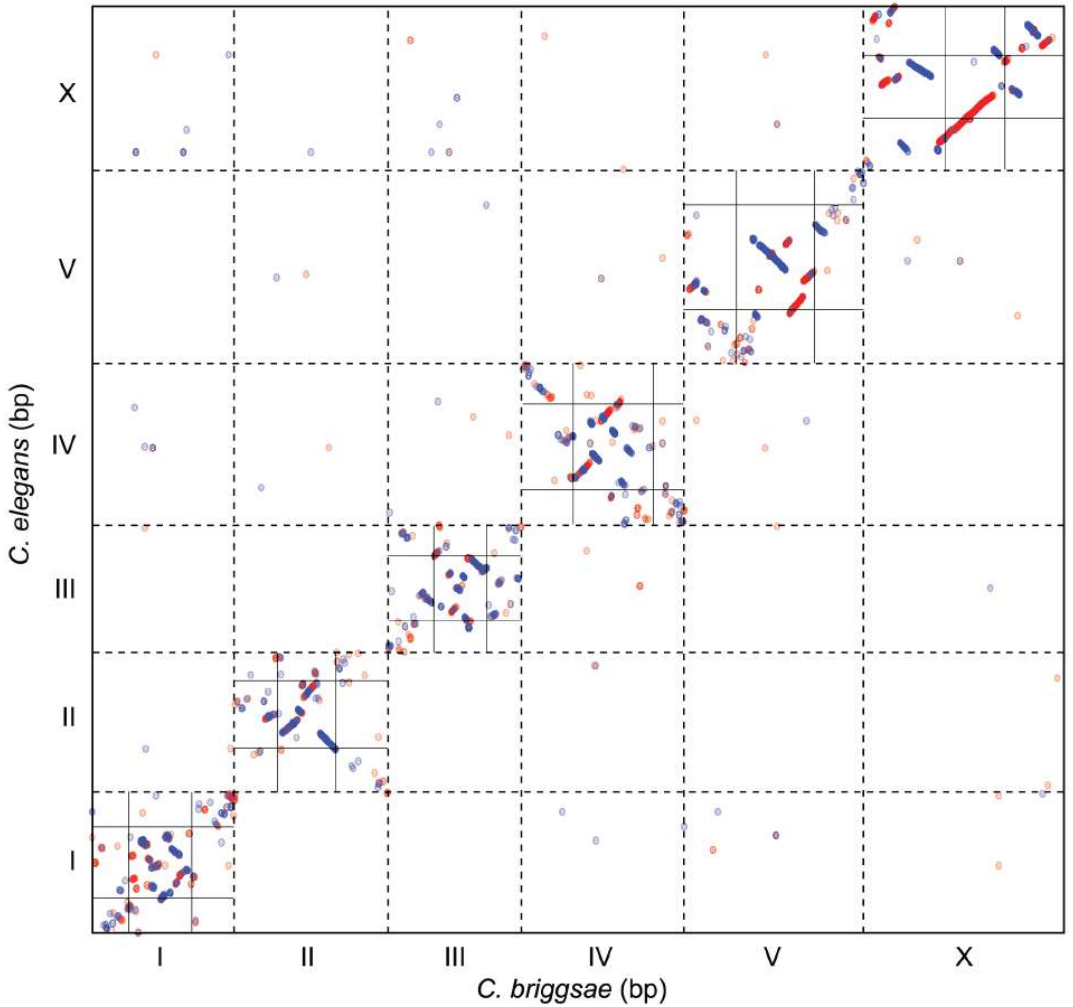
Kohn et al (2006)

Some caveats

Assembly quality likely to influence synteny observation



Stein *et al.,* PLOS Genetics (2003)



Ross *et al.,* PLOS Genetics (2011)

Syteny based scaffolding: use with caution

Tang *et al. Genome Biology* (2015) 16:3
DOI 10.1186/s13059-014-0573-1

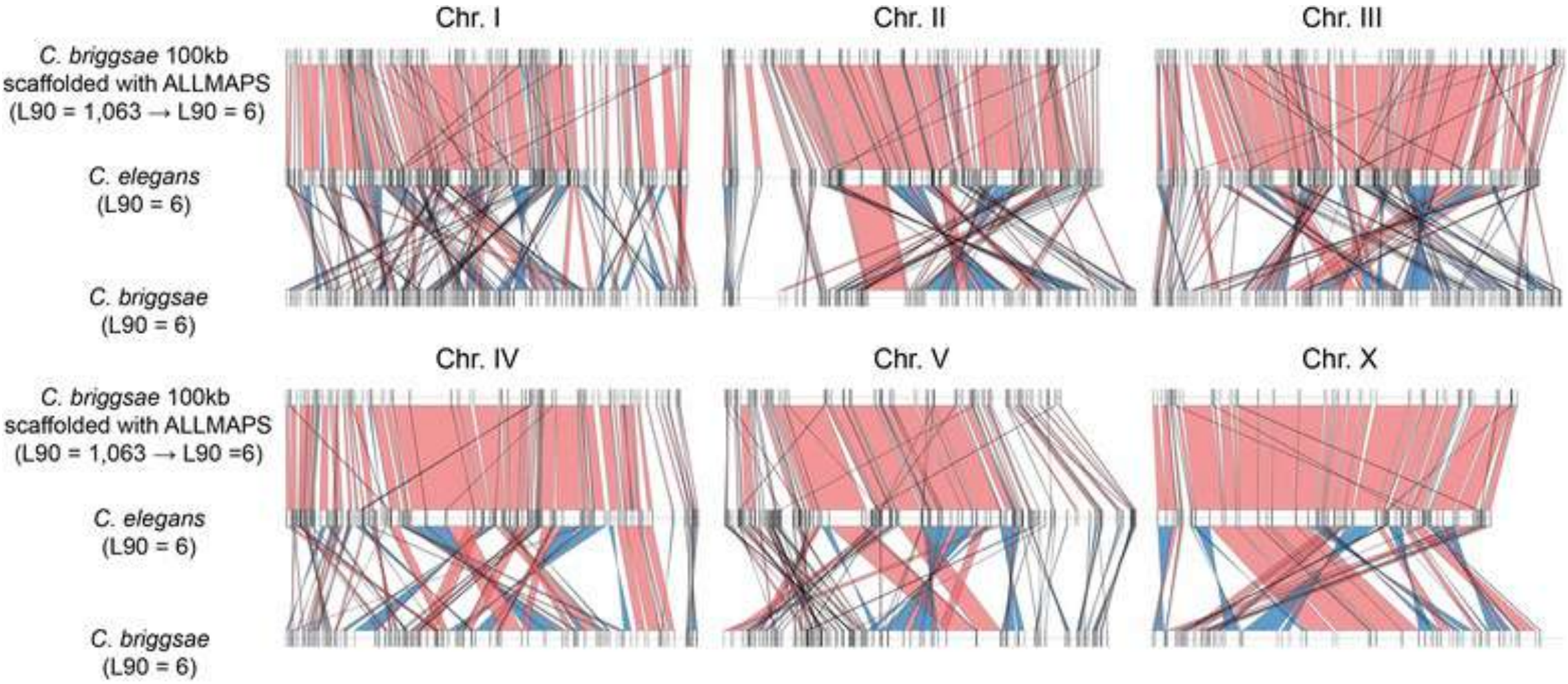
METHOD Open Access

ALLMAPS: robust scaffold ordering based on multiple maps

Haibao Tang[1,2,3*], Xingtan Zhang[4], Chenyong Miao[1], Jisen Zhang[1], Ray Ming[1], James C Schnable[3,5], Patrick S Schnable[3,6], Eric Lyons[2] and Jianguo Lu[7]

for example, in 'orphan' species where there is little research investment in the past, **we can still create consensus chromosomal assemblies based on comparative maps against multiple, closely-related genomes as a collection of 'references'** … Correct?

Syteny based scaffolding: use with caution



Dang *et al* (2018)

Comparing genomes beyond gene level

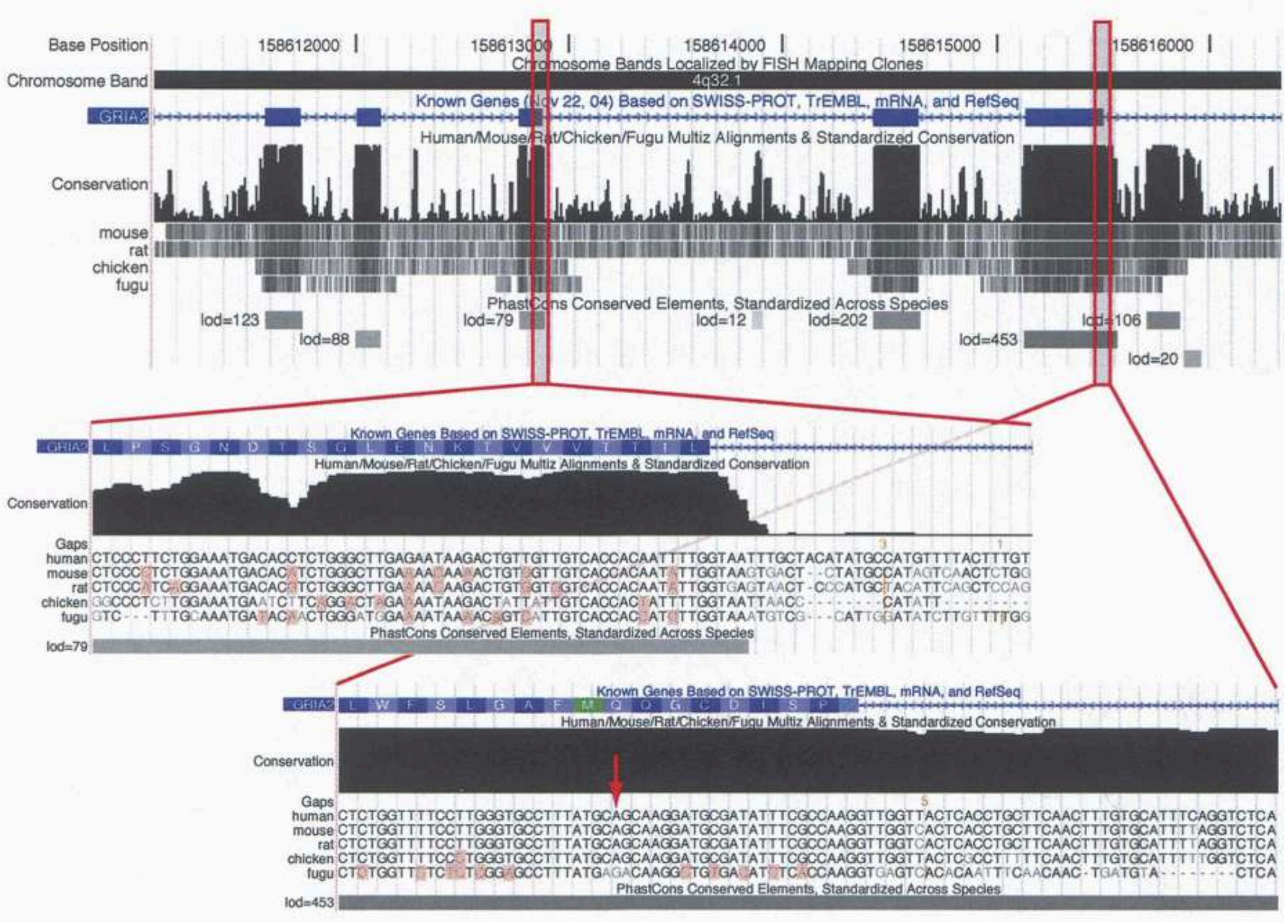
Article

Evolutionarily conserved elements in vertebrate, insect, worm, and yeast genomes

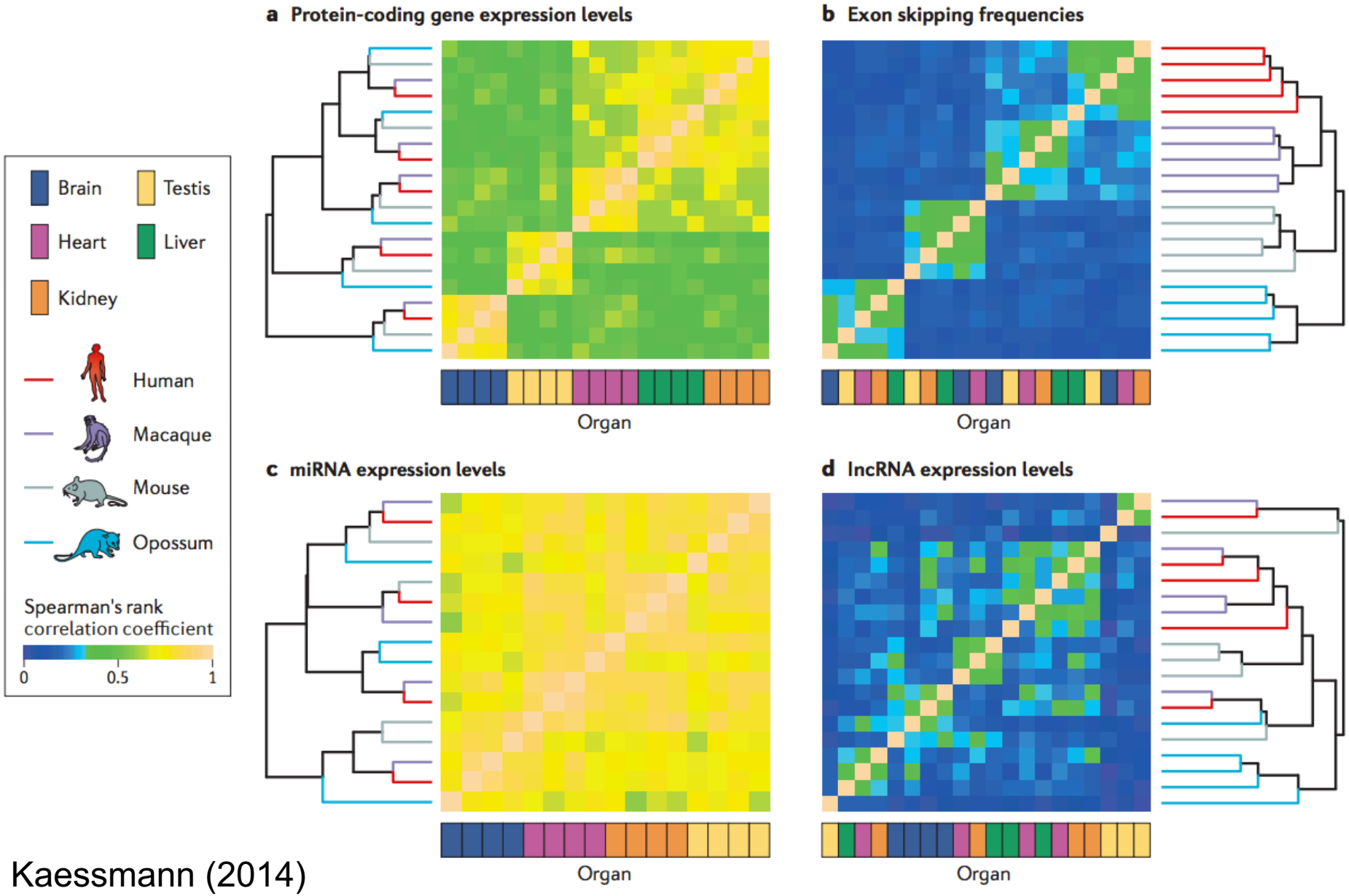
Adam Siepel,[1,6] Gill Bejerano,[1] Jakob S. Pedersen,[1] Angie
Kate Rosenbloom,[1] Hiram Clawson,[1] John Spieth,[4] LaDe
Stephen Richards,[5] George M. Weinstock,[5] Richard K. W
W. James Kent,[1] Webb Miller,[3] and David Haussler[1,2]

*[1]Center for Biomolecular Science and Engineering, [2]Howard Hughes Medical Institut
Cruz, California 95064, USA; [3]Center for Comparative Genomics and Bioinformatics
Park, Pennsylvania 16802, USA; [4]Genome Sequencing Center, Washington Universi
63108, USA; [5]Human Genome Sequencing Center, Department of Molecular and H
Houston, Texas 77030, USA*

PhastCons

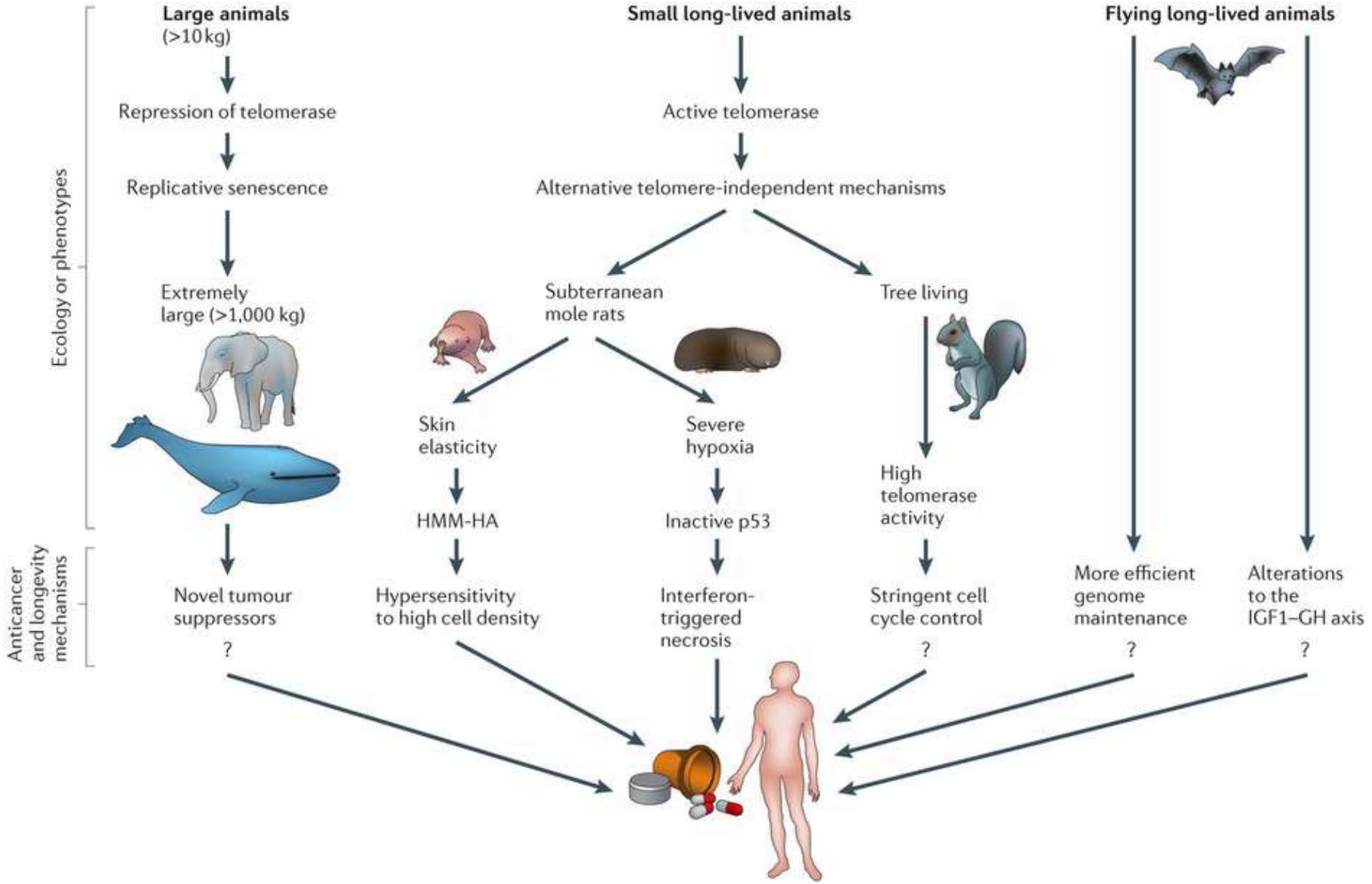


Global patterns of evolution for different aspects of the transcriptome



Necsulea and Kaessmann (2014)

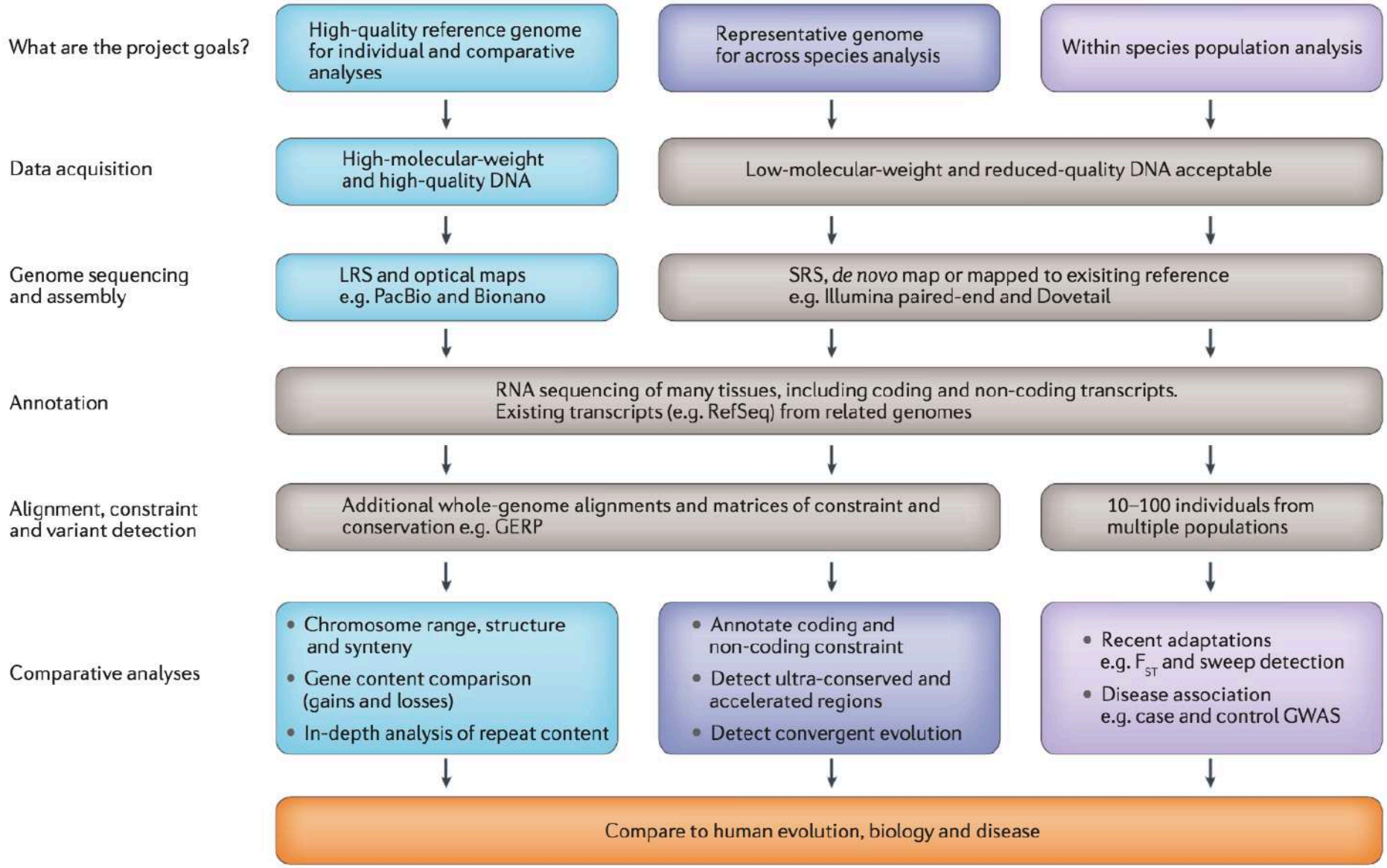
Comparative genomics of longevity ageing (with focus)



Gorbunova et al (2014)

Nature Reviews | Genetics

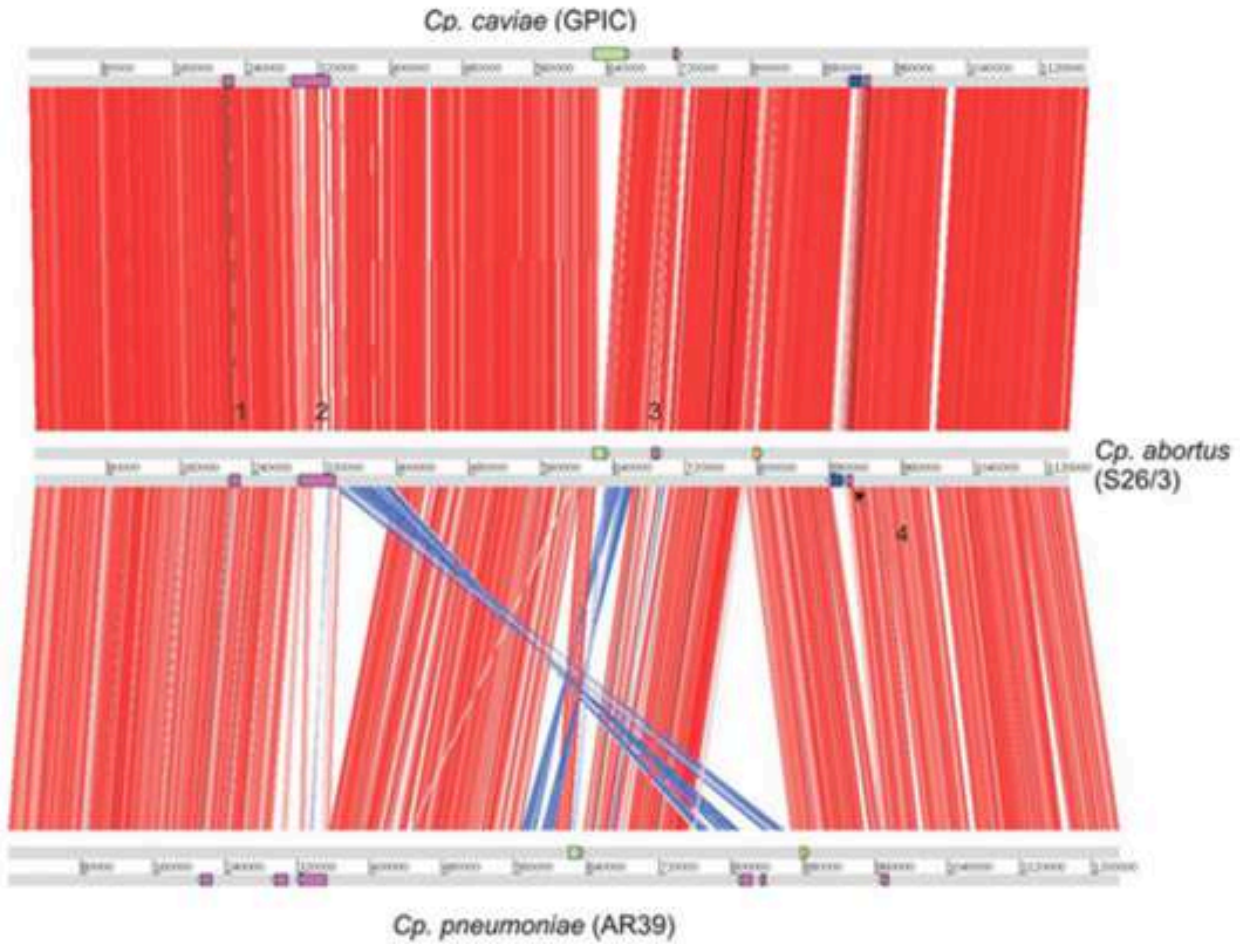
Designing a sequencing project: 2017 version



Meadows and Toh (2017) Nature Review Genetics

Genome visualisation

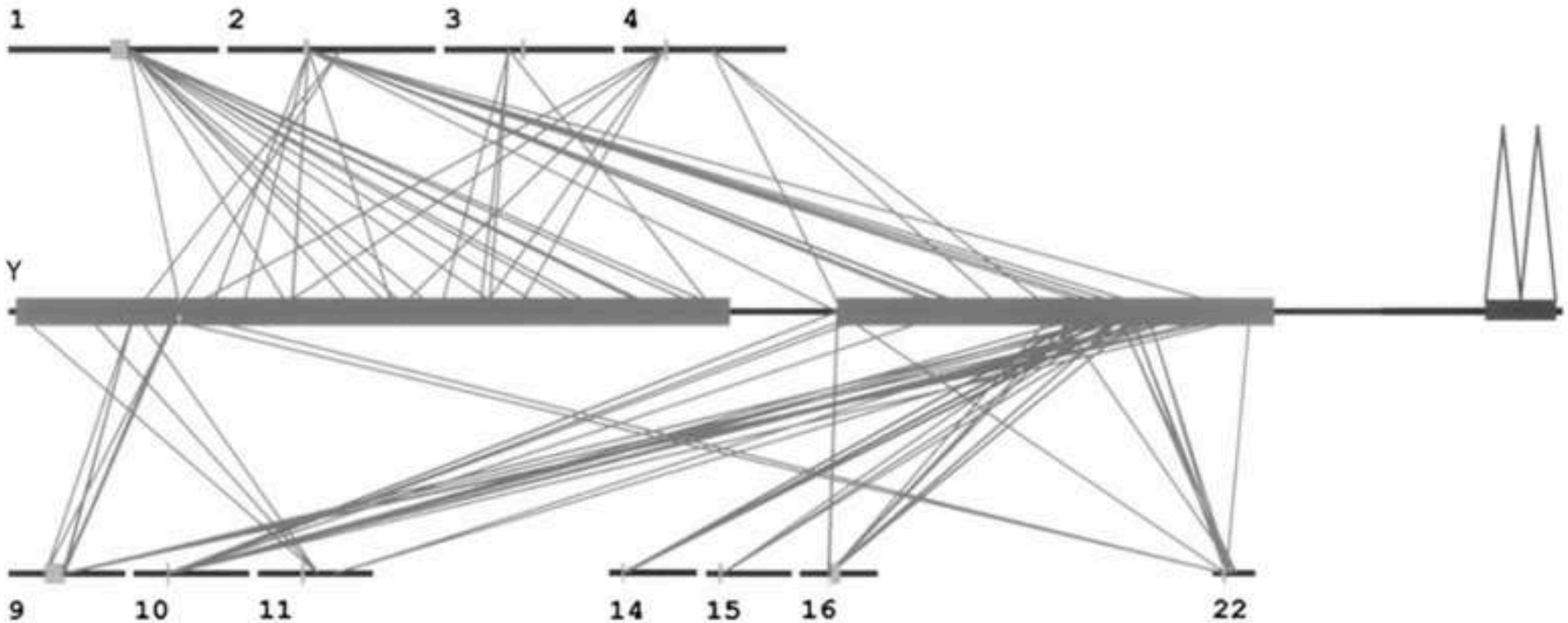
- this is the most common way to represent relationships within genomic positions
  - works when the number of cross-overs is limited



Genome Res. 2005 May;15(5):629-40

http://circos.ca/presentations/talks/circos_intro/

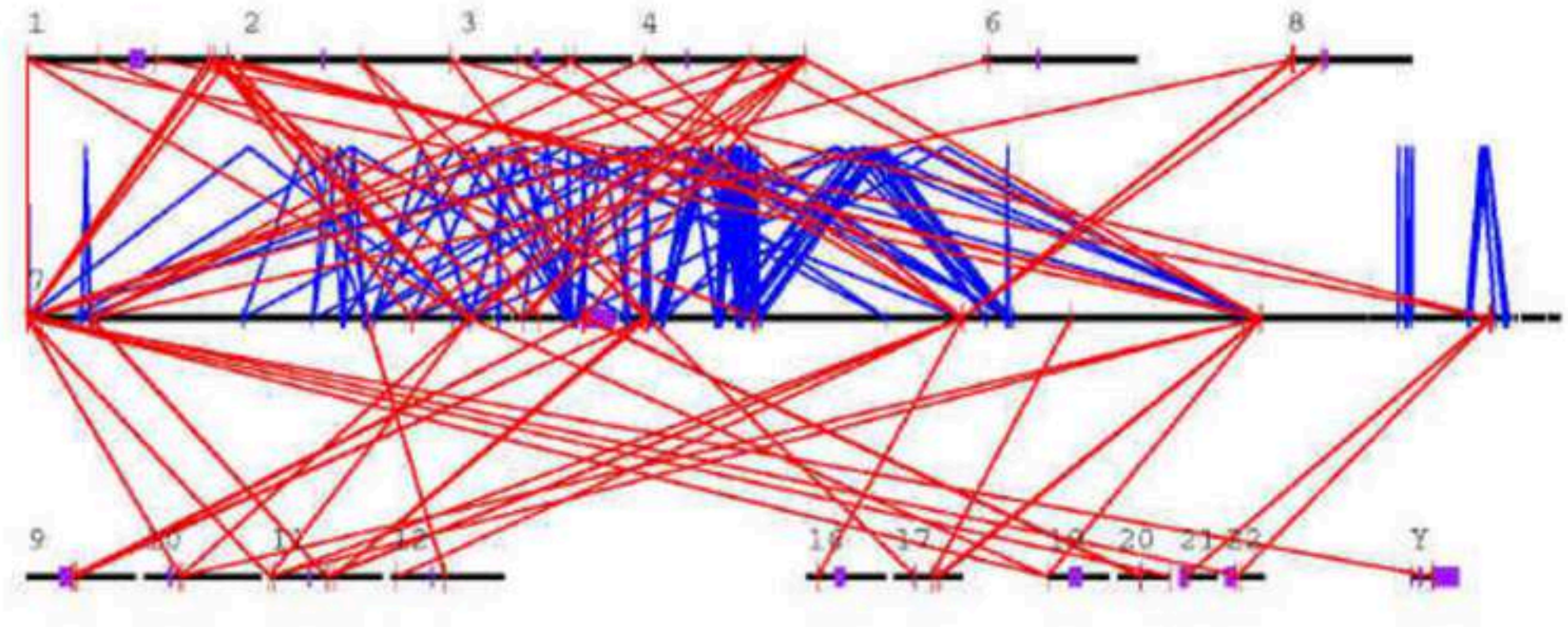
- when complexity is increased, the figure starts to lose cohesion
  - routing becomes difficult to follow
  - there is no focus point for the eye – your eye wanders over the figure



Genome Res. 2003 Jan;13(1):37-45

http://circos.ca/presentations/talks/circos_intro/

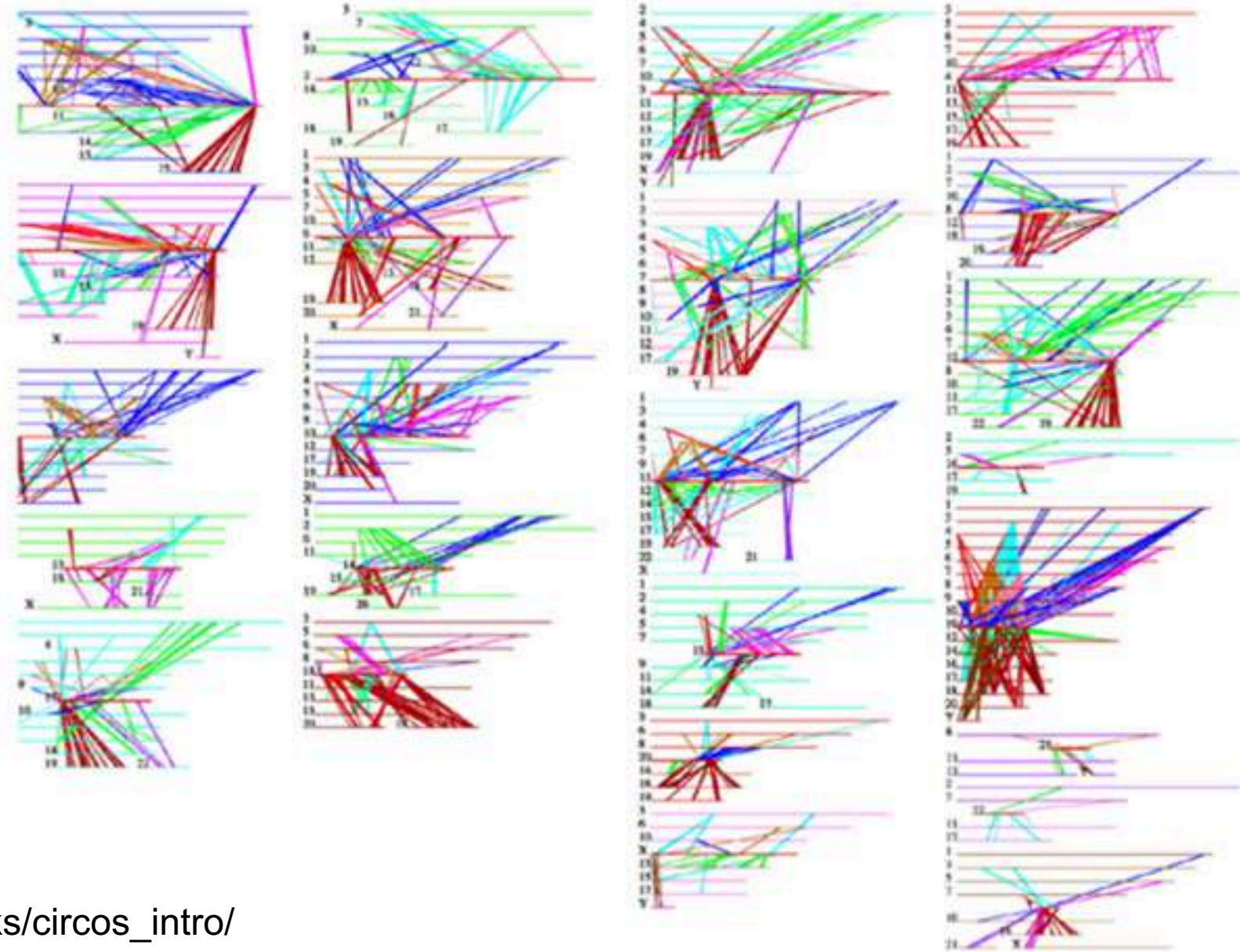
- things get worse and worse when mappings that link both neighbouring (blue) and distant (red) positions are shown



http://circos.ca/presentations/talks/circos_intro/

http://www.genome.wustl.edu/projects/human/chr7paper/chr7data/030113/segmental/index.php

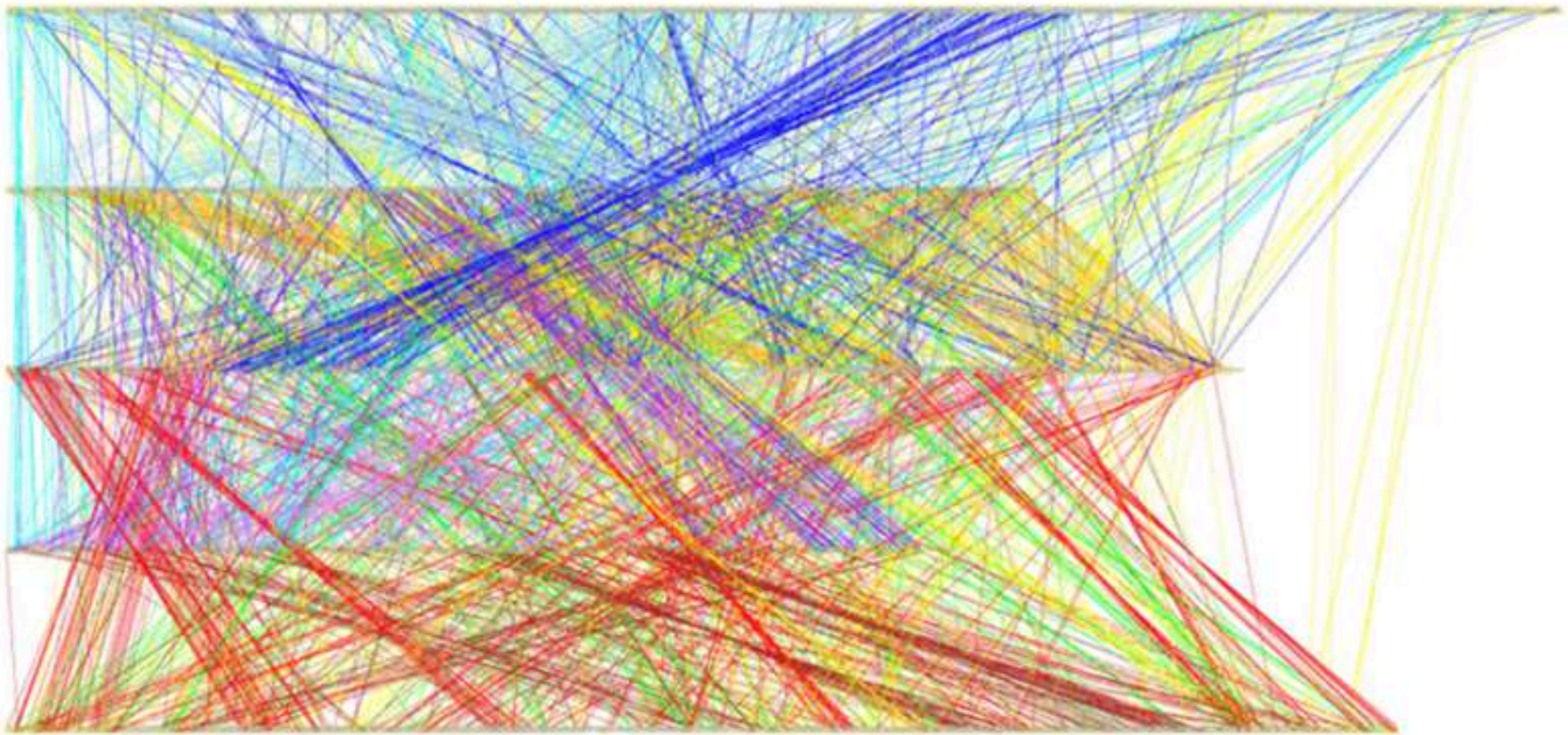
- you can try to fix things by partitioning your data set (somehow)
- mileage varies
  - generally poor



http://circos.ca/presentations/talks/circos_intro/

Venter, J. C., M. D. Adams, et al. (2001). "The sequence of the human genome." Science 291(5507): 1304-51.v

- finally, you descend into data overload and information hell
  - this is not an informative plot, although a pretty one

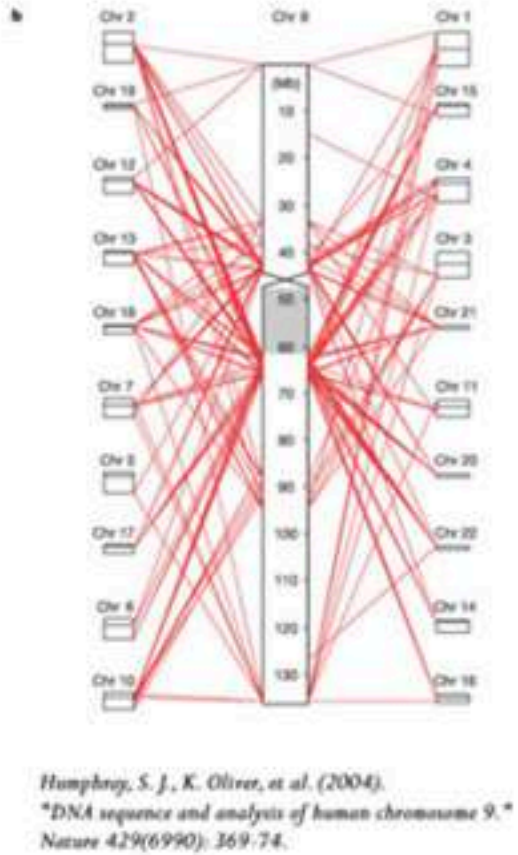


Segmental Duplications in Arabidopsis Genome. Alexander Kozik and Richard Michelmore, UC Davis, California

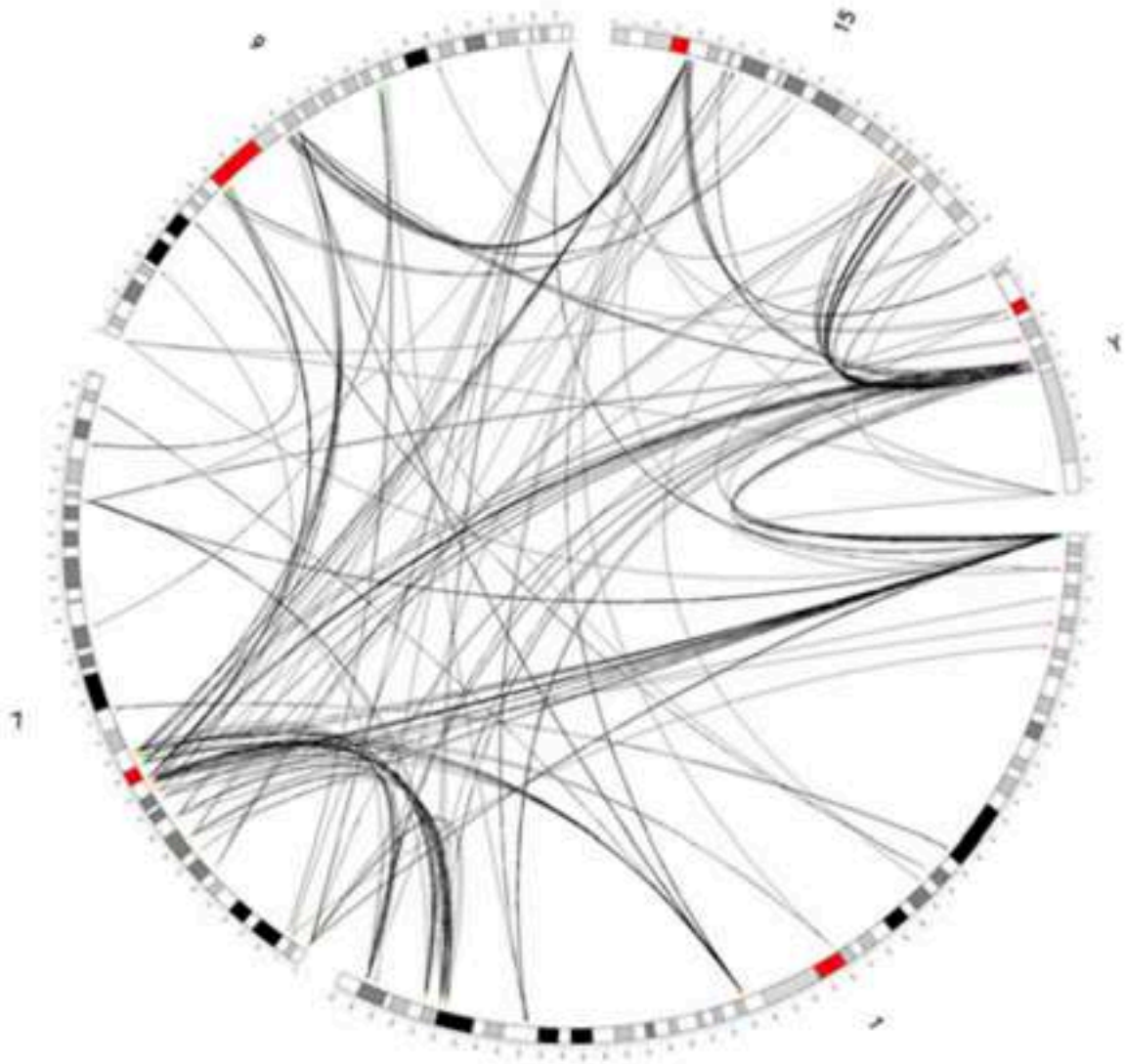
Image created with GenomePixelizer

http://circos.ca/presentations/talks/circos_intro/

Circos



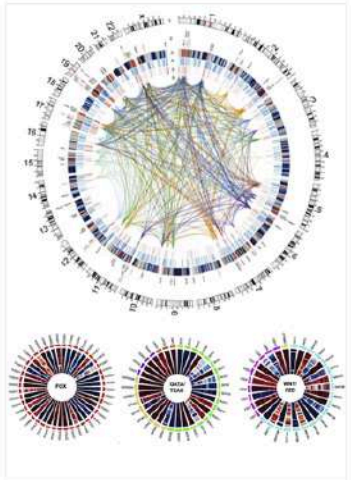
Humphray, S. J., K. Oliver, et al. (2004).
"DNA sequence and analysis of human chromosome 9."
Nature 429(6990): 369-74.



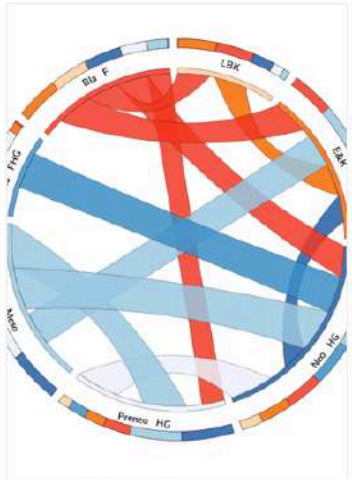
Circos image

http://circos.ca/presentations/talks/circos_intro/

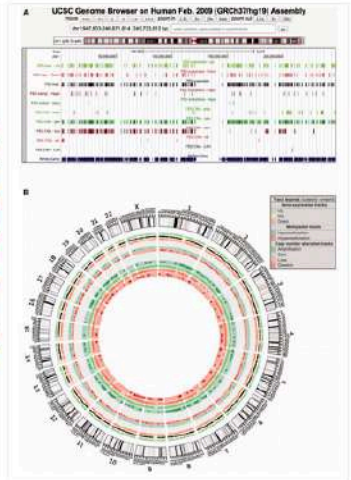
Circos



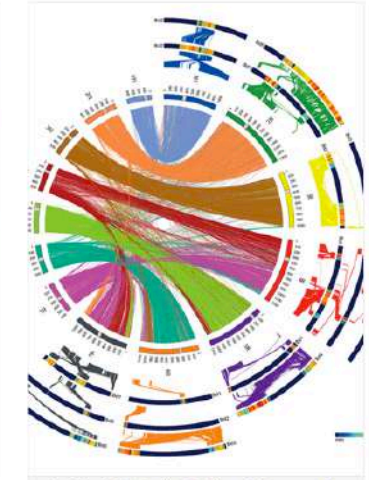
▲ 1 · 1 Dec 2013 | Saben J, Zhong Y, McKelvey S *et al.* (2014) A comprehensive analysis of the human placenta transcriptome *Placenta* **35**:125-131.



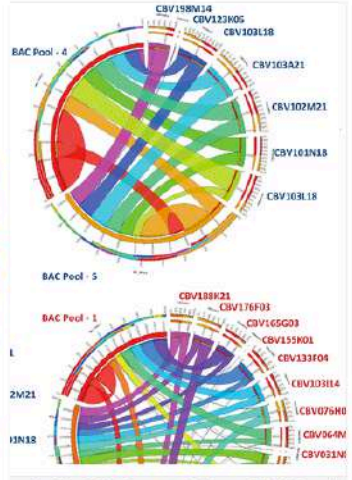
▲ 2 · 25 Oct 2013 | Bollongino R, Nehlich O, Richards MP *et al.* (2013) 2000 years of parallel societies in Stone Age Central Europe *Science* **342**:479-481.



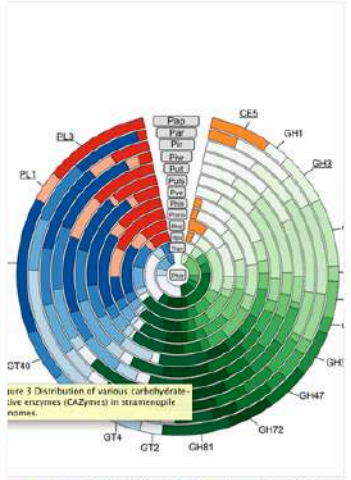
▲ 3 · 25 Oct 2013 | Dayem Ullah AZ, Cutts RJ, Ghetia M *et al.* (2013) The pancreatic expression database: recent extensions and updates *Nucleic Acids Res*



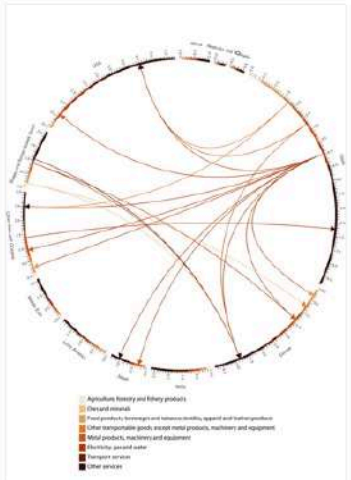
▲ 13 · 8 Oct 2013 | Martis MM, Zhou R, Haseneyer G *et al.* (2013) Reticulate Evolution of the Rye Genome *Plant Cell*



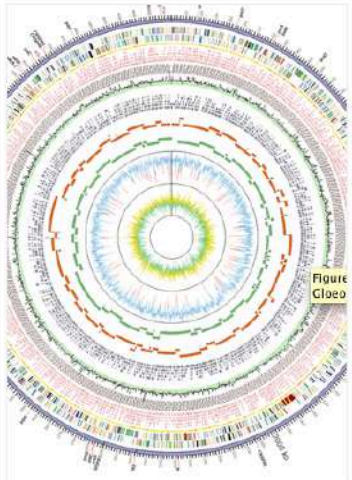
▲ 14 · 8 Oct 2013 | Buyyarapu R, Kantety RV, Yu JZ *et al.* (2013) BAC-Pool Sequencing and Analysis of Large Segments of A12 and D12 Homoeologous Chromosomes in Upland Cotton *PLoS One* **8**:e76757.



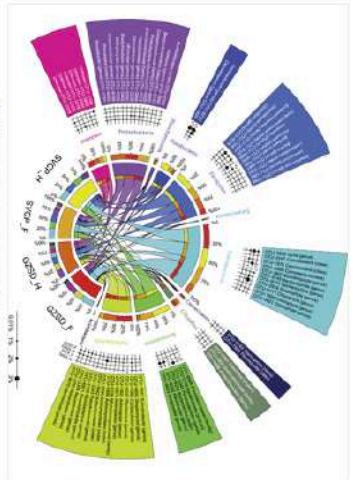
▲ 15 · 4 Oct 2013 | Adhikari BN, Hamilton JP, Zerillo MM *et al.* (2013) Comparative Genomics Reveals Insight into Virulence Strategies of Plant Pathogenic Oomycetes *PLoS One* **8**:e75072.



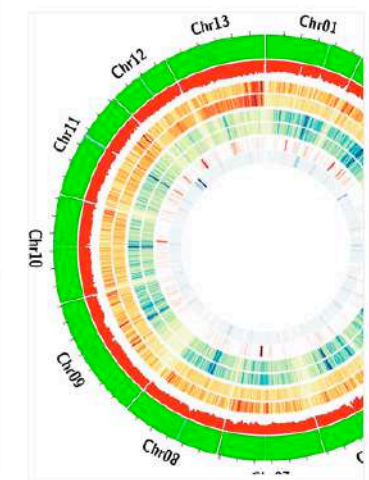
▲ 4 · 23 Oct 2013 | Kanemoto K, Moran D, Lenzen M *et al.* (2013) International trade undermines national emission reduction targets: New evidence from air pollution *Global Environmental Change*



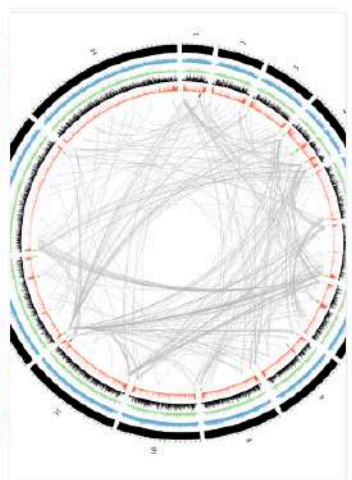
▲ 5 · 23 October 2013 | Saw JHW, Schatz M, Brown MV *et al.* (2013) Cultivation and Complete Genome Sequencing of Gloeobacter kilaueensis sp. nov., from a Lava Cave in Kilauea Caldera, Hawai'i *PLoS One* **8**:e76376.



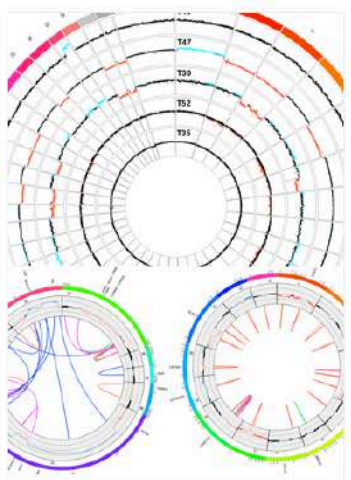
▲ 6 · 17 Oct 2013 | Ye L, Amberg J, Chapman D *et al.* (2013) Fish gut microbiota analysis differentiates physiology and behavior of invasive Asian carp and indigenous American fish *The ISME Journal*



▲ 16 · 1 Oct 2013 | Page JT, Huynh MD, Liechty ZS *et al.* (2013) Insights into the Evolution of Cotton Diploids and Polyploids from Whole-Genome Re-sequencing *G3: Genes|Genomes|Genetics* **3**:1809-1818.



▲ 17 · 30 Sep 2013 | Lemieux JE, Kyes SA, Otto TD *et al.* (2013) Genome-wide profiling of chromosome interactions in Plasmodium falciparum characterizes nuclear architecture and reconfigurations associated with antigenic variation *Molecular microbiology*



▲ 18 · 30 Sep 2013 | Beck J, Hennecke S, Bornemann-Kolatzki K *et al.* (2013) Genome Aberrations in Canine Mammary Carcinomas and Their Detection in Cell-Free Plasma DNA *PLoS One* **8**:e75485.

Applications of comparative genomics

Phylogenomics

Phylogenomics aims at inferring detailed information about the evolutionary histories of organisms by using whole genomes rather than just a single gene or a few genes. The term was coined by Jonathan Eisen in the context of prediction of gene function

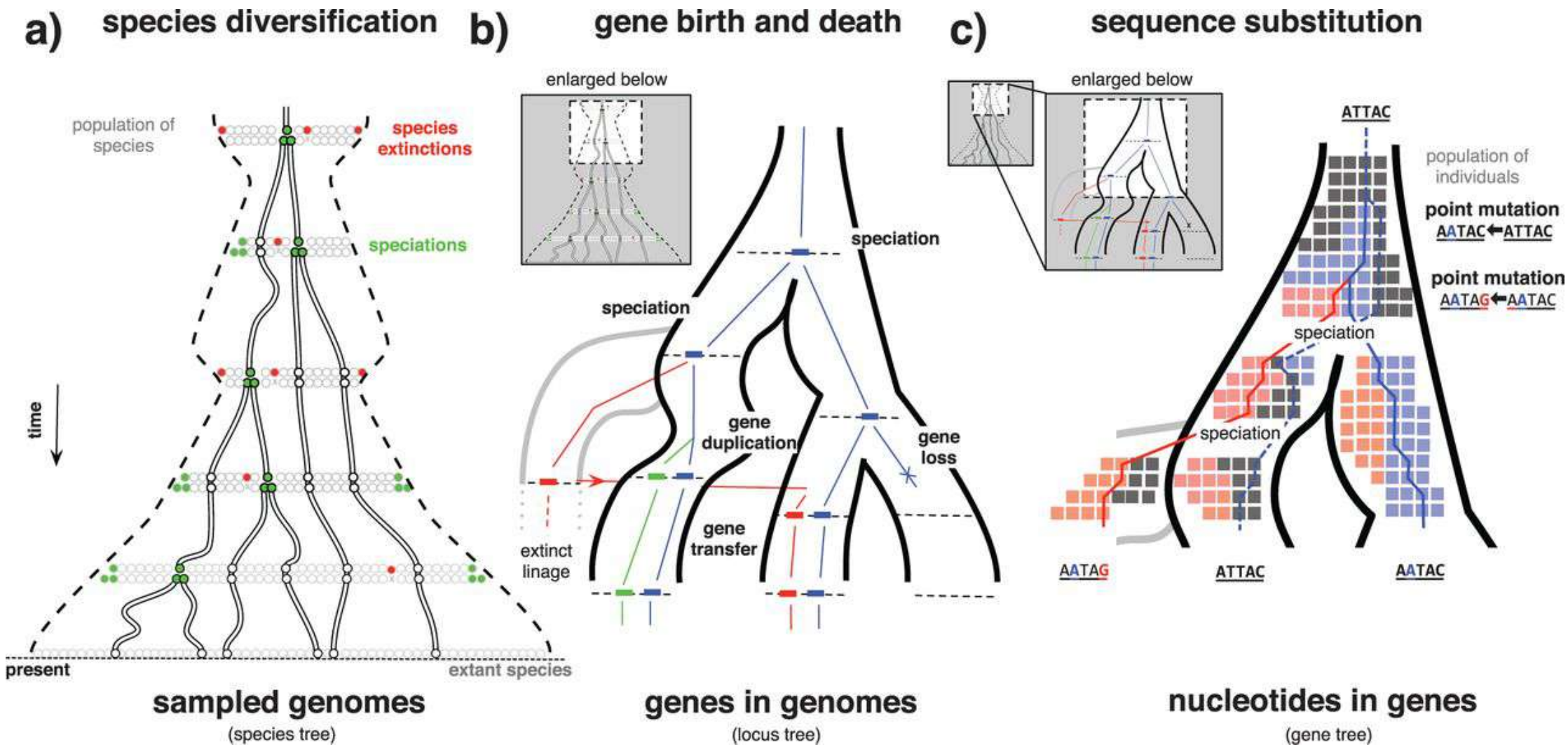
It would be difficult or impossible to understand the evolutionary history of an organism, even having available its whole genome sequence, in isolation. So it is always the case the phylogenomics is practiced for sets of genomes.

During the last 50 years, phylogeny has become more and more based on molecular data, increasingly **favoring homologous sequences over morphological characters**. This approach has been extremely fruitful, **producing constant improvement in the accuracy and resolution of phylogenetic reconstruction together with our understanding of evolutionary processes at the molecular level**.

However, we have known all along that we are barking up the wrong trees: with increasing sophistication in the models of sequence evolution, **we have been reconstructing trees describing the history of fragments of genomic sequence, which we will liberally call "gene" in this review, but never the history of species. Gene trees are not species trees** (Maddison 1997).

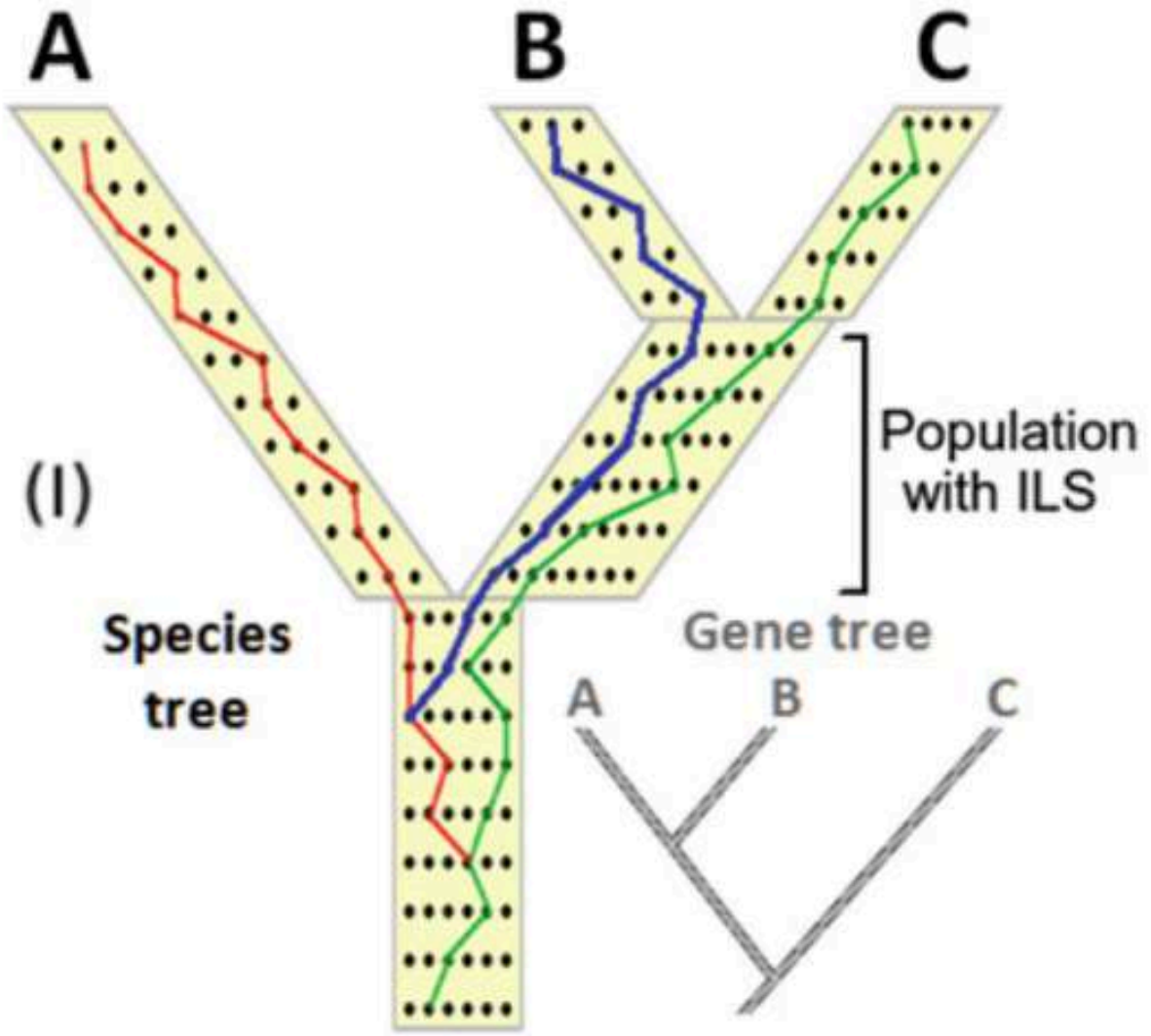
https://academic.oup.com/sysbio/article/64/1/e42/1634124

Each level of the hierarchy contributes to generating phylogenetic signal that can lead to differences between reconstructed gene trees.



Szöllősi *et al* (2014) Systematic Biology

Processes that may induce gene trees that are different than the actual species tree

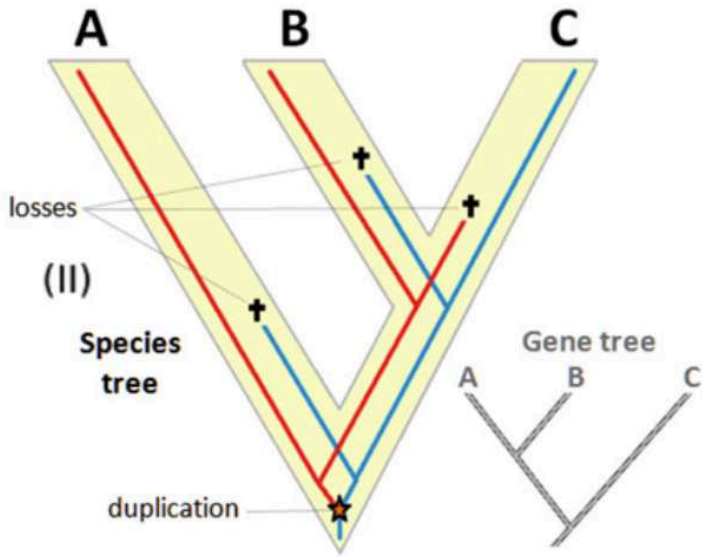


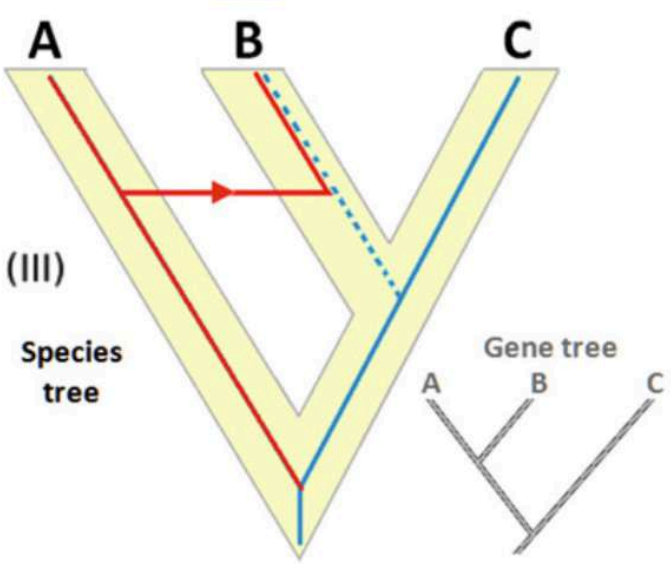
i) Incomplete lineage sorting

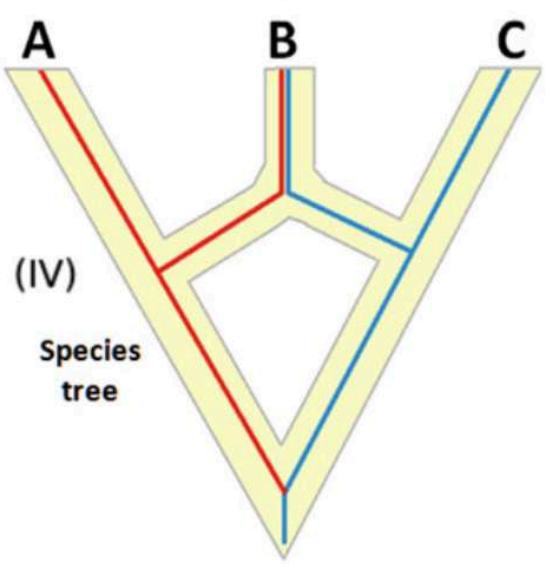
When a species splits in two, allelic lineages sort into the two descendant species, and this lineage sorting varies along the genome.

If speciation events are close in time, the lineage sorting process may be incomplete at the second speciation event and lead to gene genealogies that do not match the species phylogeny

Processes that may induce gene trees that are different than the actual species tree





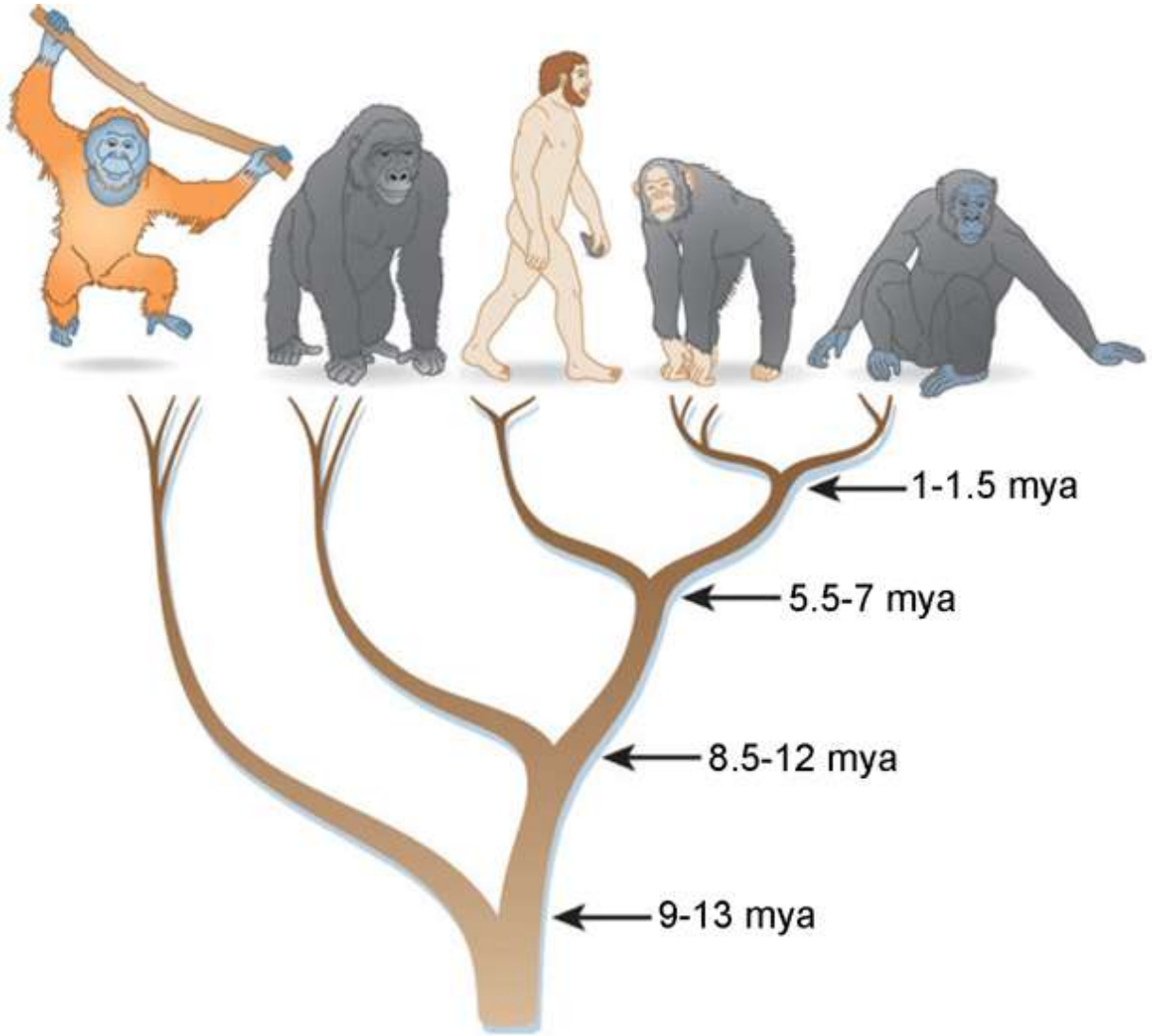


(II) **Duplication and Loss**
a locus may generate a duplicate somewhere in the genome, and then both may be inherited or just a single copy is maintained in each lineage.

(III) **Horizontal Gene Transfer**
(HGT): a donor DNA segment (from taxon A) is transmitted and incorporated into the host's genome (taxon B)

(IV) **Hybridization/Introgression**
in extreme cases of lateral transfer, or upon mixing of related species, different regions of the genome will bear two distinct evolutionary histories;

Why is Studying (Ape) Speciation Important? (Example)



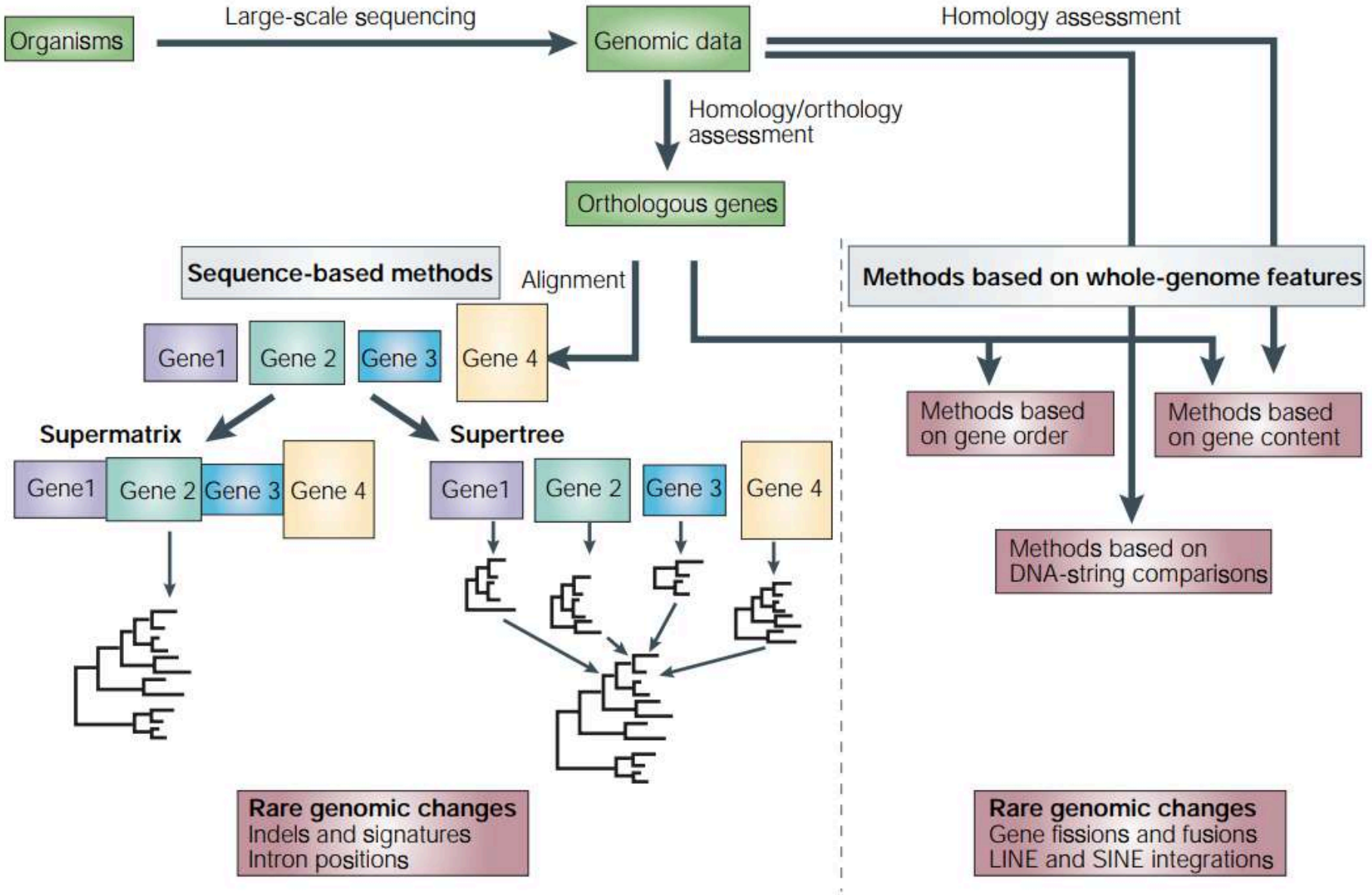
These studies also led to rich discussions about the suite of **factors that may have contributed to promoting speciation in the last common ancestor of humans and African apes**, as well as the **factors that might have contributed to creating the amazing diversity of Hominins that co-existed with each other during the Pliocene and Pleistocene** (Foley 2002).

For many years, there was considerable debate about which of the African apes is our closest relative…. The general consensus that emerged is that we share a more recent relationship with chimpanzees (*Pan troglodytes*) and bonobos (*Pan paniscus*) than we do with gorillas (*Gorilla gorilla*) (Ruvolo 1997, Chen & Li 2001).

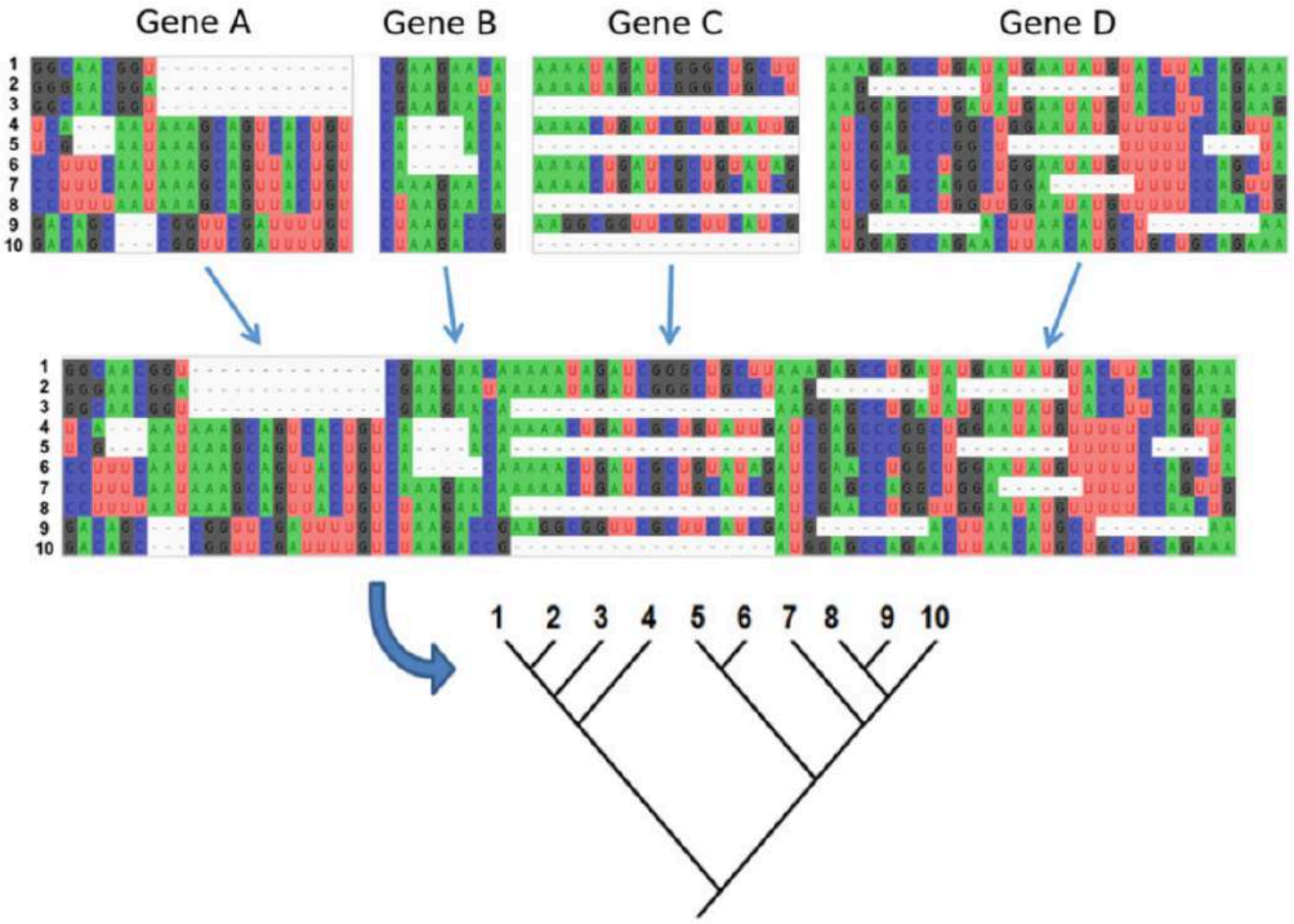
Current estimates indicate that up to 30% of the sequence of the human genome is more closely related to Gorilla than to Chimpanzee due to this process (Scally et al. 2012).

https://www.nature.com/scitable/knowledge/library/primate-speciation-a-case-study-of-african-96682434

Probably the most common (easy) way to construct alignment of concatenated gene shared across all species



Probably the most common (easy) way to construct alignment of concatenated gene shared across all species (but this is wrong)

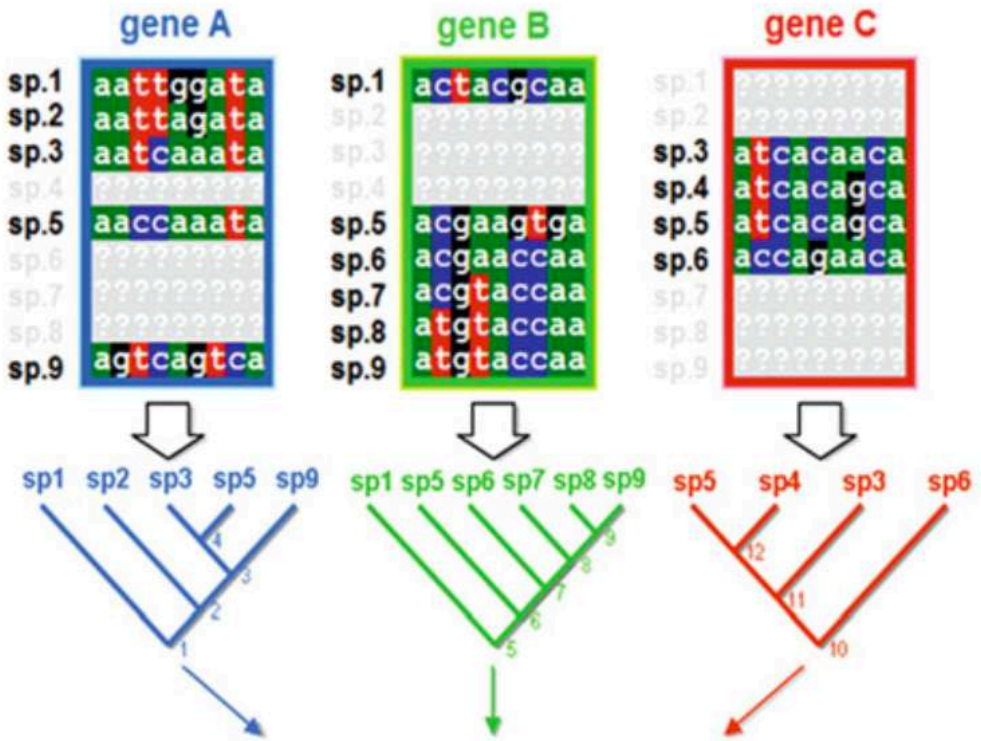


Important drawbacks:

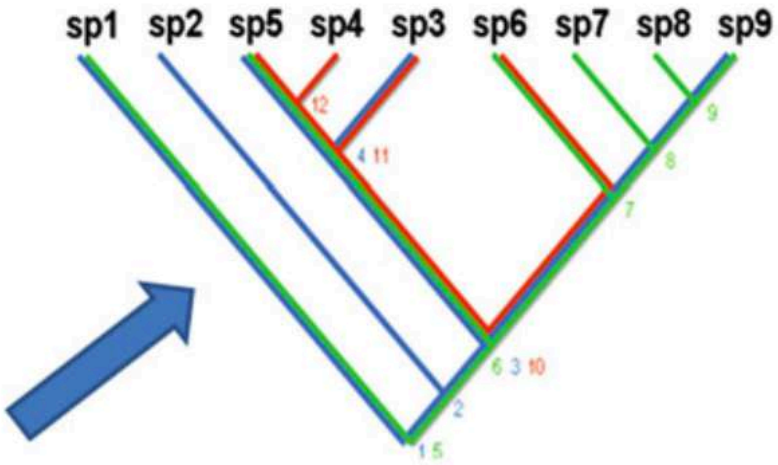
(1) it hinders variation among gene trees by assuming implicitly that all of them conform to a single species tree;
(2) if sampling was heterogeneous across species there may be too much missing data, which can affect topological reconstruction; Or limited number of genes shared among all species
(3) large data sampling effects inflate credibility in some clades;
(4) spurious hidden support can lead to support for non-existent clades; and
(5) in case of moderate to severe levels of ILS, supermatrix can become statistically inconsistent.

From genes to supertrees

Instead of forcing all gene trees to comply to a single tree, **supertree methods infer the best topology for each gene (using the same phylogenetic method for each), and then a topological consensus is obtained**. Such methods are able to make consensus trees even if the number of leaves among gene trees differs but overlaps to some extent, for example when a gene has not been sequenced for some taxa

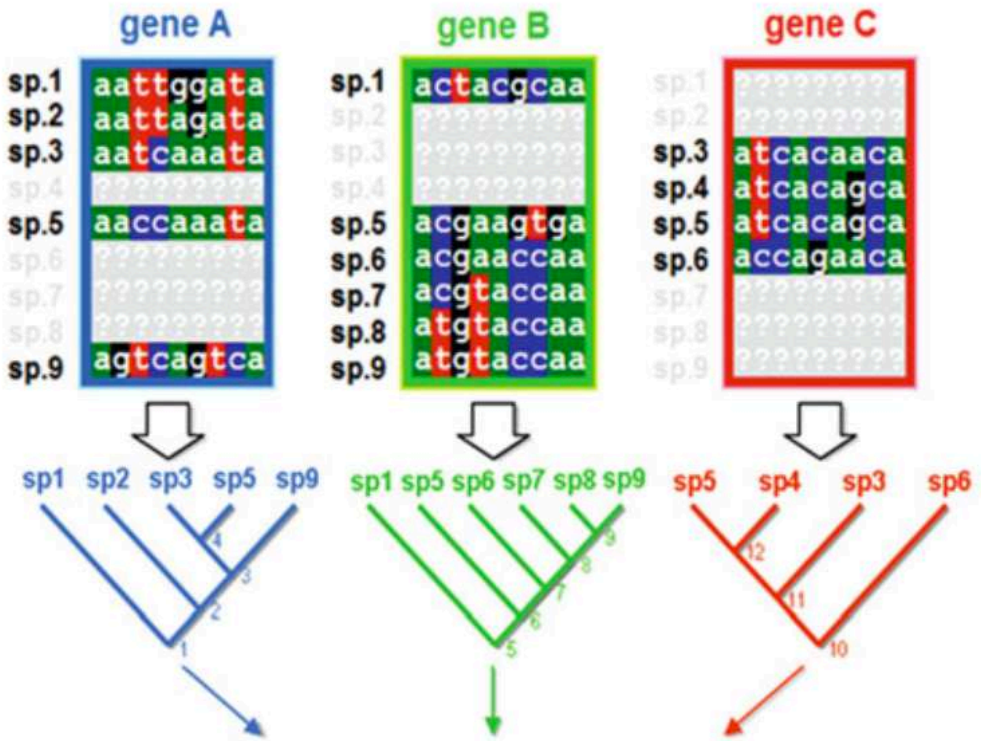


MRP	1	2	3	4	5	6	7	8	9	10	11	12
sp1	1	0	0	0	1	0	0	0	0	?	?	?
sp2	1	1	0	0	?	?	?	?	?	?	?	?
sp3	1	1	1	1	?	?	?	?	?	1	1	0
sp4	?	?	?	?	?	?	?	?	?	1	1	1
sp5	1	1	1	1	1	1	0	0	0	1	1	1
sp6	?	?	?	?	1	1	1	1	0	1	0	0
sp7	?	?	?	?	1	1	1	1	0	?	?	?
sp8	?	?	?	?	1	1	1	1	1	?	?	?
sp9	1	1	1	0	1	1	1	1	1	?	?	?

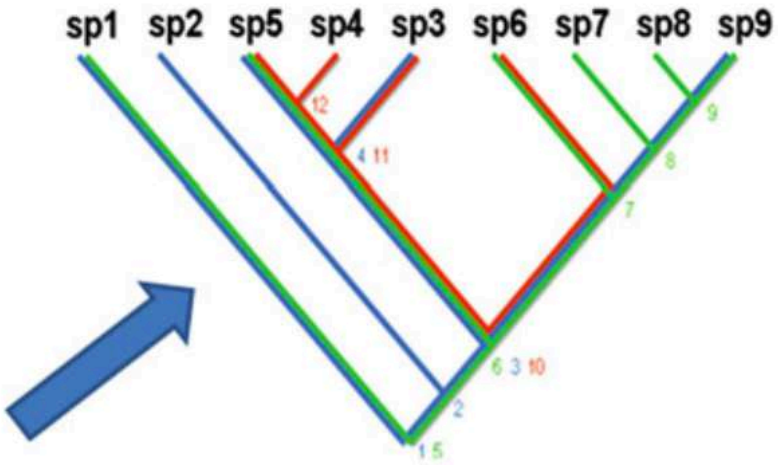


Current methods

A step beyond supertrees is the use of methods that take into consideration specific evolutionary processes that may be responsible for differences in gene topologies, and then estimate the species tree which would most likely have generated such gene trees, under different scenarios



MRP	1	2	3	4	5	6	7	8	9	10	11	12
sp1	1	0	0	0	1	0	0	0	0	?	?	?
sp2	1	1	0	0	?	?	?	?	?	?	?	?
sp3	1	1	1	1	?	?	?	?	?	1	1	0
sp4	?	?	?	?	?	?	?	?	?	1	1	1
sp5	1	1	1	1	1	1	0	0	0	1	1	1
sp6	?	?	?	?	1	1	1	1	0	1	0	0
sp7	?	?	?	?	1	1	1	1	0	?	?	?
sp8	?	?	?	?	1	1	1	1	1	?	?	?
sp9	1	1	1	0	1	1	1	1	1	?	?	?



nature ecology & evolution

ARTICLES

PUBLISHED: 10 APRIL 2017 | VOLUME: 1 | ARTICLE NUMBER: 0126

Contentious relationships in phylogenomic studies can be driven by a handful of genes

Xing-Xing Shen[1], Chris Todd Hittinger[2] and Antonis Rokas[1]*

…Here, we use a maximum likelihood framework to quantify the distribution of phylogenetic signal among genes and sites for 17 contentious branches and 6 well-established control branches in plant, animal and fungal phylogenomic data matrices. **We find that resolution in some of these 17 branches rests on a single gene or a few sites, and that removal of a single gene in concatenation analyses or a single site from every gene in coalescence-based analyses diminishes support and can alter the inferred topology**

Shen *et al* (2017) Nature Ecology and Evolution

Visualizing phylogenetic signal in a phylogenomic data matrix

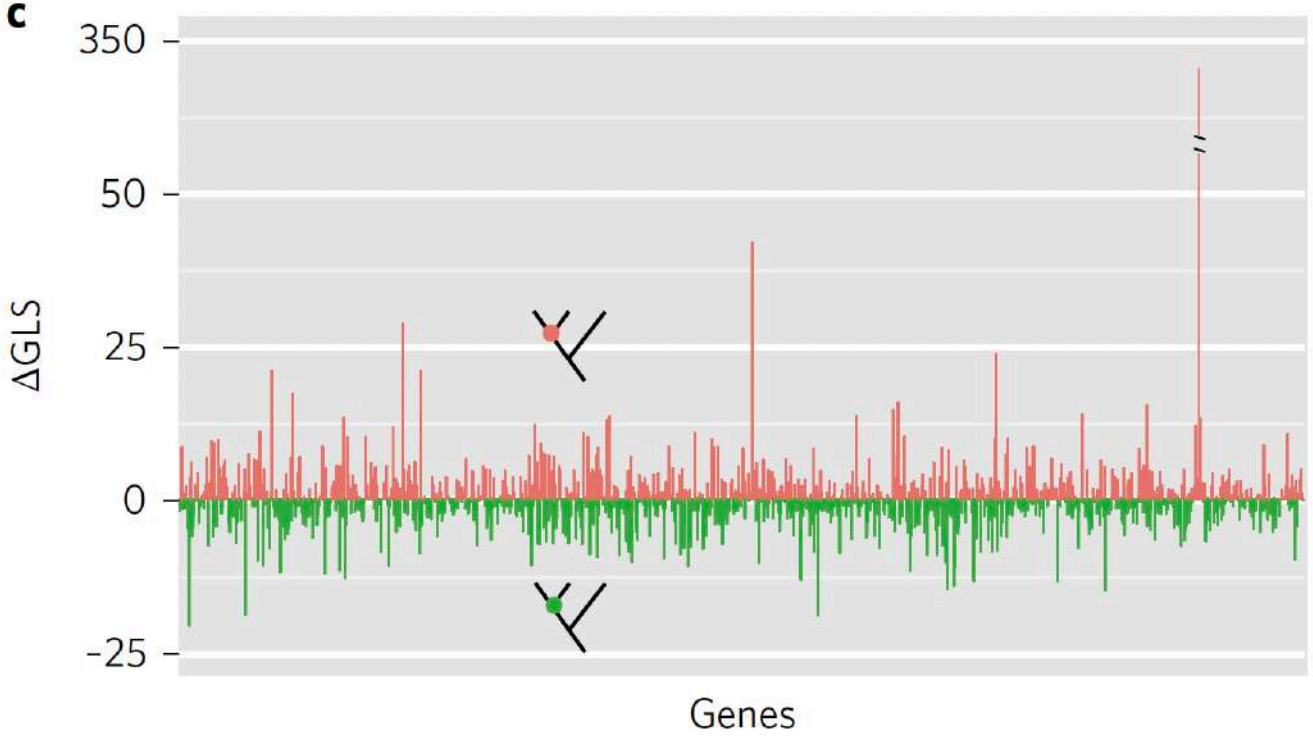
a

b

Supermatrix

	Gene1	Gene2	Gene3	.....	Gene$_i$
T1	ln L(G1|T1)	ln L(G2|T1)	ln L(G3|T1)	.....	ln L(G$_i$|T1)
T2	ln L(G1|T2)	ln L(G2|T2)	ln L(G3|T2)	.....	ln L(G$_i$|T2)
Δln L	-1.8766	-0.3983	0.1187	.....	ΔGLS$_i$

c



Shen *et al* (2017) Nature Ecology and Evolution

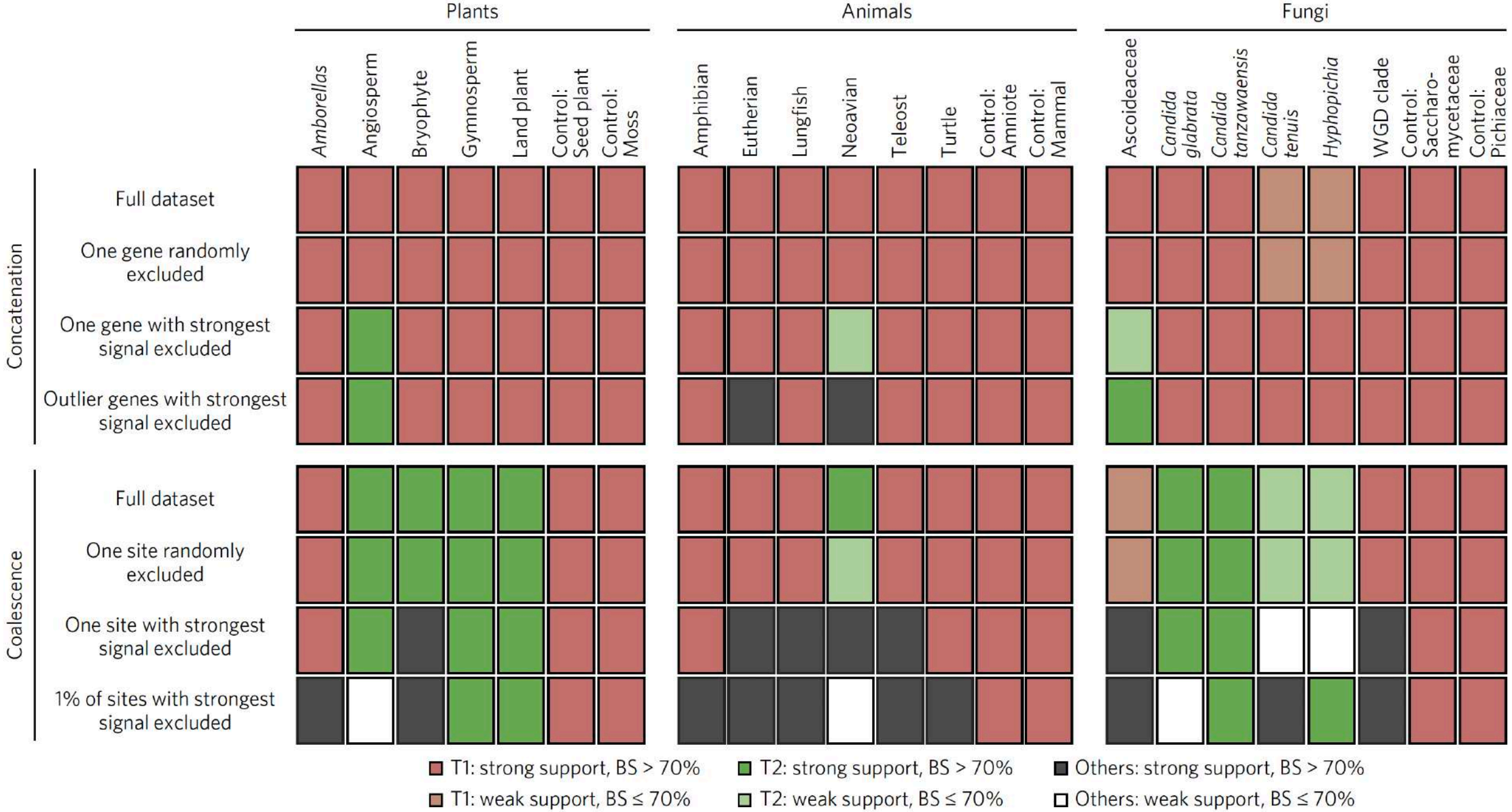
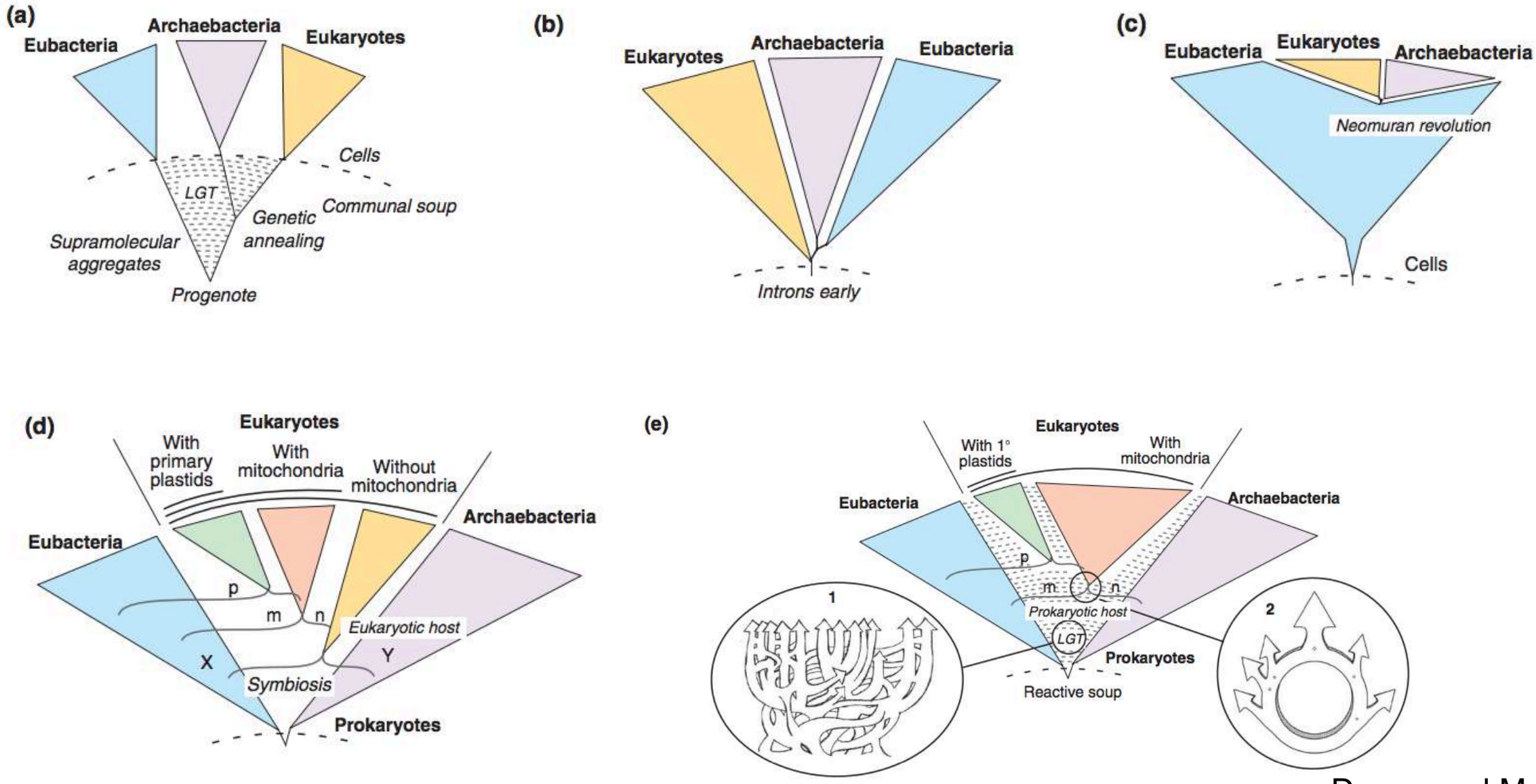


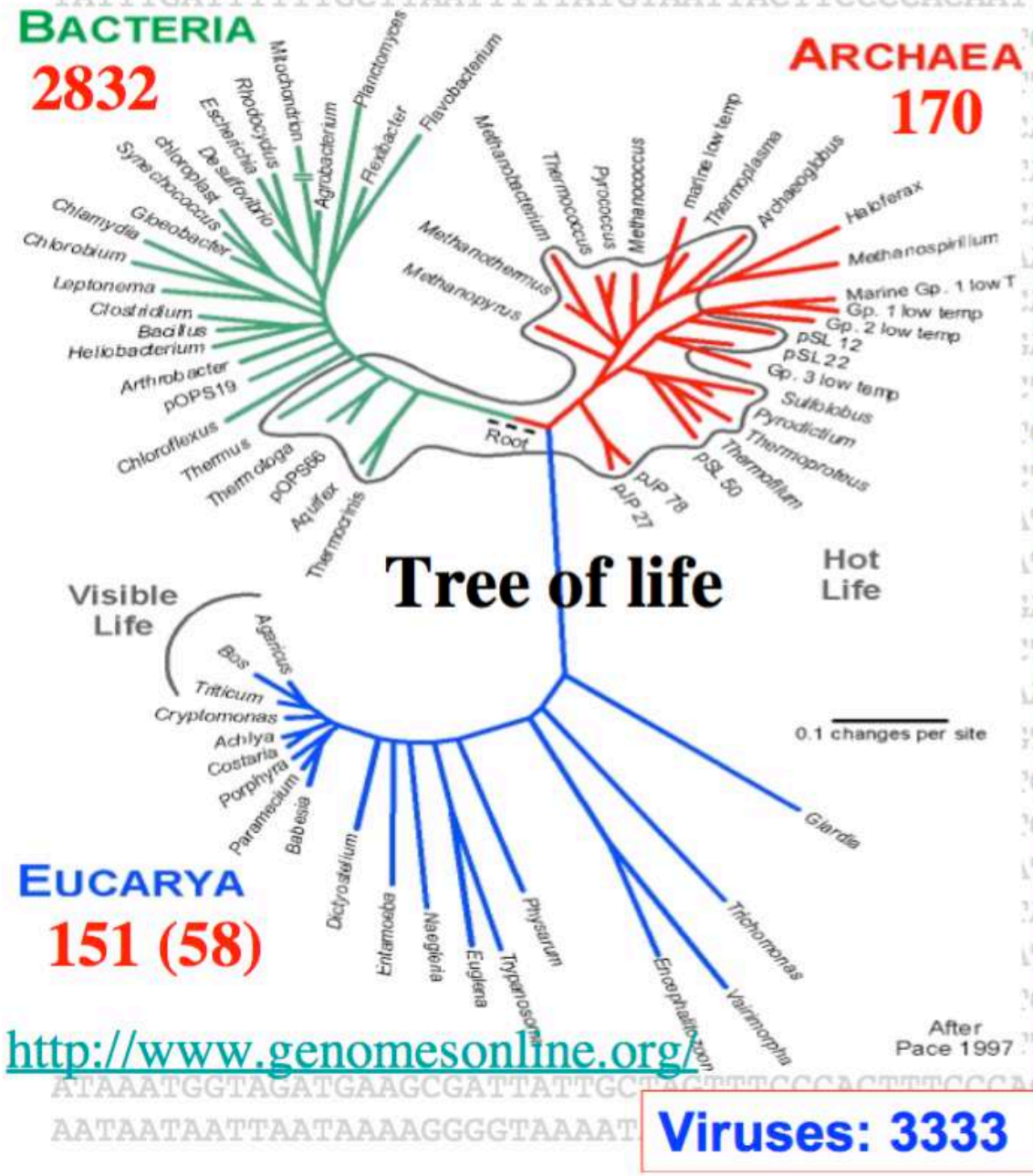
Figure 4 | Tiny amounts of data exert decisive influence in the resolution of certain contentious branches in phylogenomic studies. The effect of the

Five models models of tree of life



Dagan and Martin (2006)

Tree of life



Complete finished genomes: 3060 (04/09/14)

- 2832 Bacteria
- 170 Archaea
- 58 eukaryotes

Incomplete genomes projects: 38262

- 32068 Bacteria
- 664 Archaea
- 5530 Eukaryotes

Transciptomes: 947

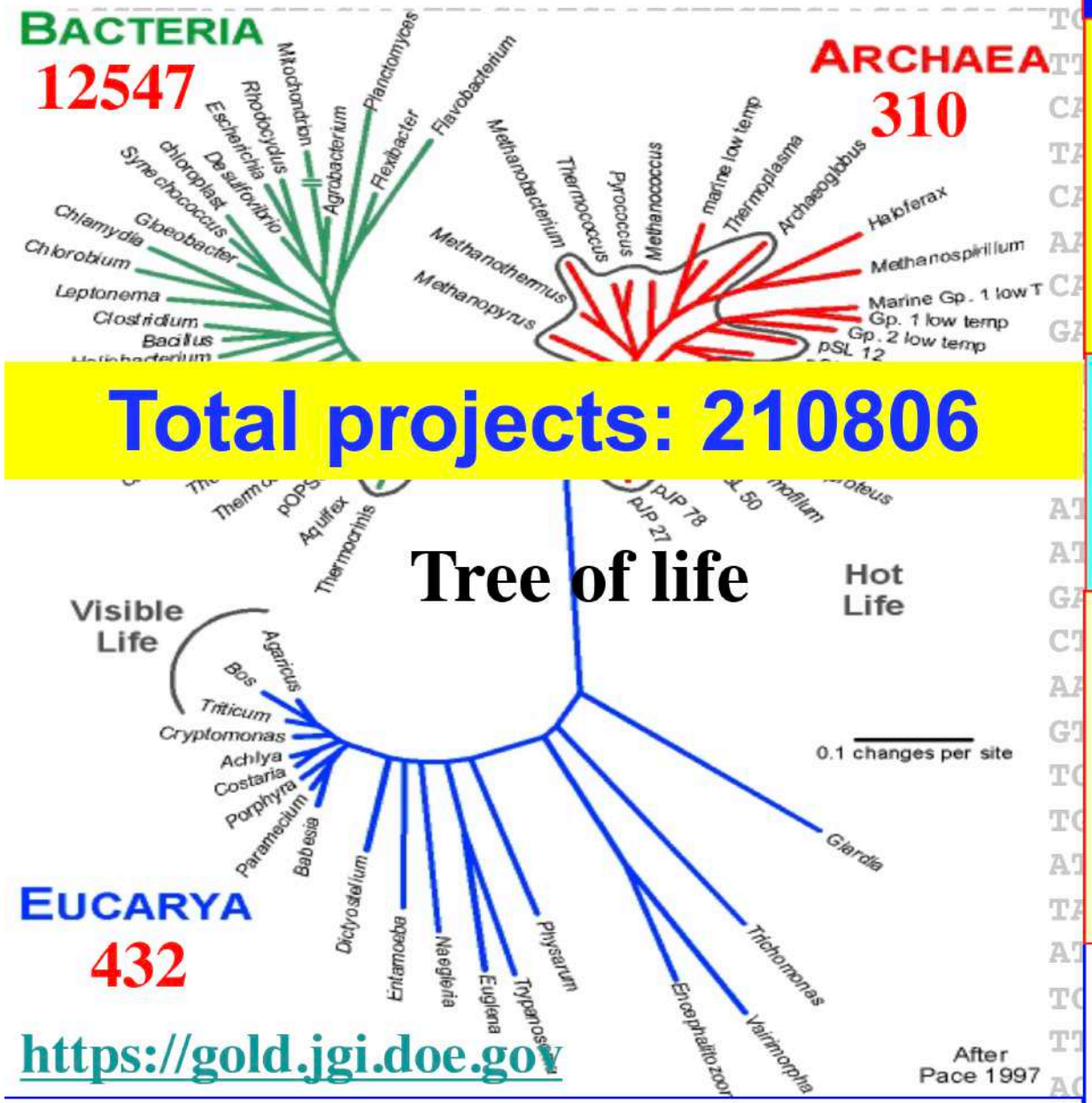
- 76 Bacteria
- 11 Archaea
- 860 Eukaryota

Viruses: 3333

http://www.genomesonline.org/

Slide of Fredj Tekaia

Tree of life



Total projects: 210806

Viruses: • **Completed: 3503** • **Permanent draft: 5079**

20/05/2019

Complete sequenced genomes: 13290
- 12547 Bacteria
- 310 Archaea
- 432 Eukaryotes

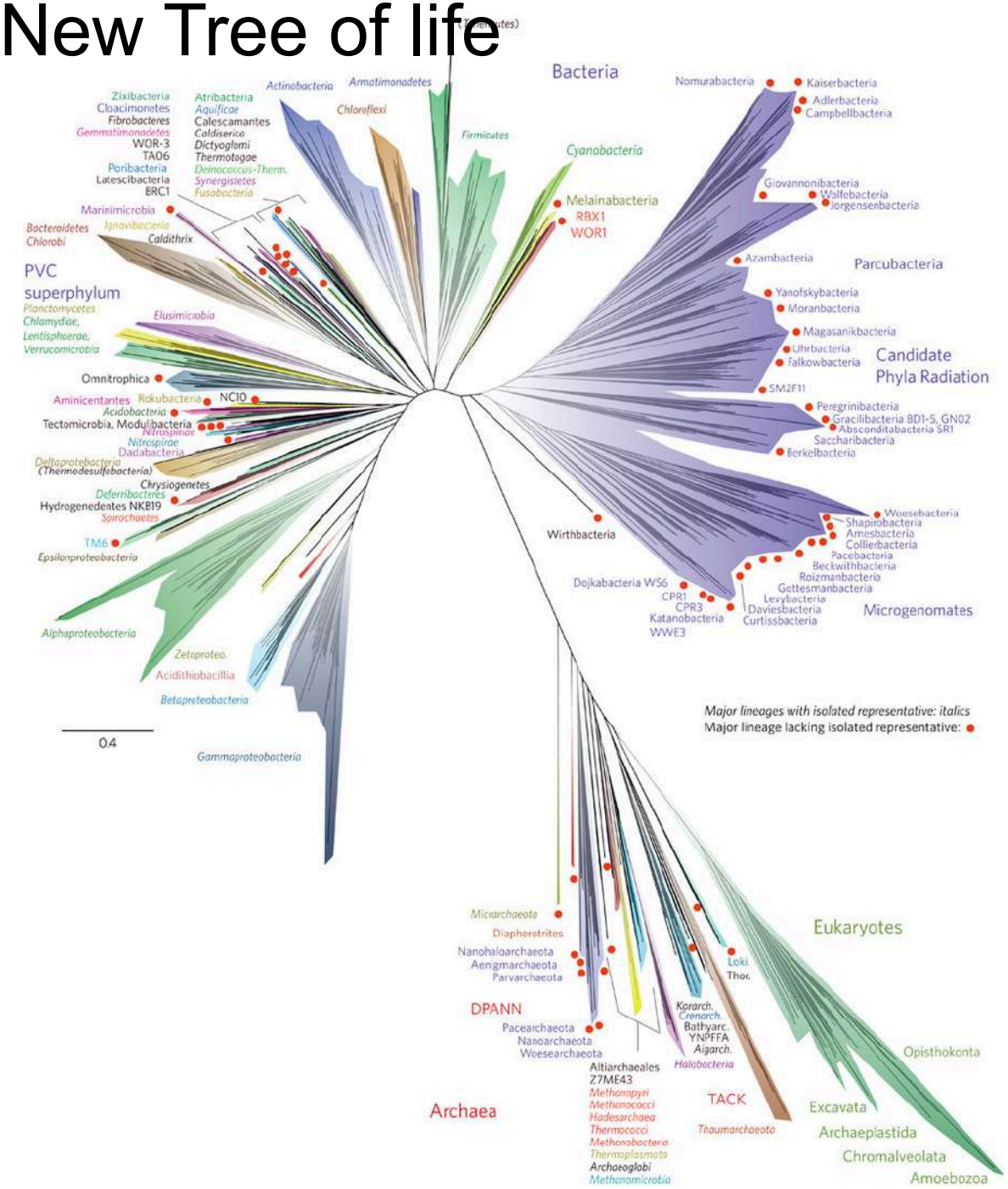
Incomplete genomes: 17939
- 11159 Bacteria
- 242 Archaea
- 6538 Eukaryotes

Permanent Draft genomes: 129958
- 124606 Bacteria
- 898 Archaea
- 4454 Eukaryotes

Transciptomes: 75/25843
- 51/1763 Bacteria
- 0/162 Archaea
- 22/23926 Eukaryota

Slide of Fredj Tekaia

New Tree of life



The third trunk that Woese and his colleagues identified included little-known [microbes that live in extreme places] like hot springs and oxygen-free wetlands. Woese and his colleagues called this third trunk Archaea.

Dr. Banfield said she expected new branches to be discovered for eukaryotes, especially for tiny species such as microscopic fungi. “That’s where I think the next big advance might be found,” Dr. Banfield said.

Dr. Hug disagreed that scientists were done with bacteria. “I’m less convinced we’re hitting a plateau,” she said. “There are a lot of environments still to survey.”

Hug et al (2016)

http://www.nytimes.com/2016/04/12/science/scientists-unveil-new-tree-of-life.html?_r=0

New Tree of life

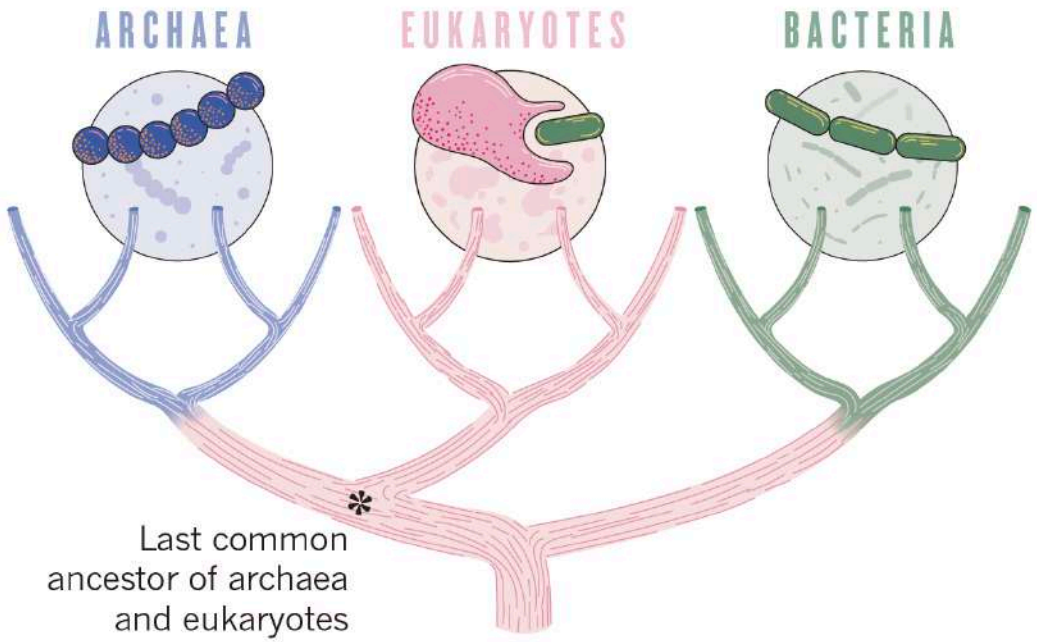
THE TRICKSTER MICROBES SHAKING UP THE TREE OF LIFE

Mysterious groups of archaea — named after Loki and other Norse myths — are stirring debate about the origin of complex creatures, including humans.

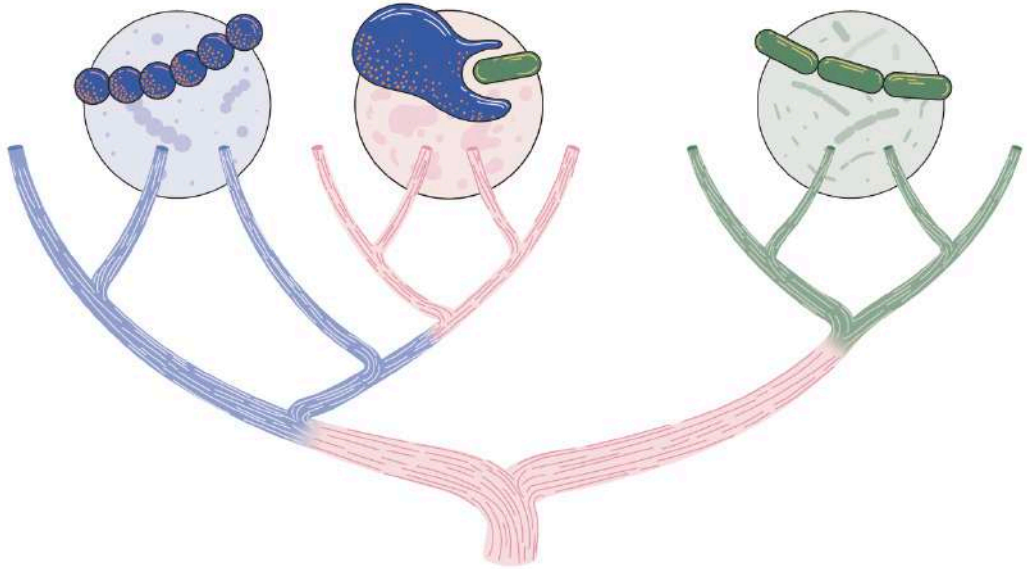
https://www.nature.com/articles/d41586-019-01496-w

Domains in debate

An organism related to archaea engulfed one related to modern bacteria eons ago, resulting in eukaryotes — complex organisms whose cells contain membrane-wrapped structures such as mitochondria. But it is unclear what the engulfing cells were. A three-domain model holds that they shared a common ancestor with archaea.



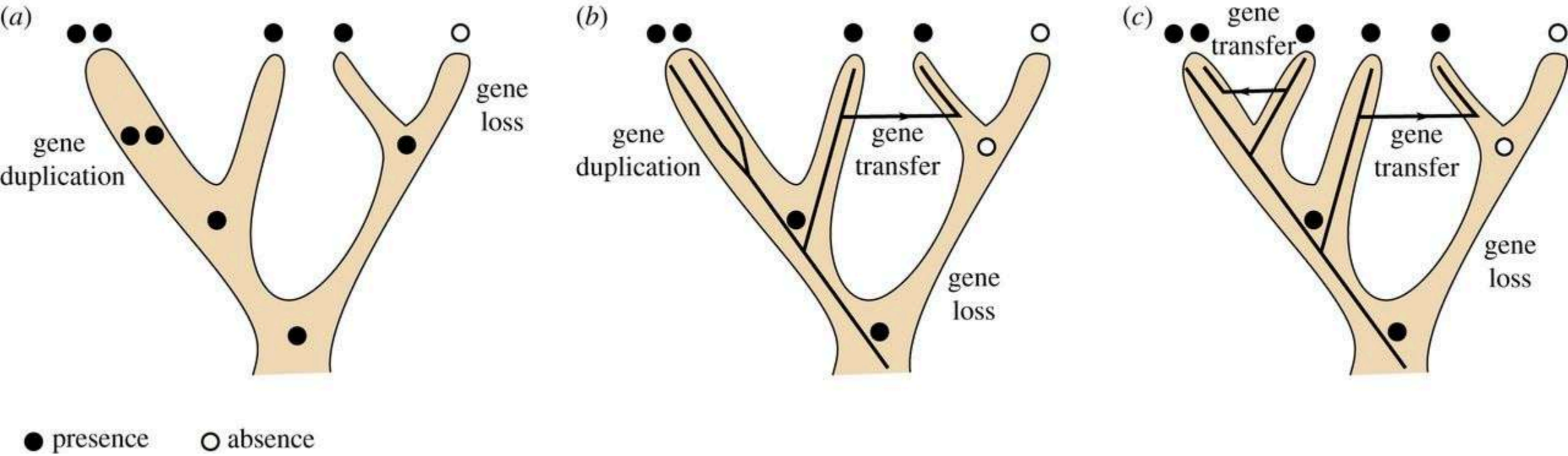
Supporters of a two-domain model argue that the engulfing cell was an archaeon and that all eukaryotes — humans included — descend from archaea.



https://www.nature.com/articles/d41586-019-01496-w

Horizontal gene transfer (HGT)

Inferring HGT require
1) species phylogeny ; 2) gene phylogeny
3) extensive taxon sampling



Szöllősi et al (2015)

Complicated history of genes: dig into finer details

Gene fusion

Gene fission

Domains shuffling

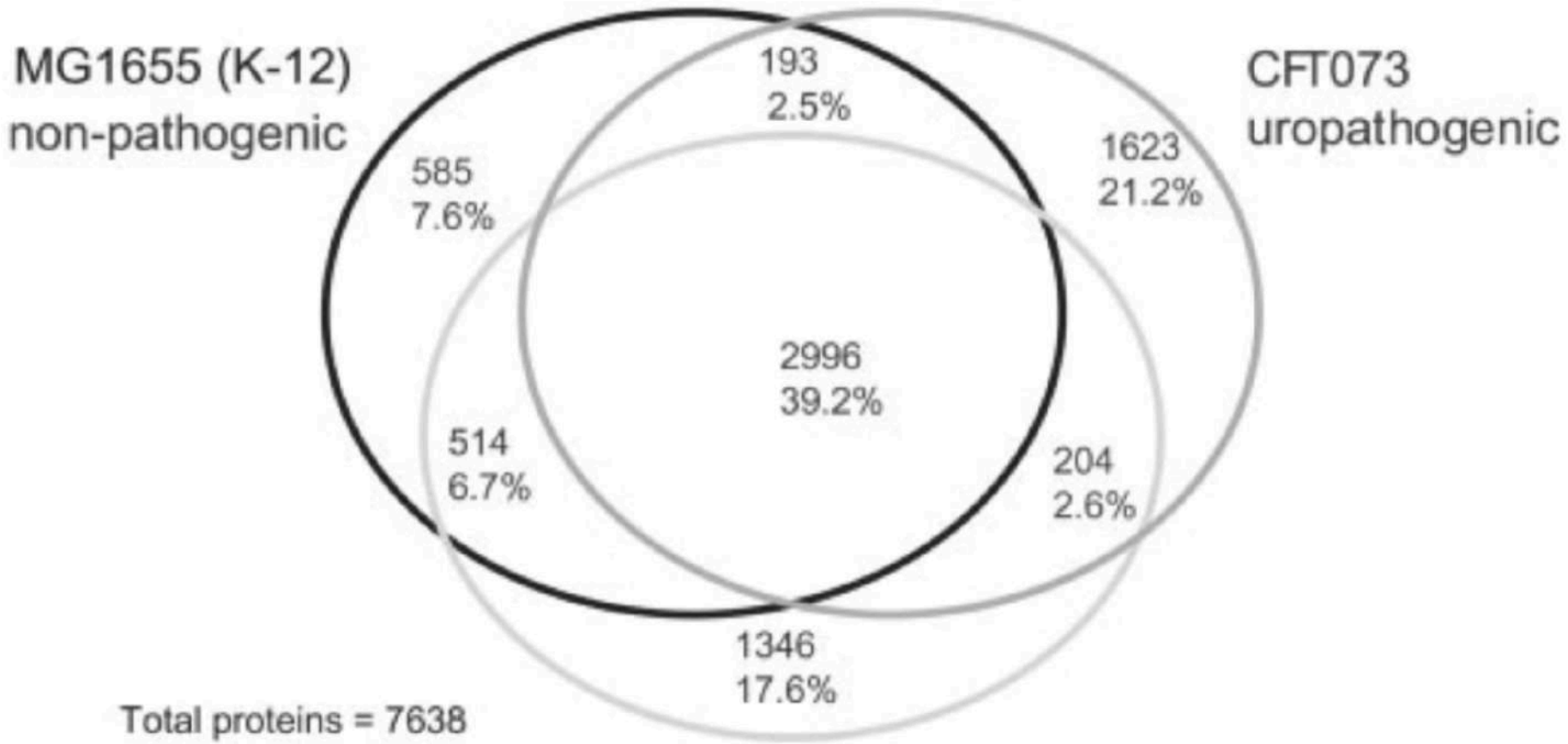
Visualisation of gene content / families

Extensive mosaic structure revealed by the complete genome sequence of uropathogenic *Escherichia coli*

R. A. Welch*, V. Burland†‡, G. Plunkett III†, P. Redford*, P. Roesch*, D. Rasko§, E. L. Buckles¶, S.-R. Liou†‖, A. Boutin†**, J. Hackett†,††, D. Stroud†, G. F. Mayhew†, D. J. Rose†, S. Zhou†‡‡, D. C. Schwartz†‡‡, N. T. Perna§§, H. L. T. Mobley§, M. S. Donnenberg¶, and F. R. Blattner†

*Department of Medical Microl
Sciences, University of Wisconsi
Department of Medicine, Unive

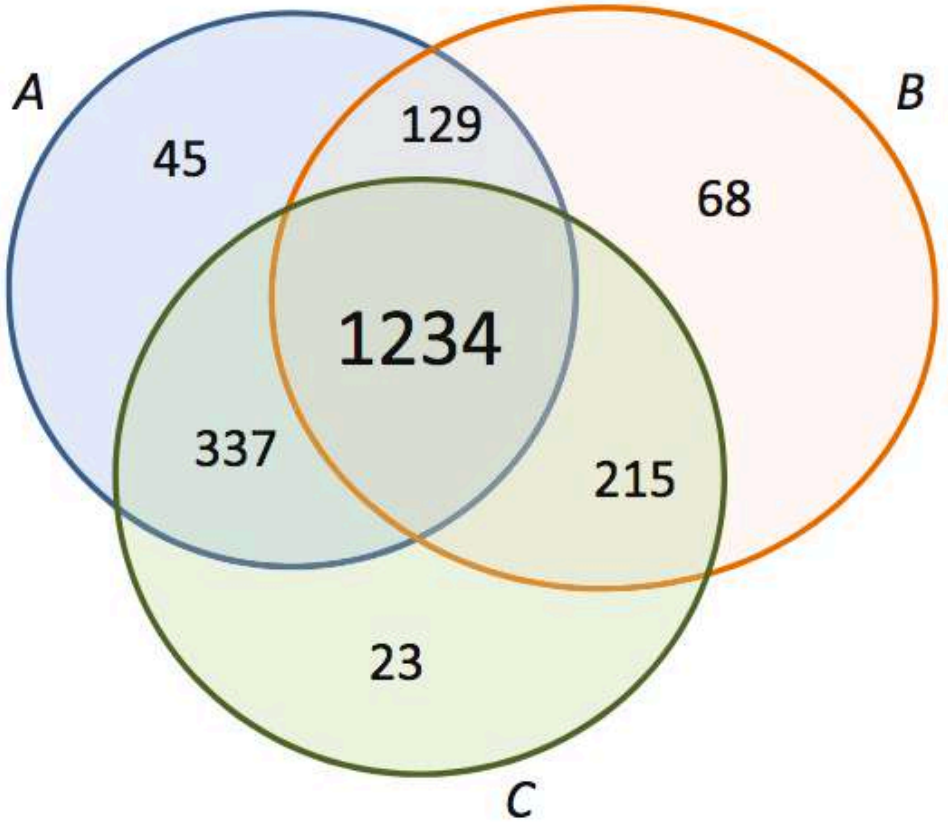
Edited by John J. Mekalanos, H



Welch *et al* (2002)

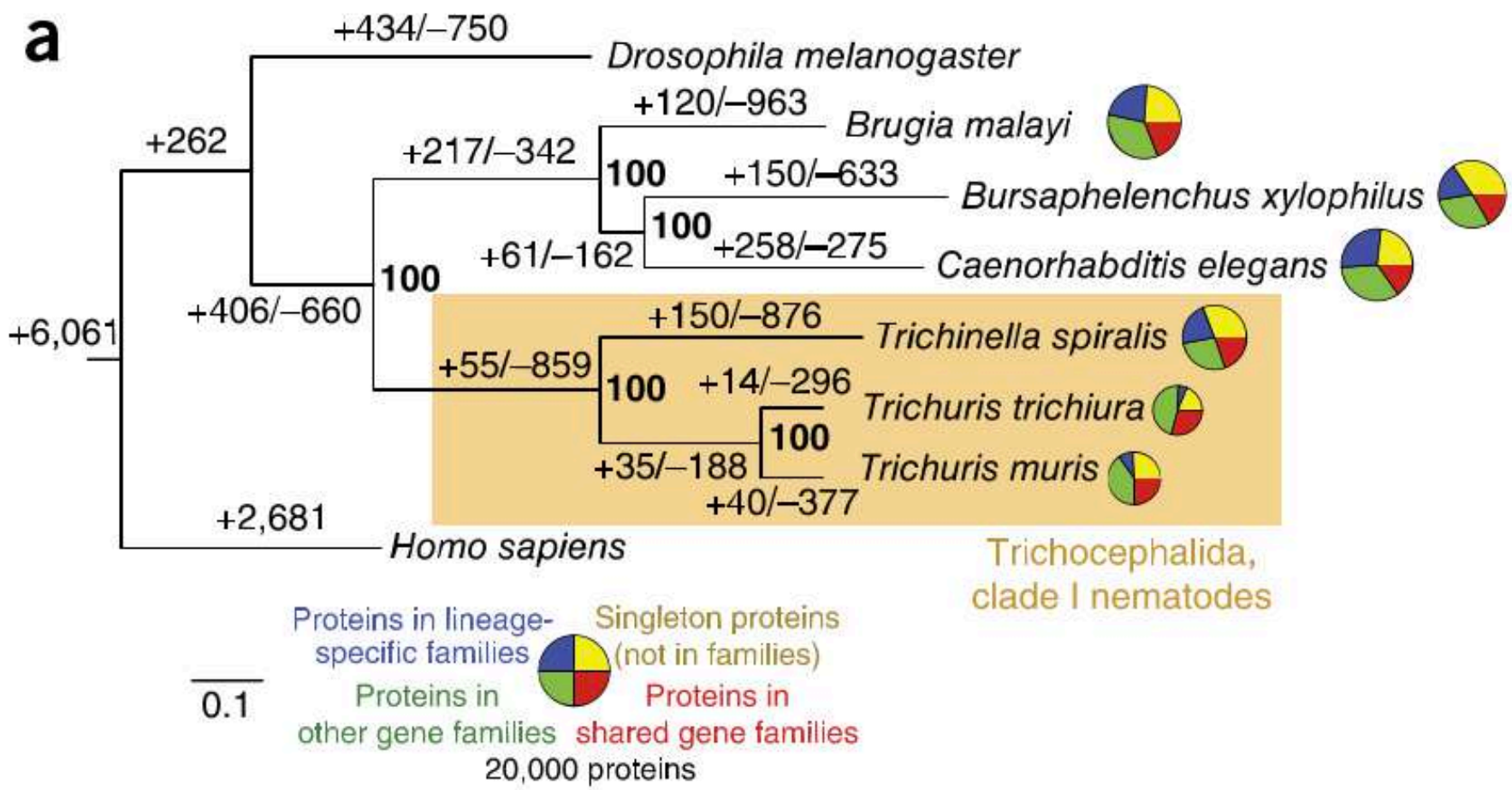
Illustration of a gene content Venn diagram for three hypothetical genomes A , B, and C

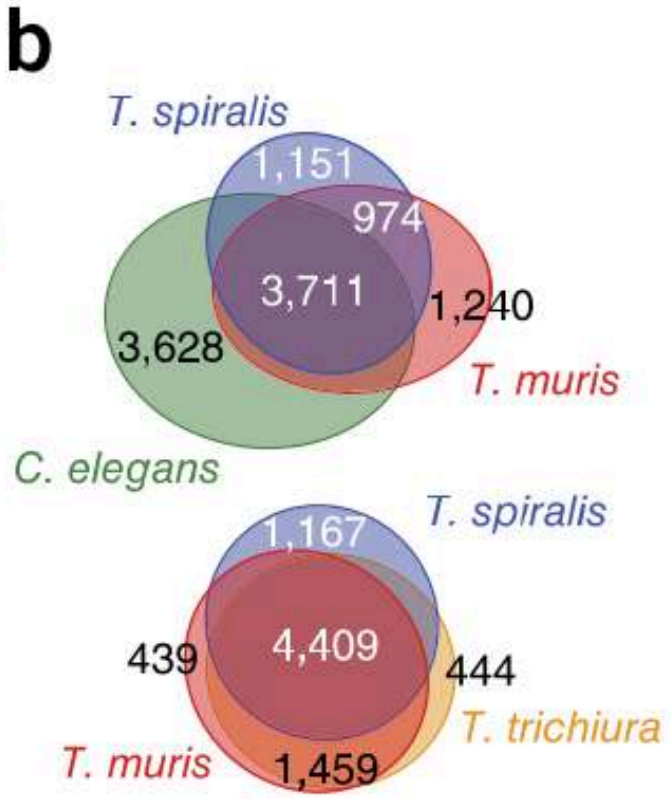
	Genome						
Gene	A	B	C	D	E	F	G
1	✓	✓			✓	✓	
2	✓		✓	✓	✓	✓	✓
3		✓		✓			
4		✓			✓		
5				✓			
6			✓		✓	✓	
7		✓		✓			✓



Schematic representation of a presence/absence gene matrix. Genomes are represented in columns, and gene families are represented in rows

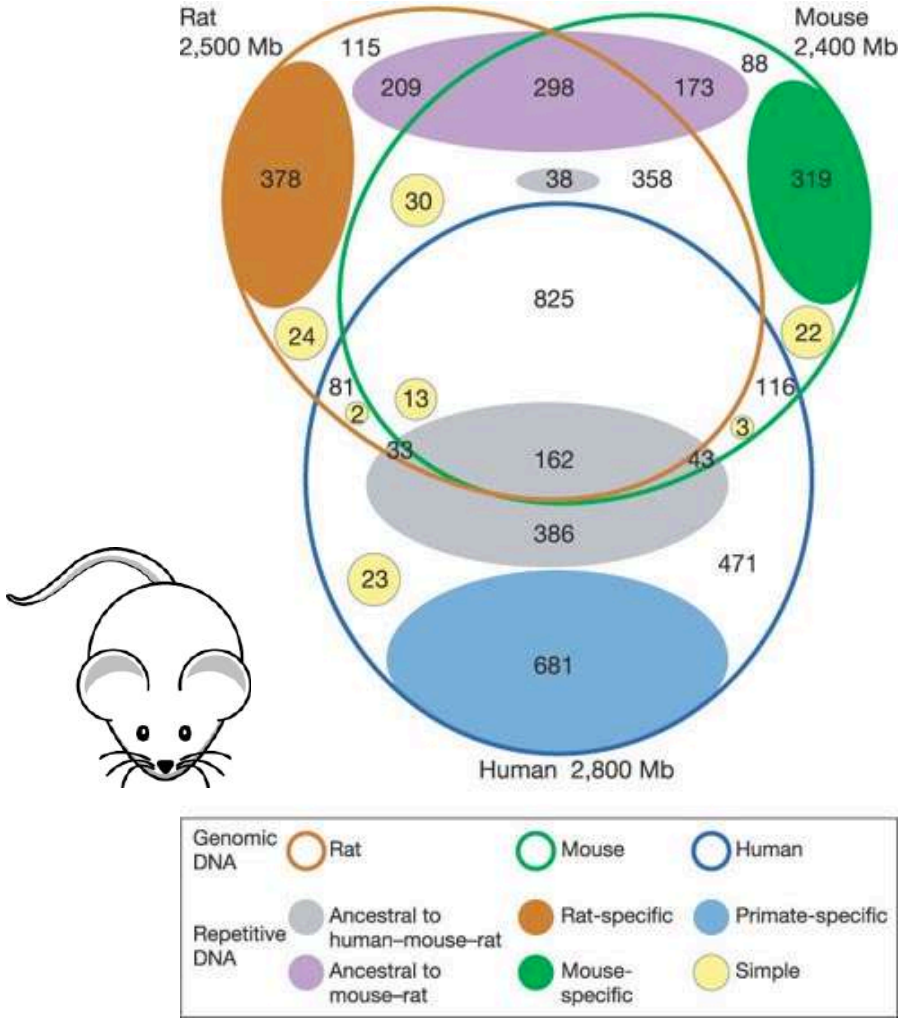
Phylogeny + Venn diagram to show expansion/loss

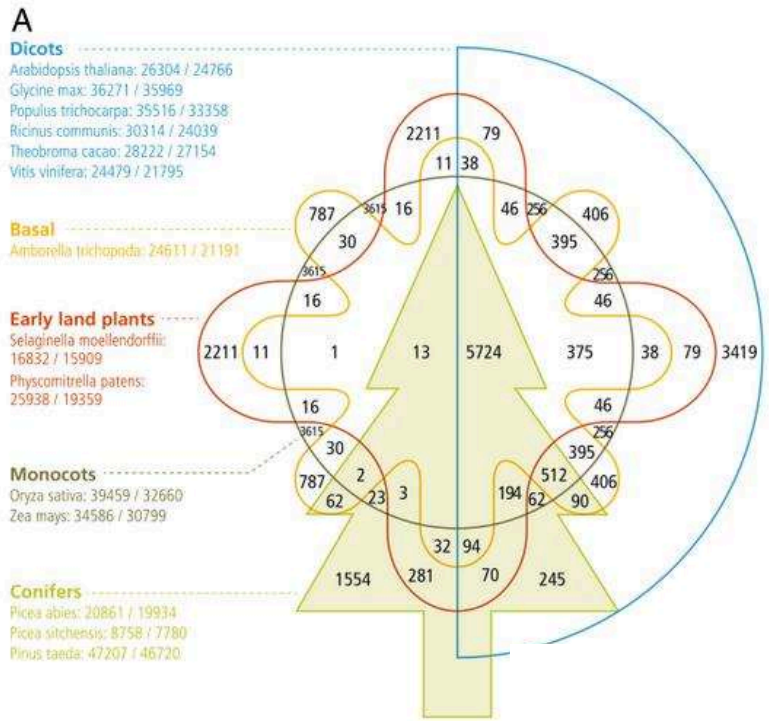


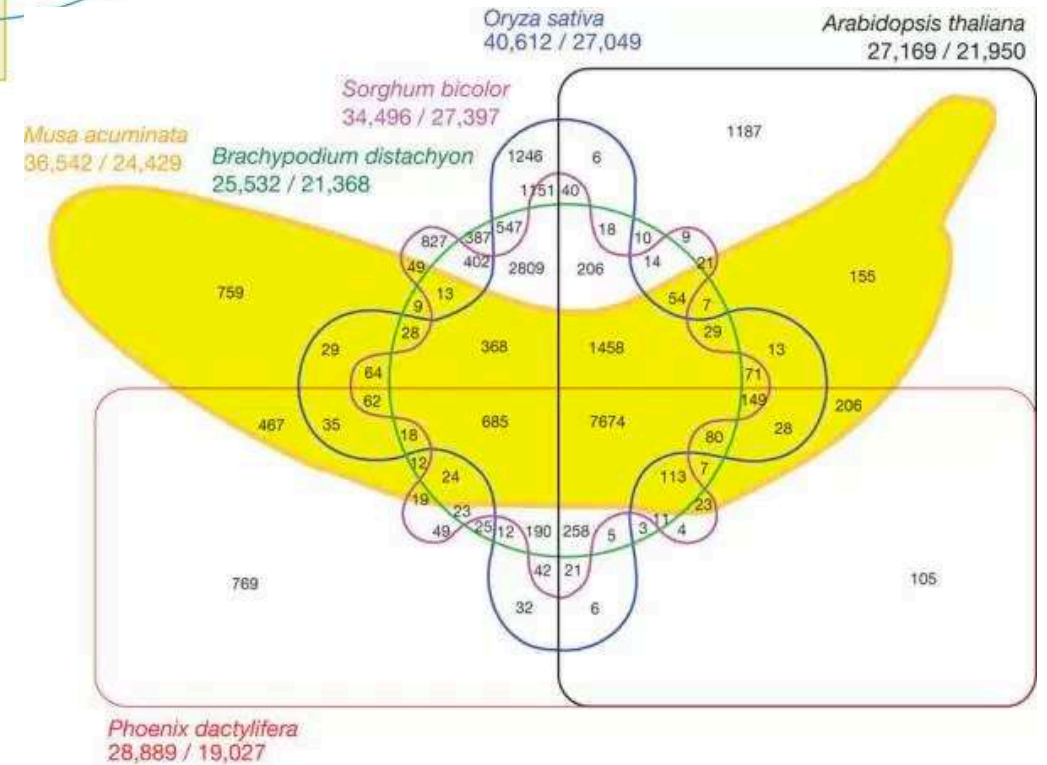


Foth (2014)

Trend of venn diagram…



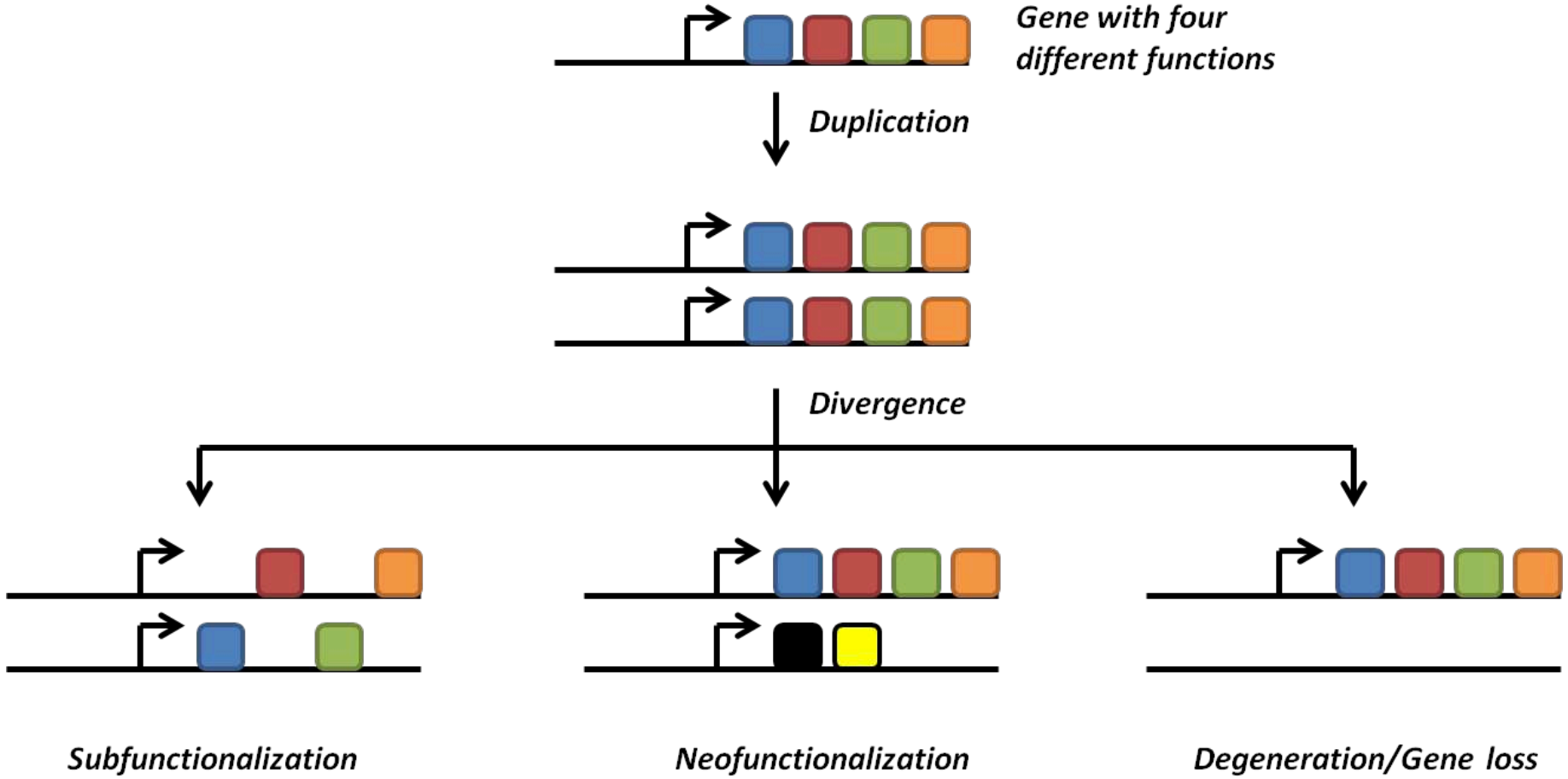




Gene and genome duplication

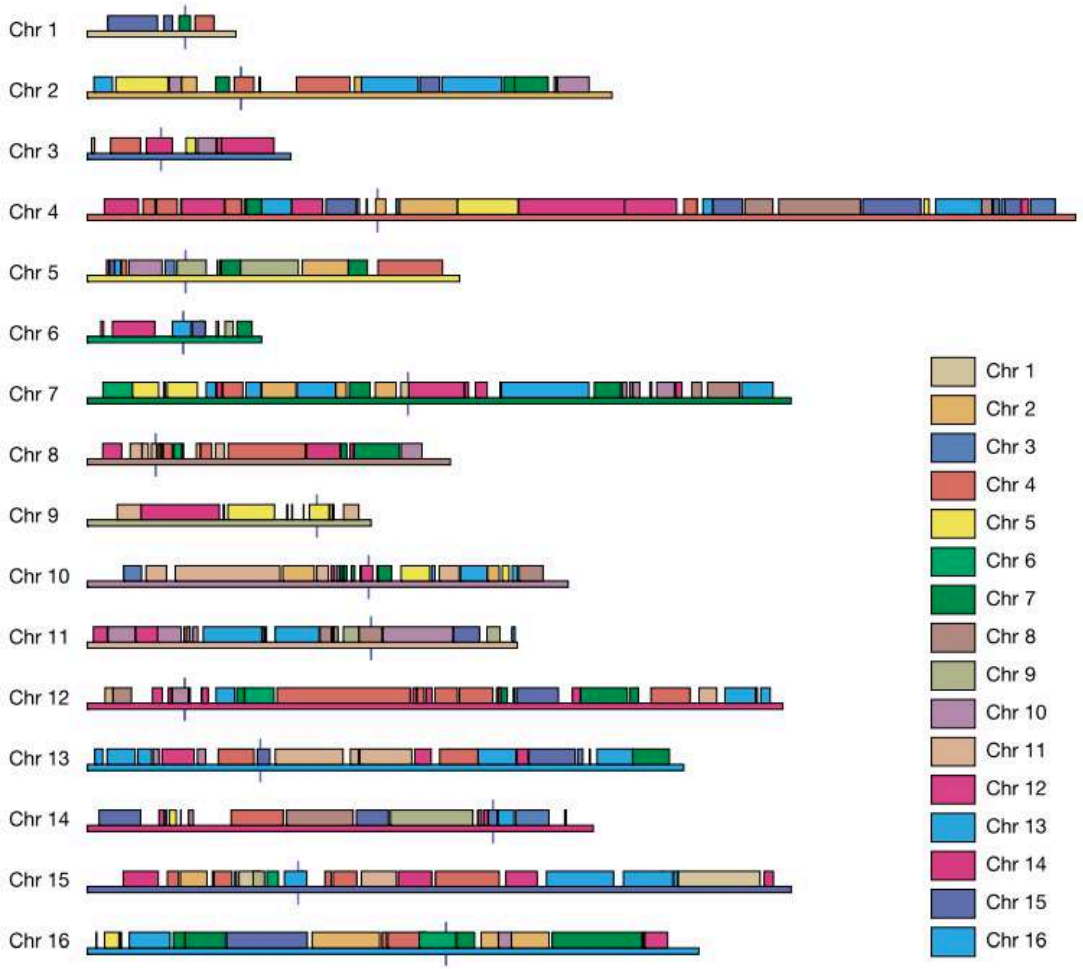
Why study gene duplication?

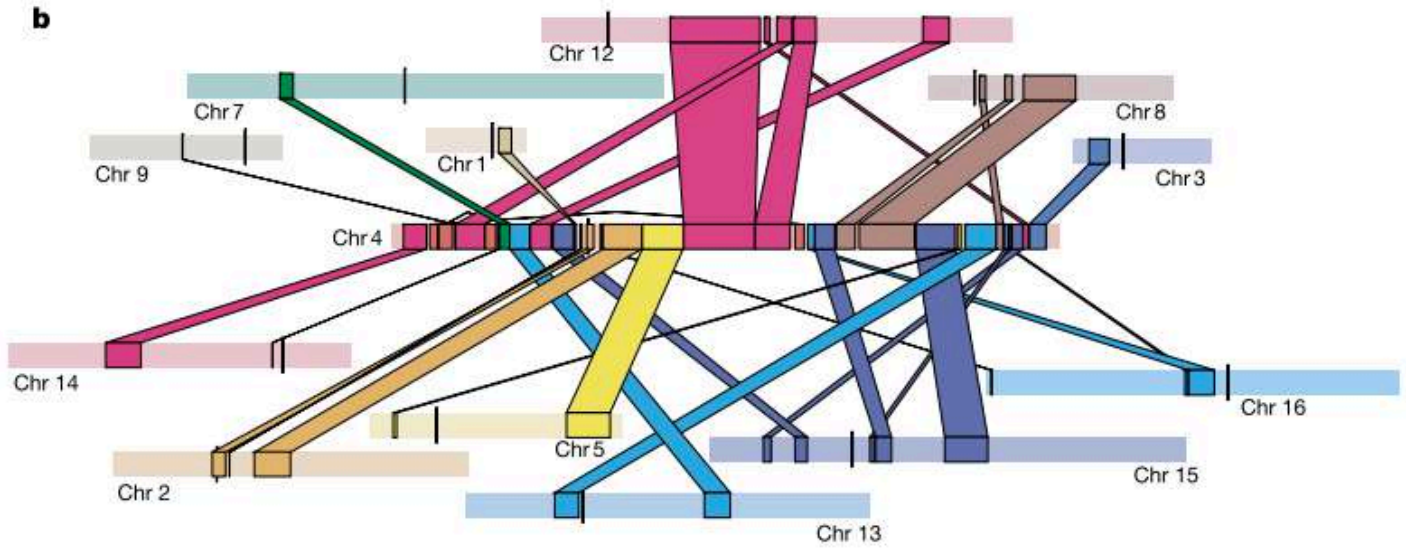
Gene duplications are traditionally considered as a major evolutionary source for protein new functions



Wiki

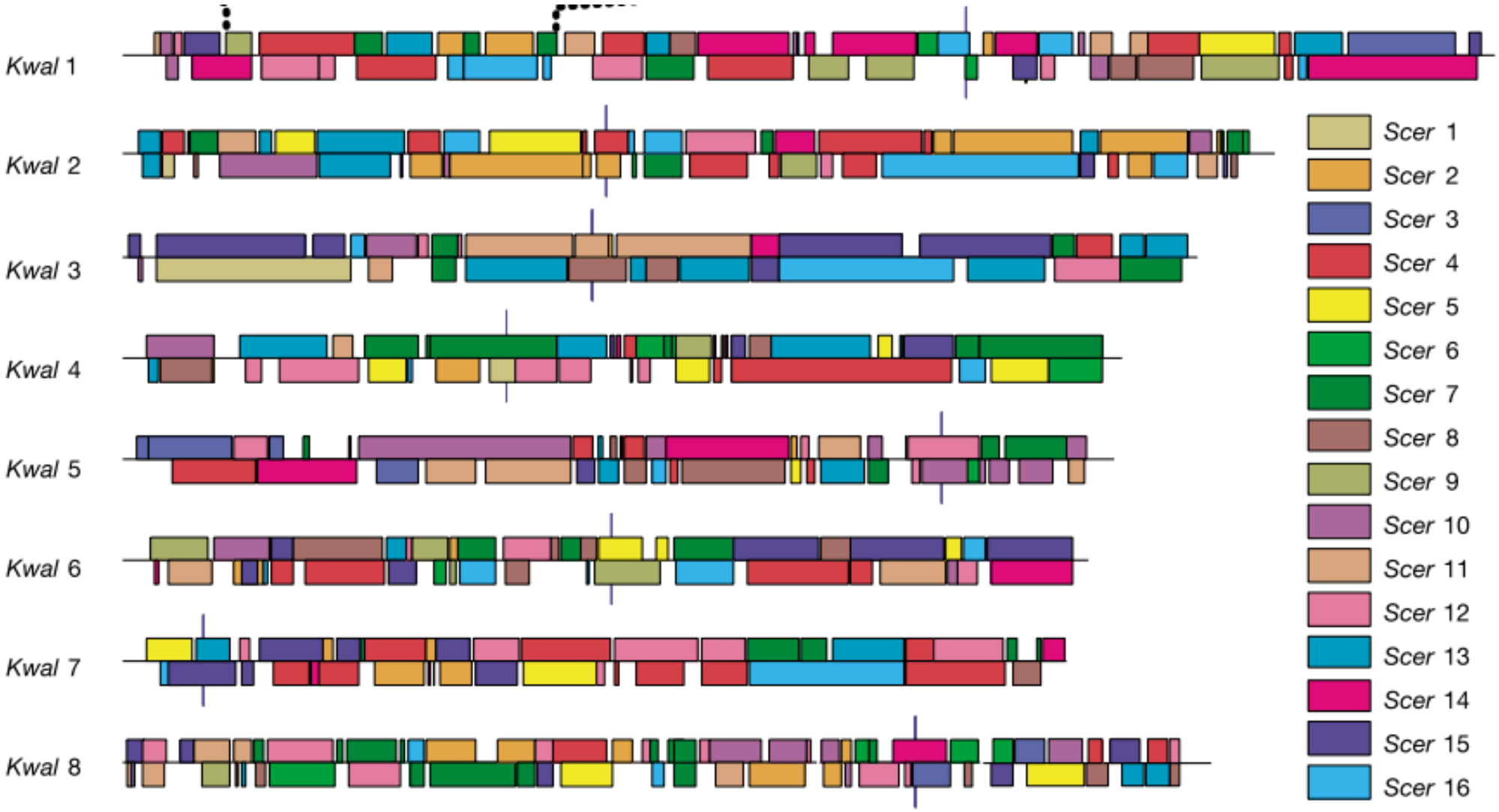
Within species





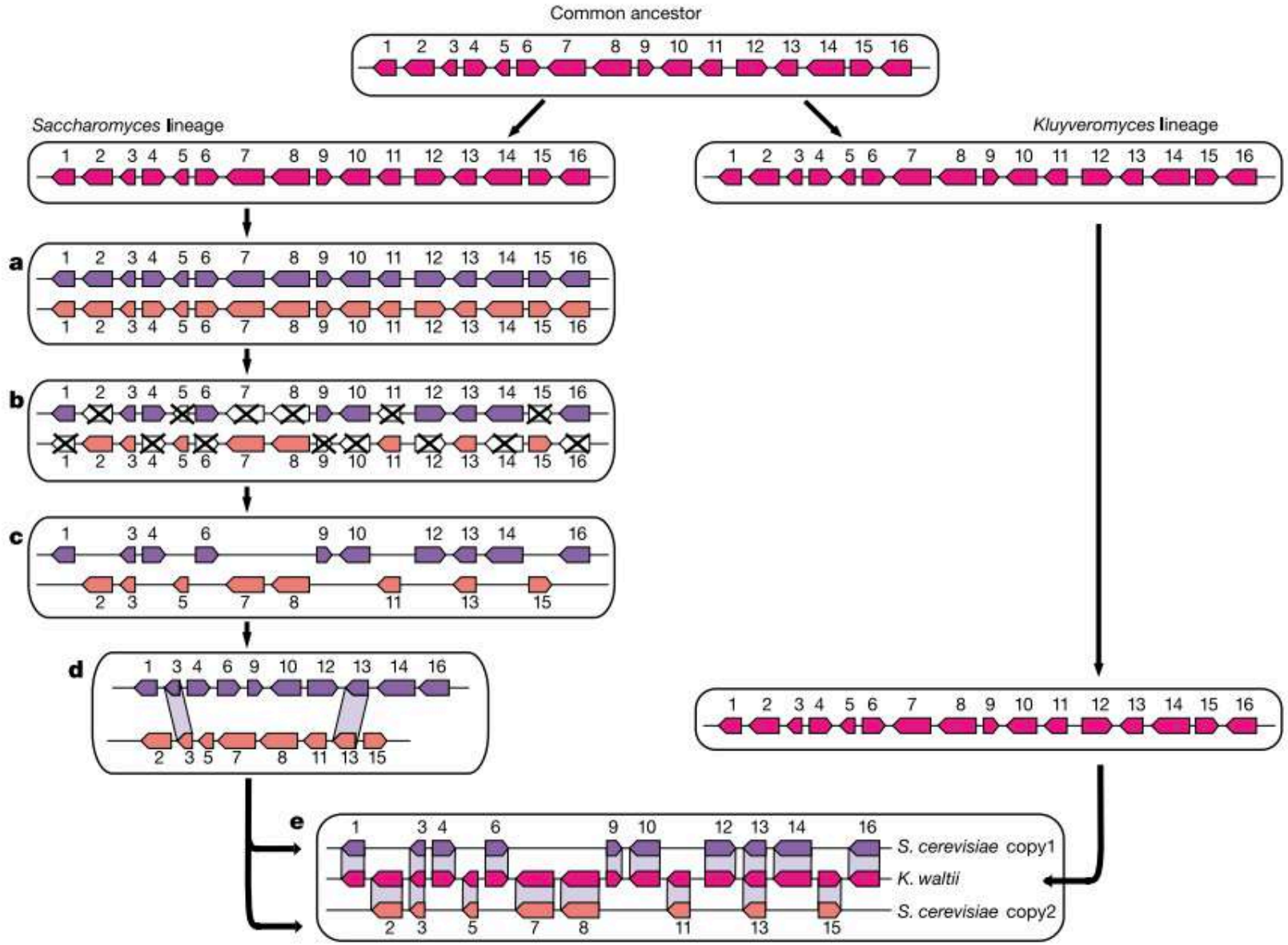
Kellis et al (2004)

Between species



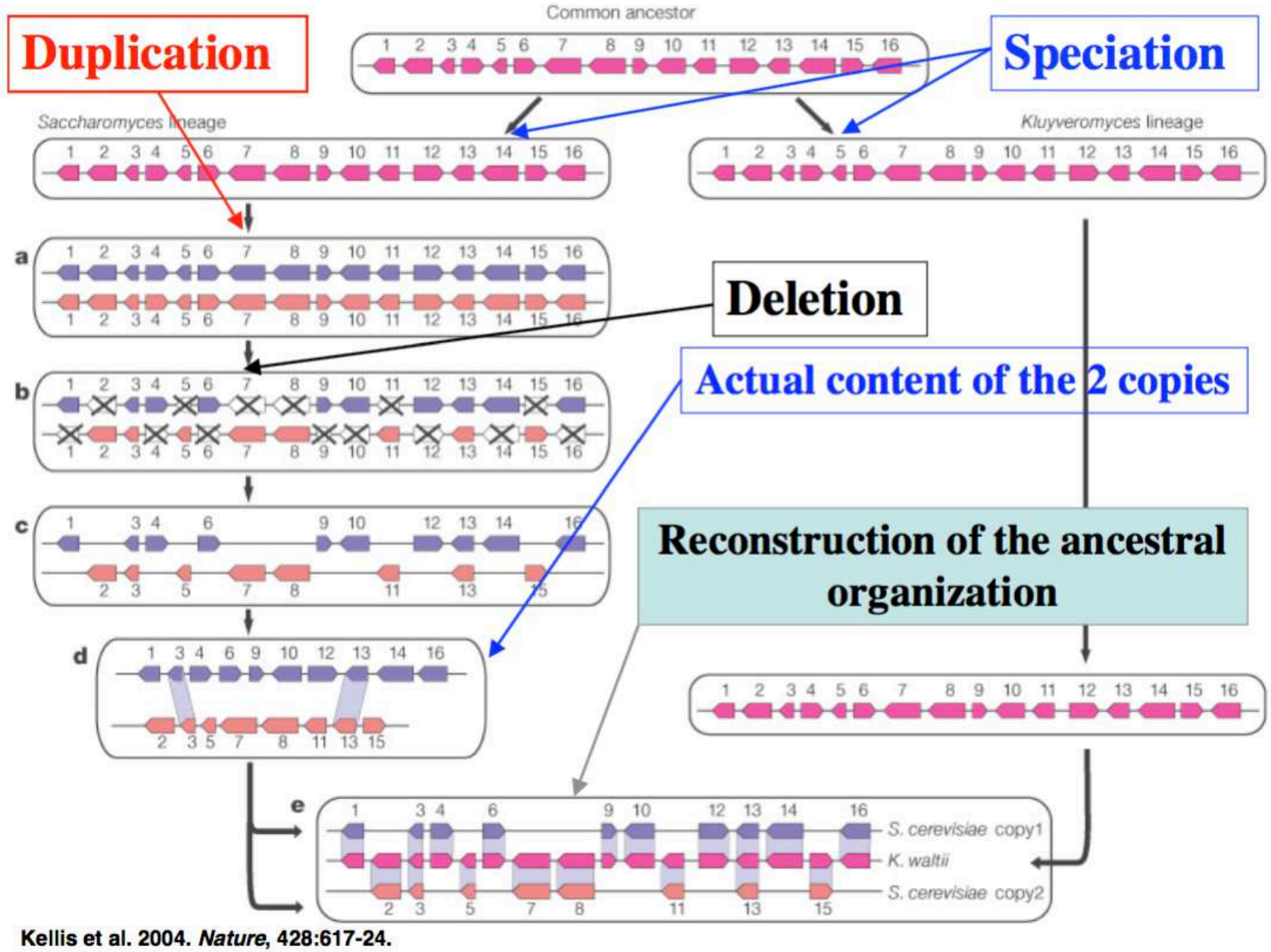
Kellis et al (2004)

Whole genome duplication model



Kellis et al (2004)

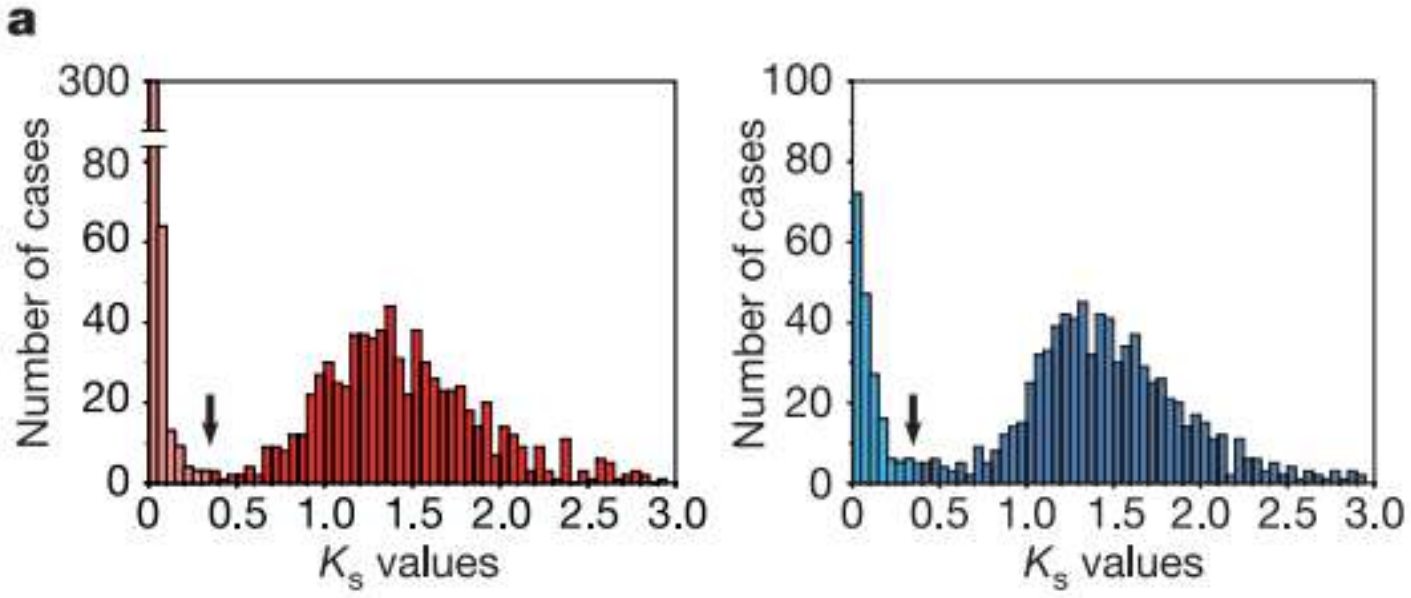
Determining ancestral conservation

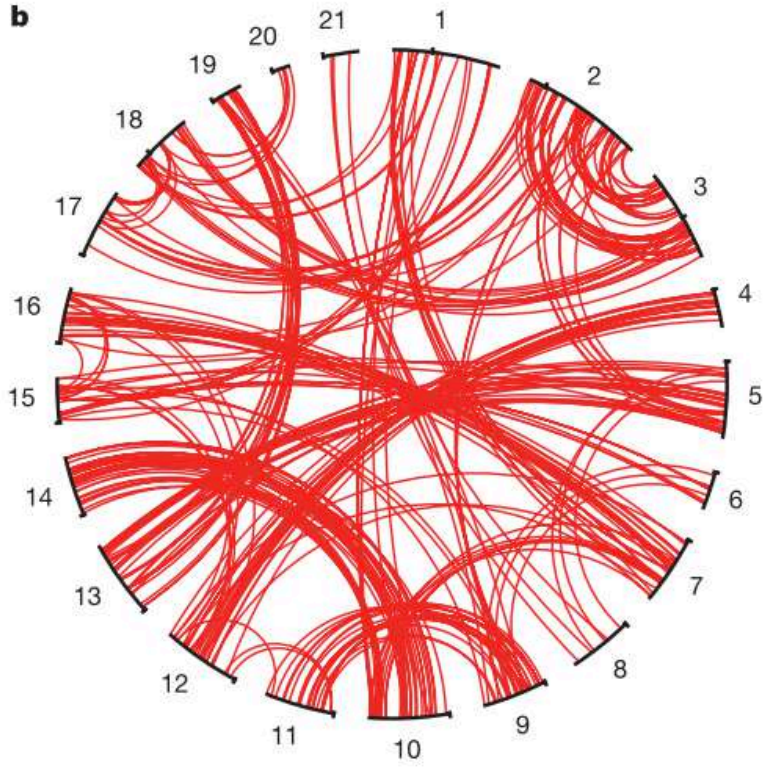


Kellis et al. 2004. *Nature*, 428:617-24.

Slide of Fred Tekaia

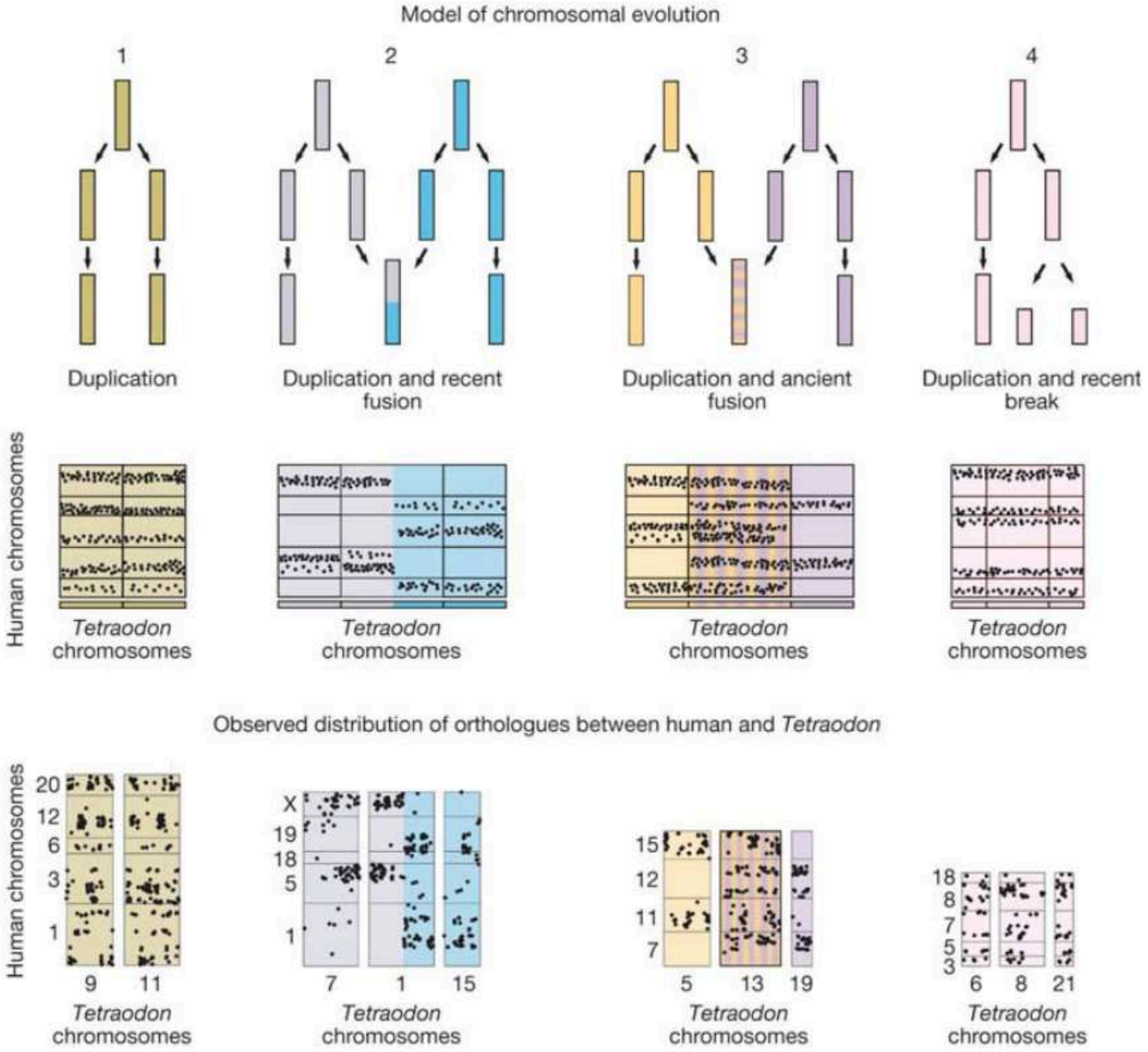
Genome duplication in the teleost fish *Tetraodon nigroviridis* reveals the early vertebrate proto-karyotype





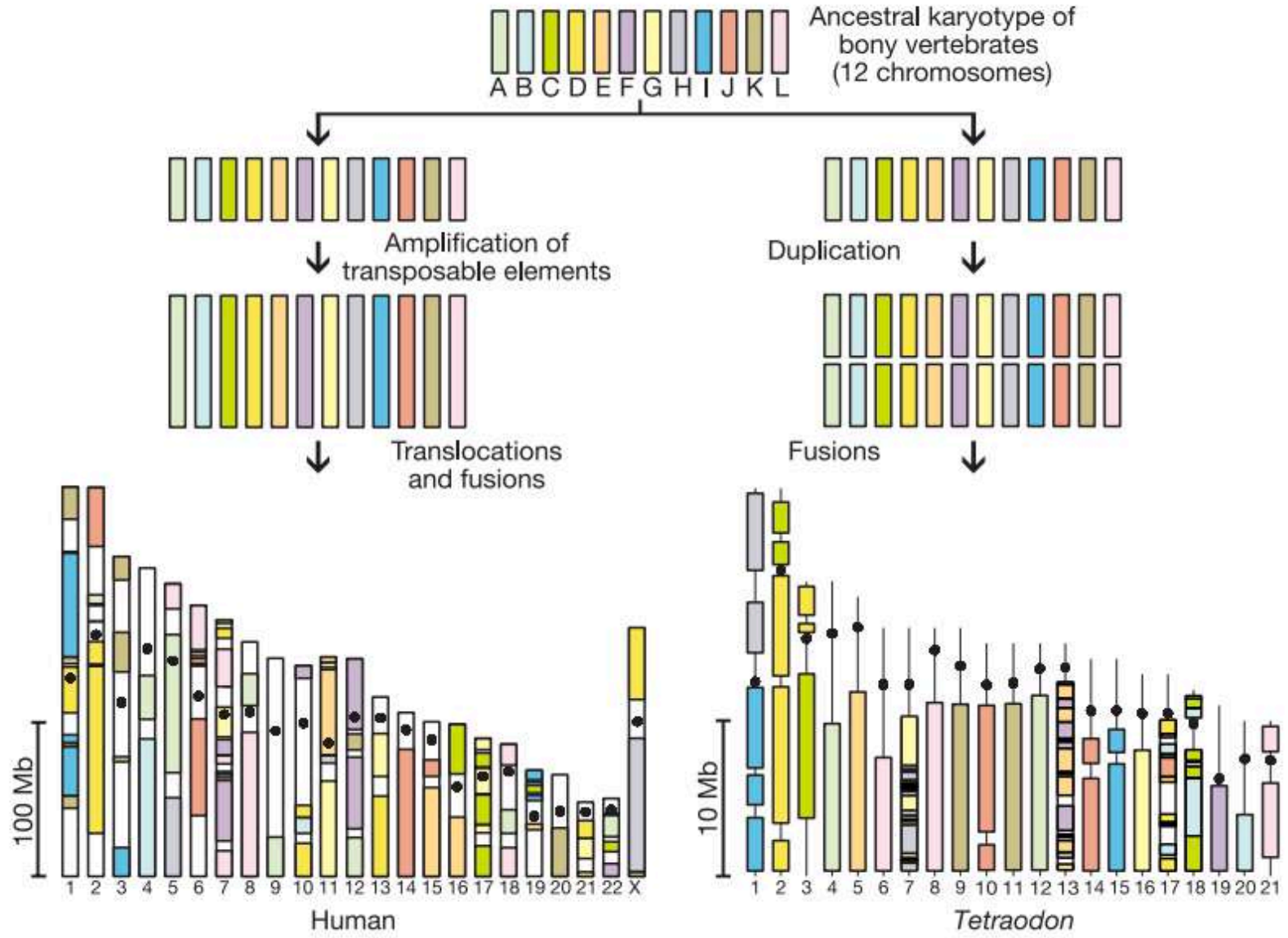
Jaillon et al (2004)

Reconstructing ancient genome rearrangement



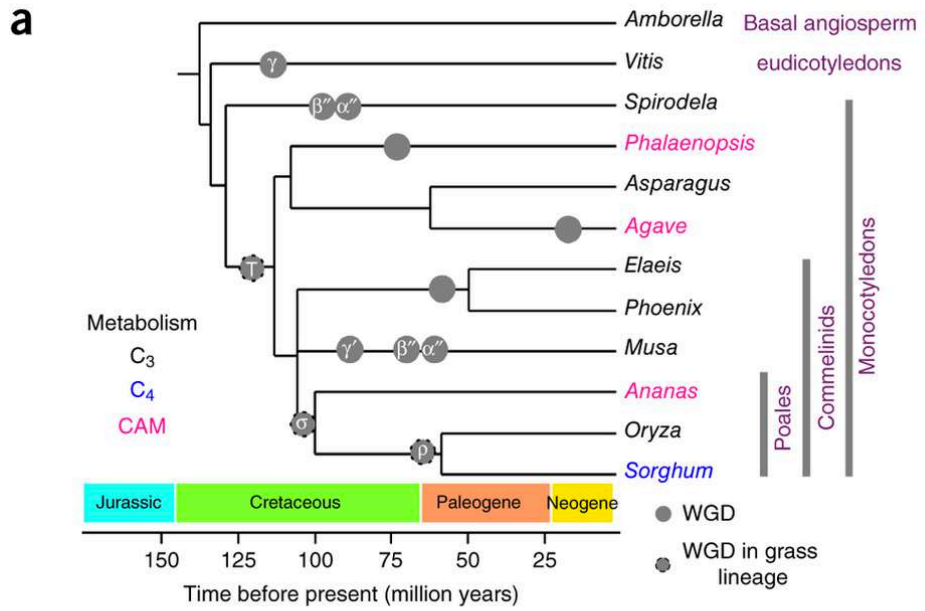
Jaillon et al (2004)

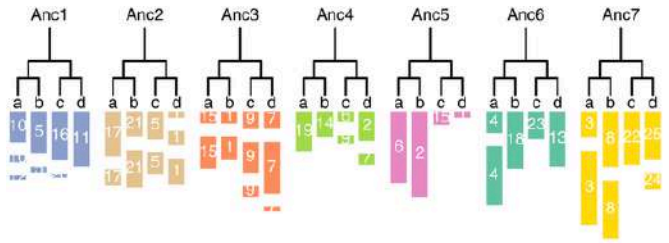
Reconstructing ancient genome rearrangement

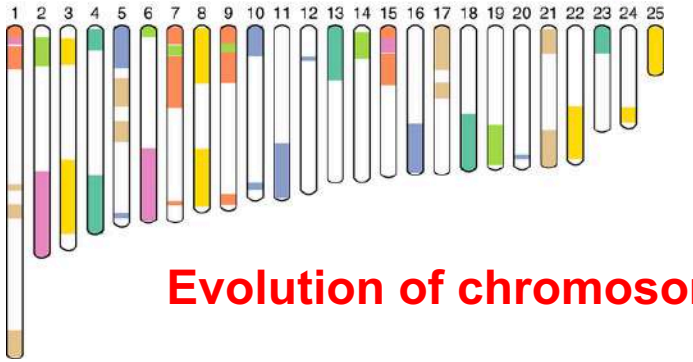


Jaillon et al (2004)

Pineapple genome

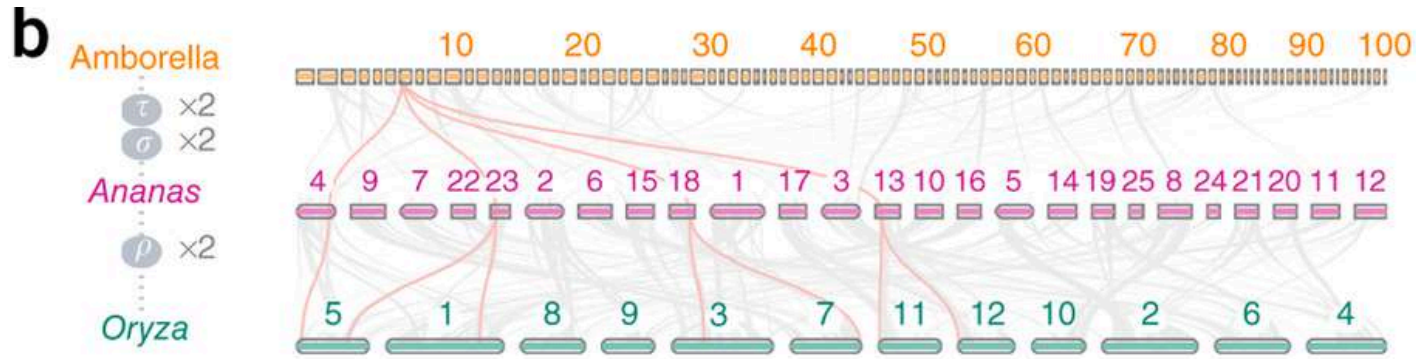


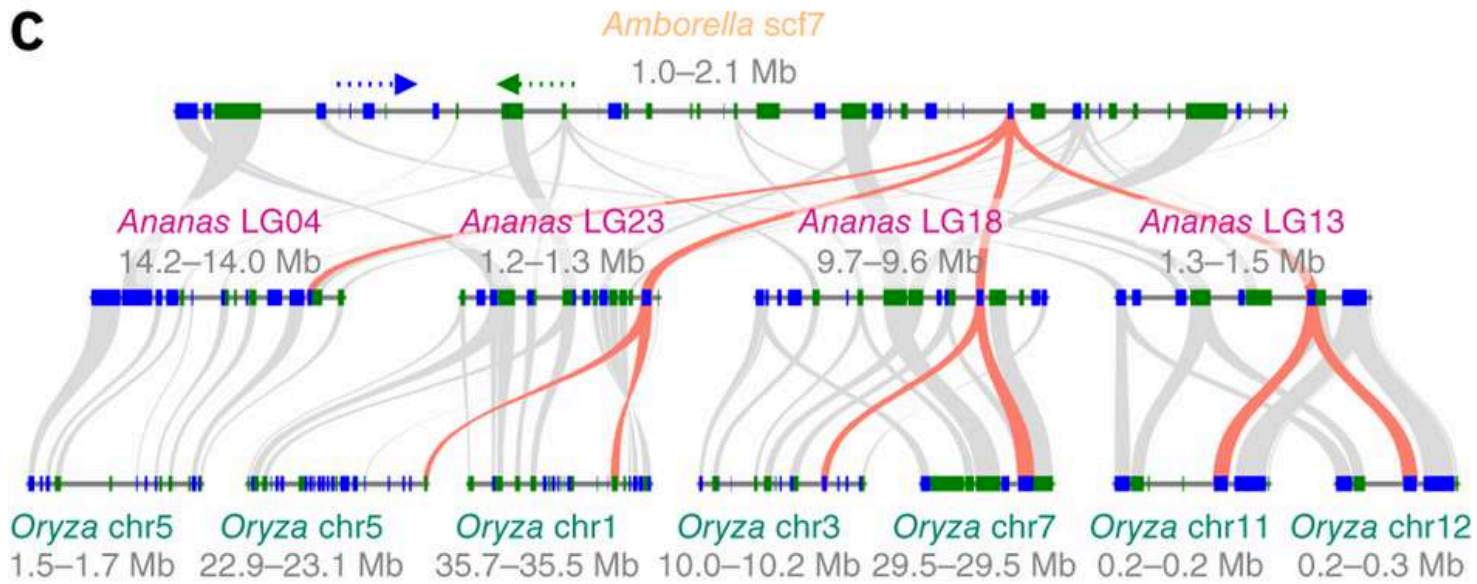




Evolution of chromosomes

Genome alignment

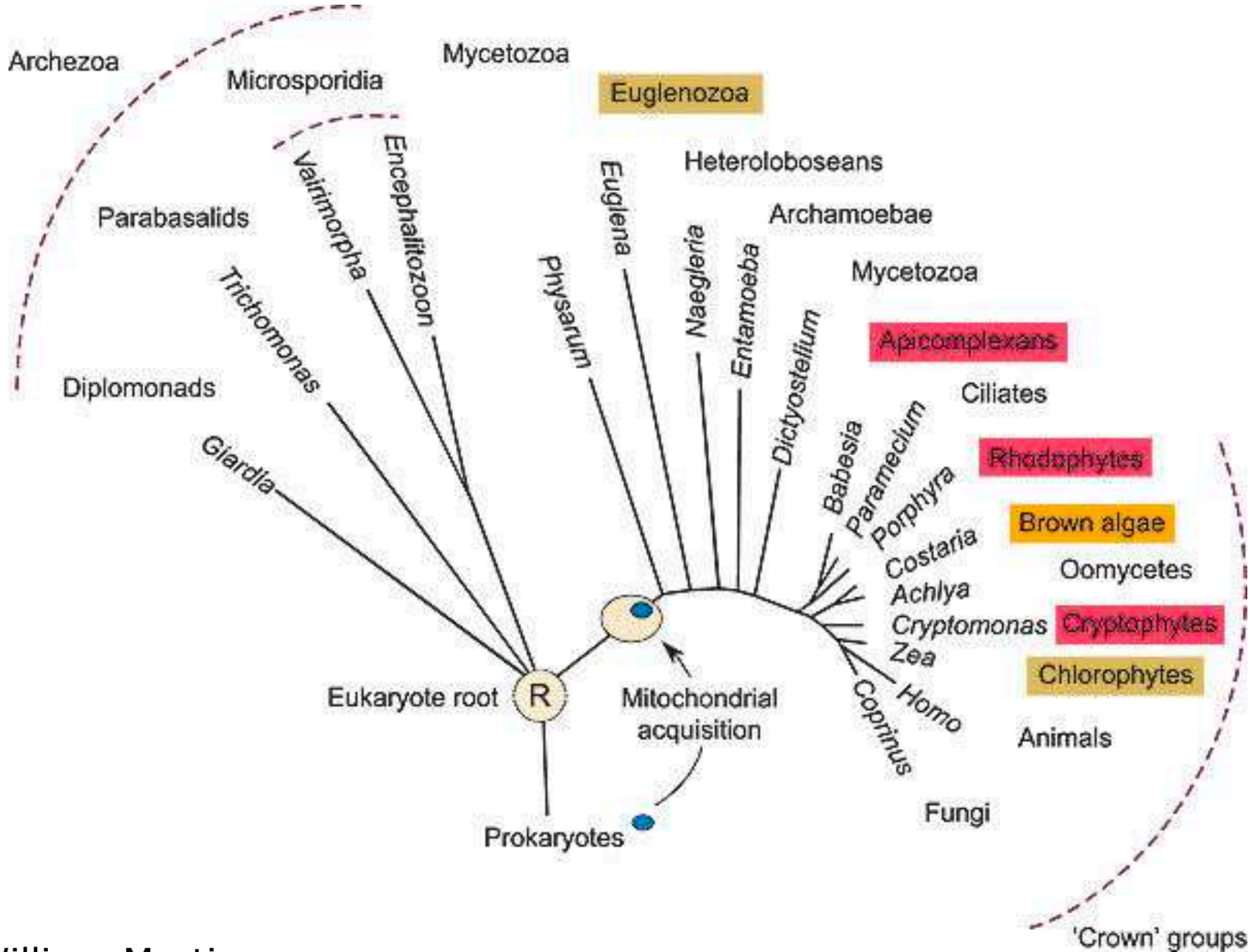




Colinearity of genes

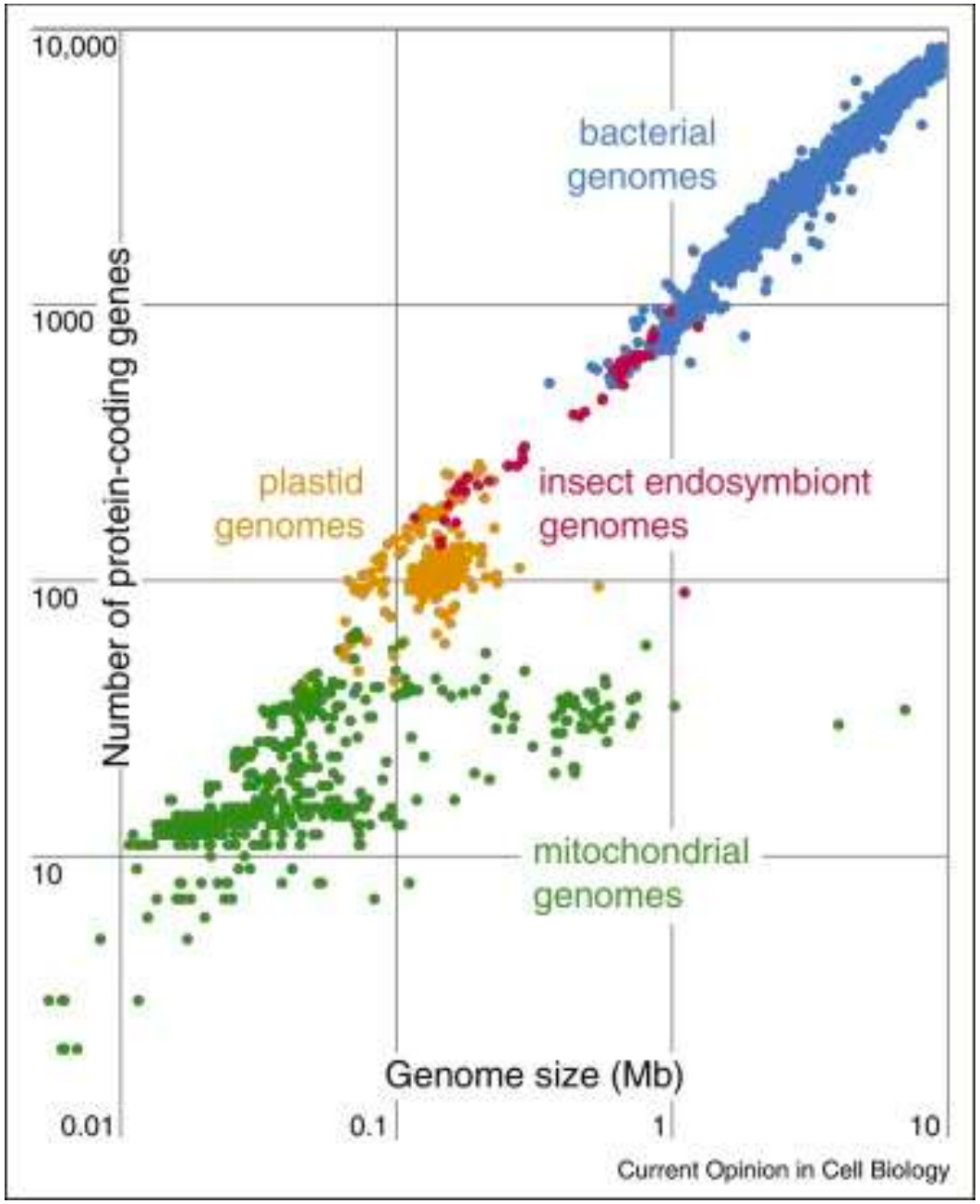
Ming et al (2015)

Symbiosis



Martin Embley & William Martin
Nature **440**, 623-630(30 March 2006)

Genomes from bacteria, insect endosymbionts, chloroplasts, and mitochondria form an unbroken continuum of size and coding density. The plot is truncated at 10 Mb and 10,000 genes.

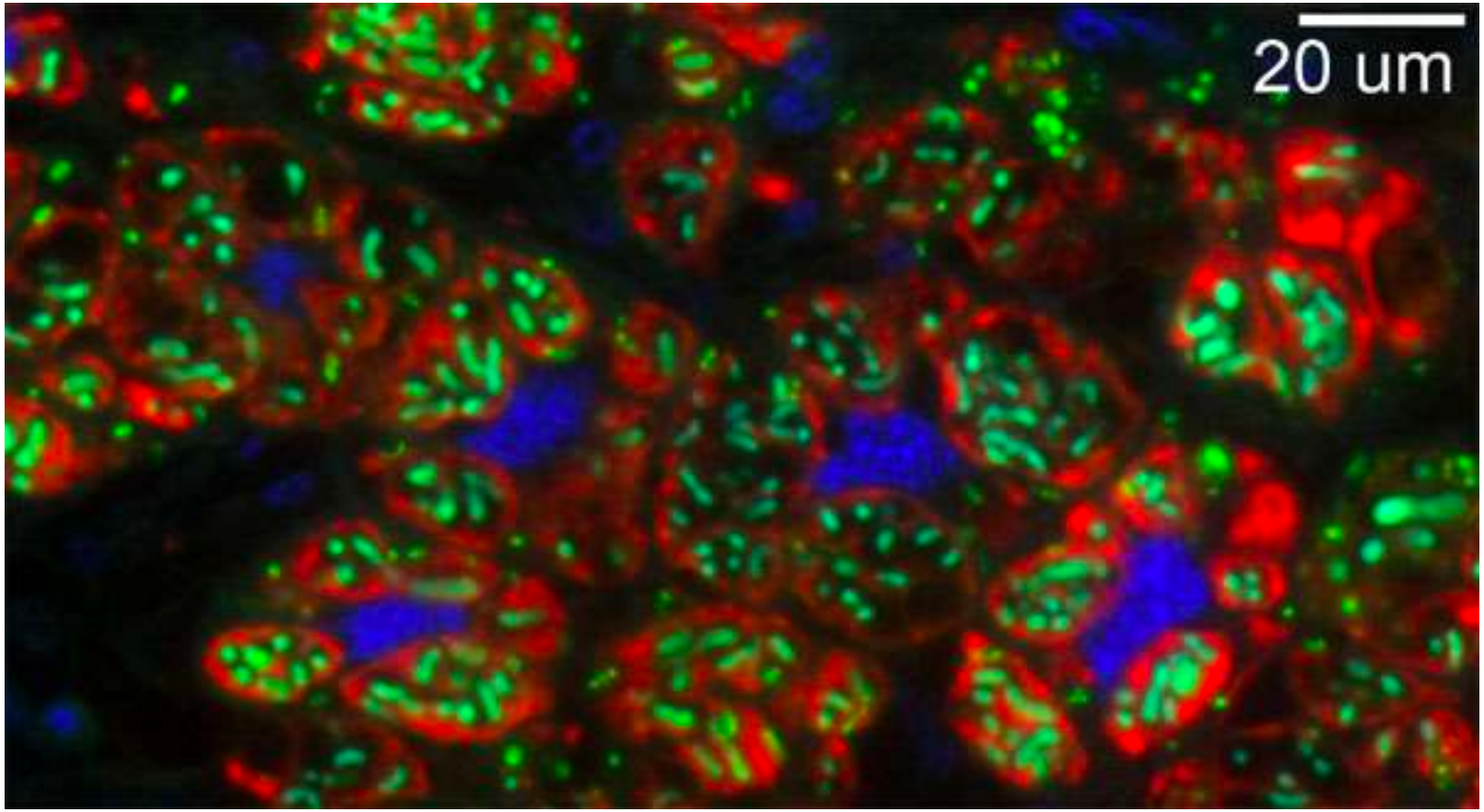


“Insect endosymbionts are missing (genomic) links between bacteria and organelles. It is now widely appreciated that all animals form symbioses with bacteria. Insects are especially interesting in this regard because they form many intracellular symbioses — that is, they allow bacteria to live inside their cells — that are not pathogenic from the host perspective”

McCutcheon (2016) Current Opinion in Cell Biology

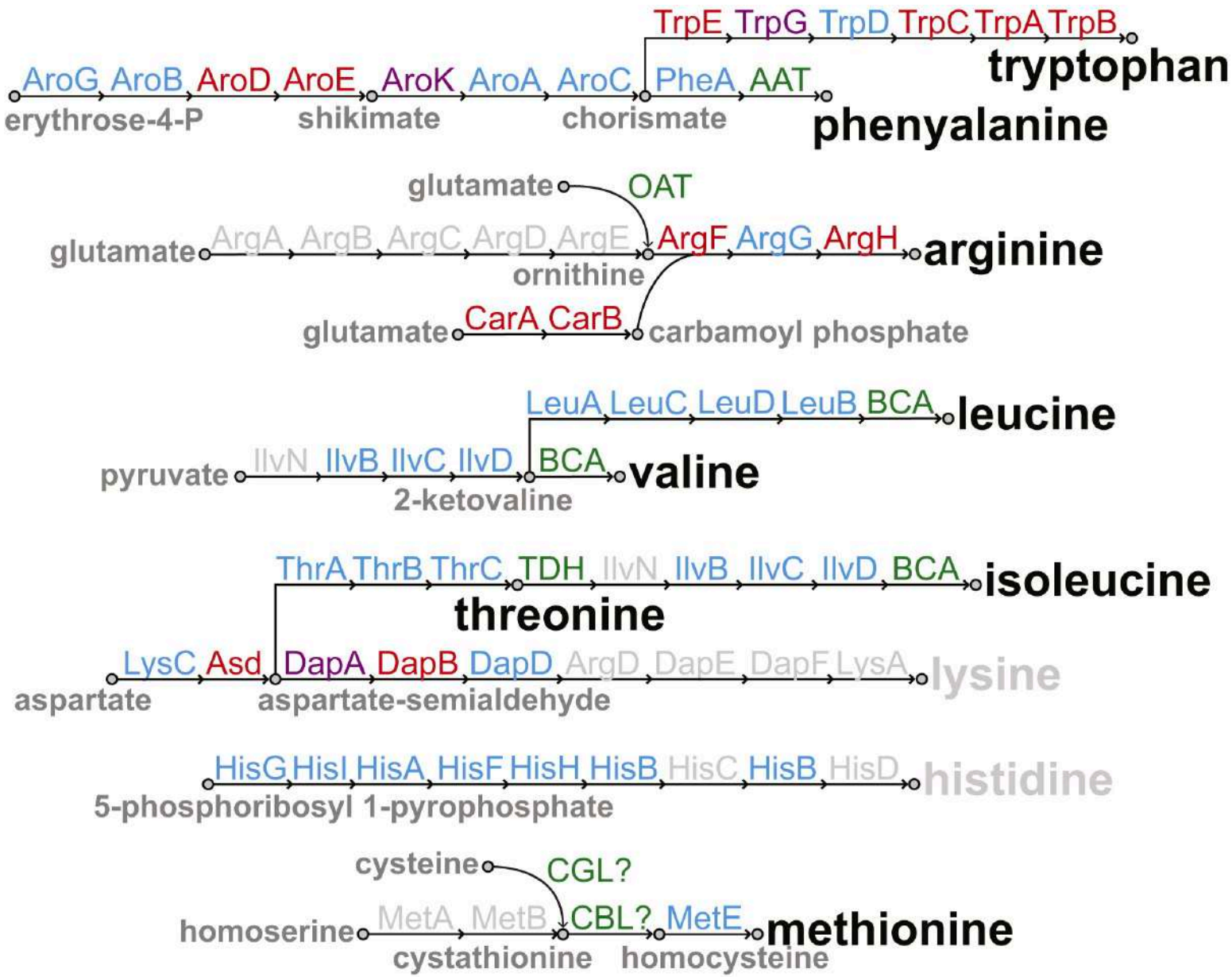
Case study: Mealybugs

Triple Symbiotic Relationship between Mealybugs, *Tremblaya princeps*, and *Moranella endobia*



Mealybug cells, showing Tremblaya (red), Moranella (green) and mealybug nuclei (blue).
Credit: Ryuichi Koga, National Institute of Advanced Industrial Science and Technology, Japan

Predicted Essential Amino Acid Metabolic Contributions of the Mealybug-Tremblaya-Moranella Symbiosis



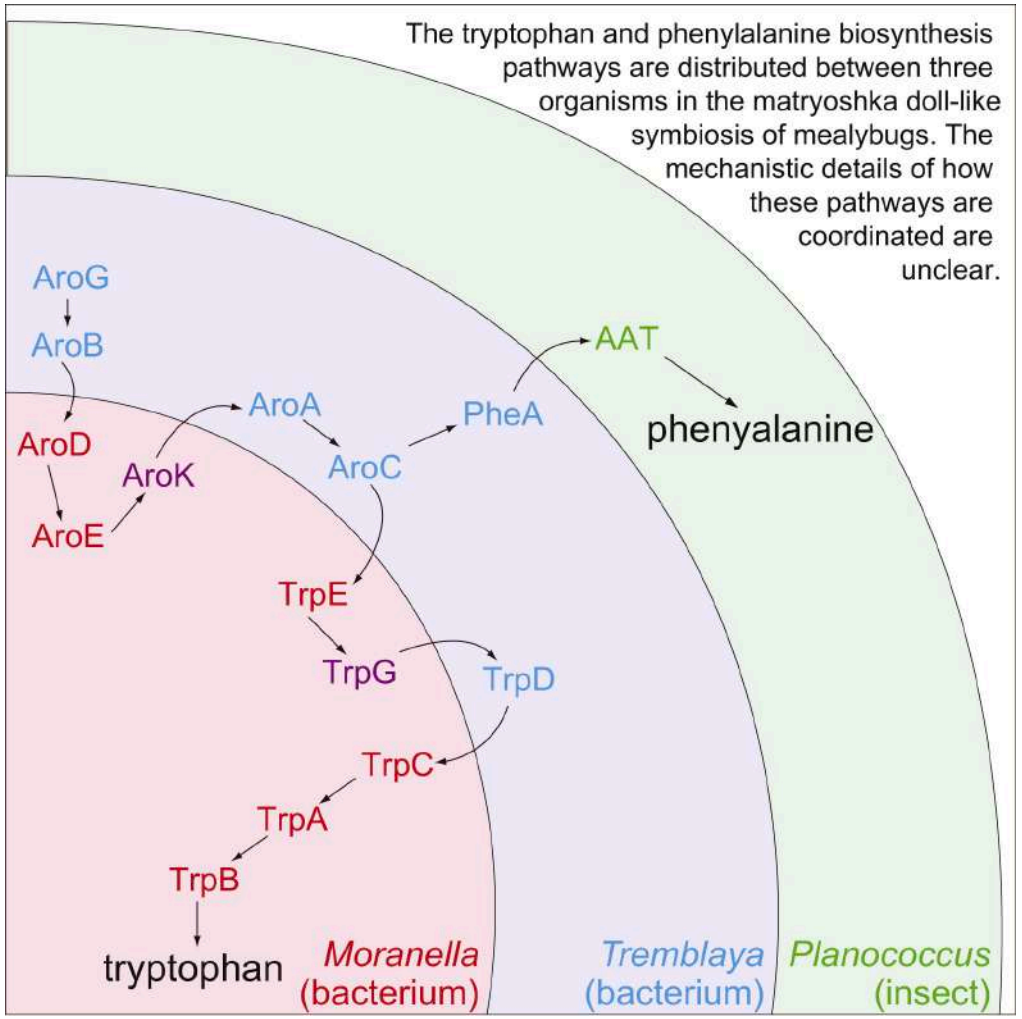
Gene homologs found in the Tremblaya genome are blue; the Moranella genome, red; both the Tremblaya and Moranella genomes, purple; neither the Tremblaya nor the Moranella genome, gray; activities not found in either bacterial genome but predicted to be encoded in the mealybug genome, green.

McCutcheon and Dohlen (2011) Current Biology

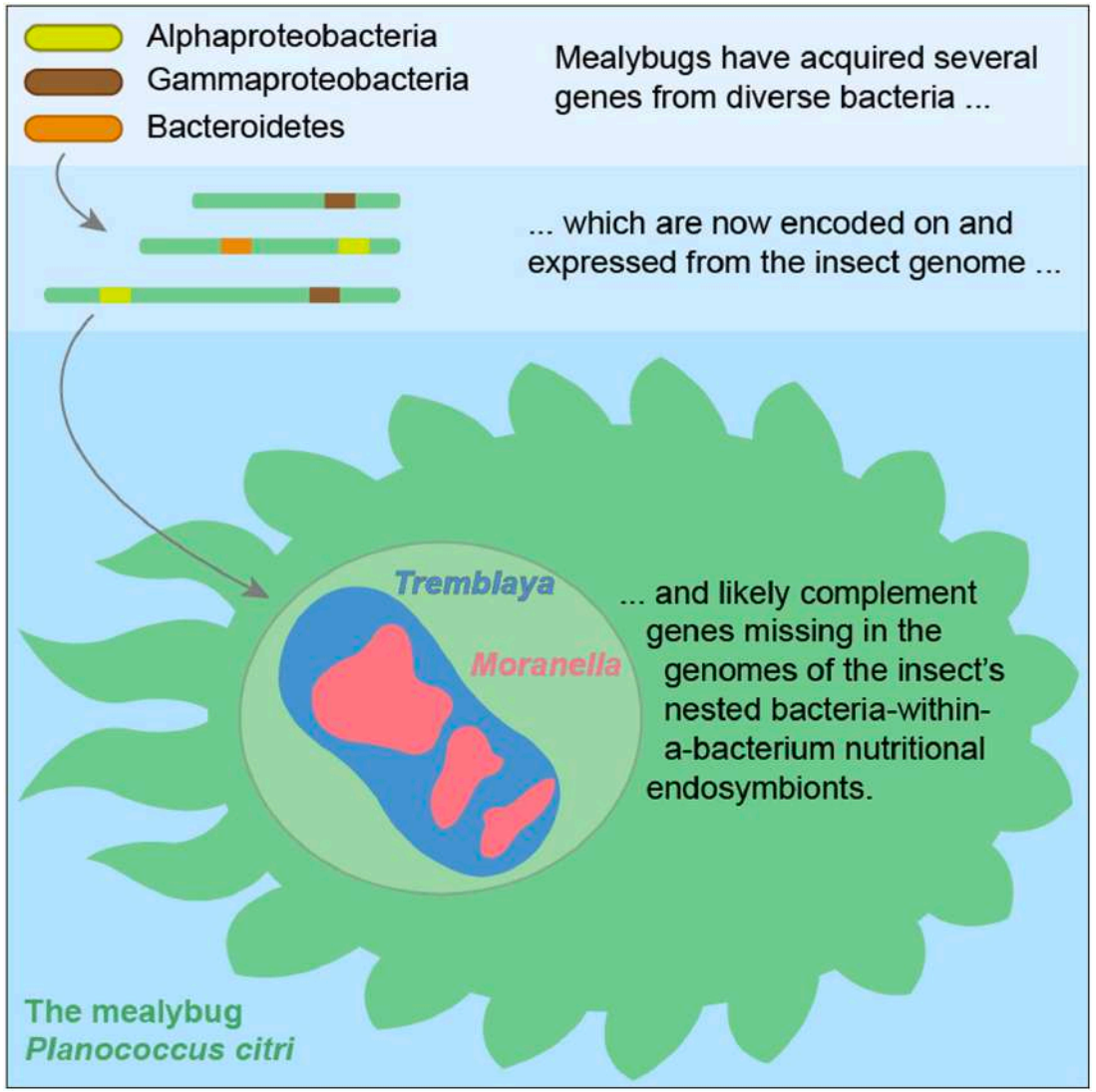
Genome degeneracy of a bacterial endosymbiont is driven by its own endosymbiont

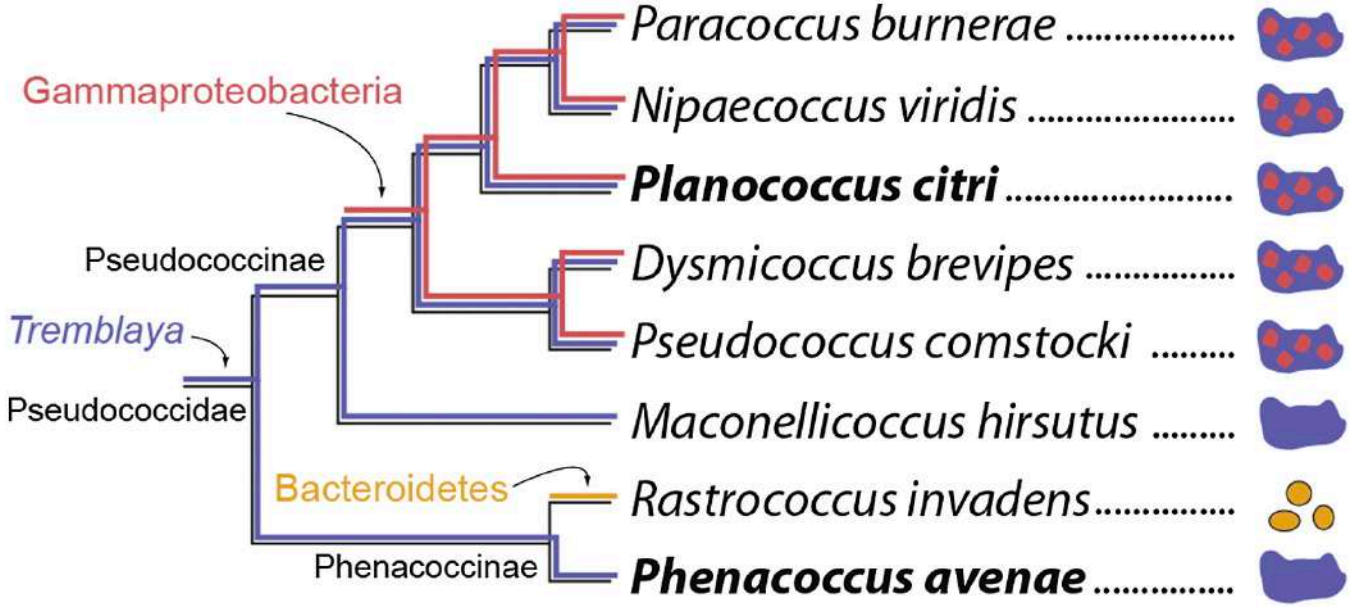
•HGT from diverse bacteria to the insect host genome support the three-way symbiosis

•Endosymbiont genomes can massively degrade without transfer of genes to the host

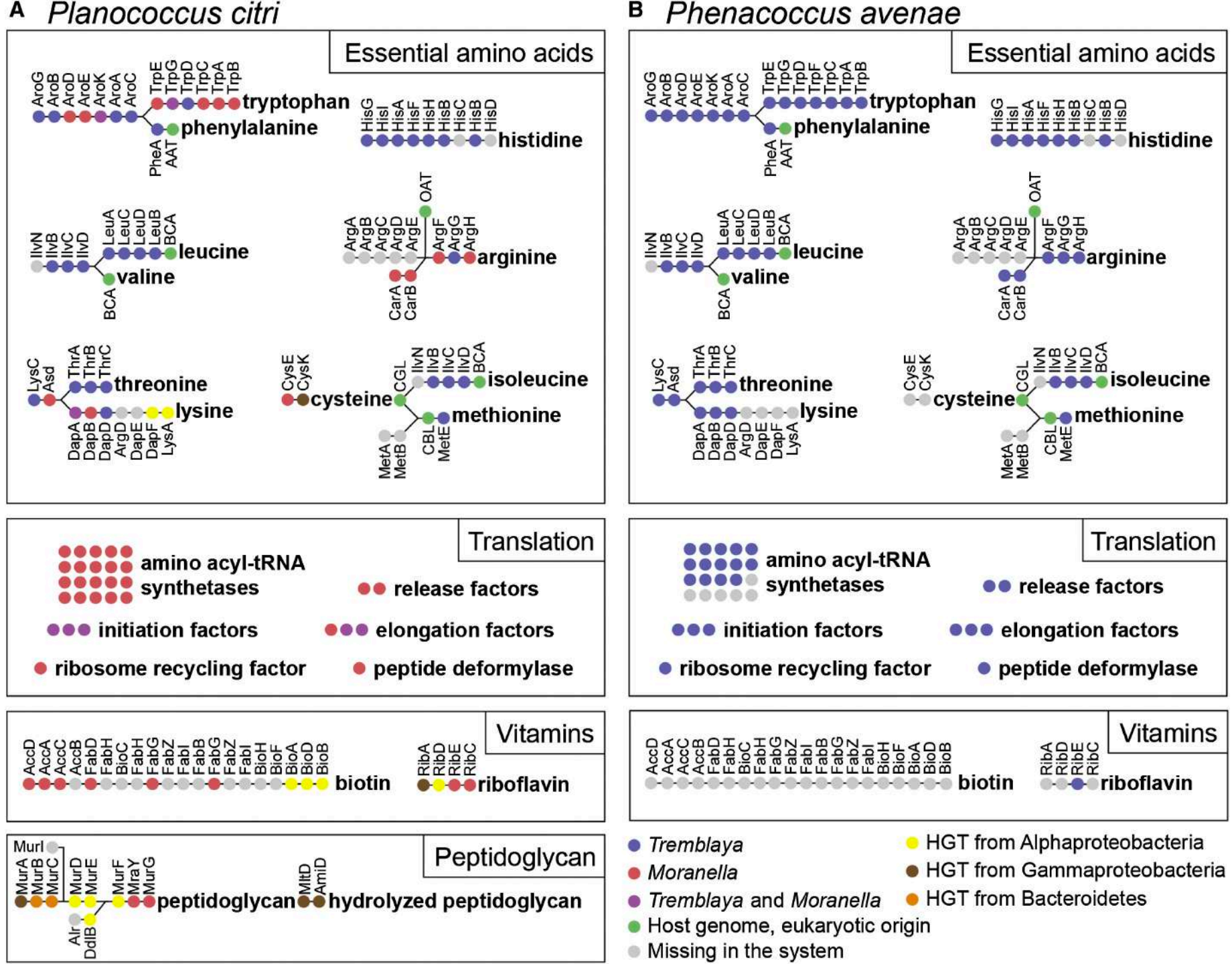


Horizontal Gene Transfer from Diverse Bacteria to an Insect Genome Enables a Tripartite Nested Mealybug Symbiosis





FilipHusnik et al., (2013) Cell


A Planococcus citri
Essential amino acids
AroG AroB AroD AroE AroK AroA AroC
TrpE TrpG TrpD TrpC TrpA TrpB
tryptophan
phenylalanine
PheA AAT
HisG HisI HisA HisF HisH HisB HisC HisB HisD
histidine
IlvN IlvB IlvC IlvD
LeuA LeuC LeuD LeuB BCA
leucine
valine
BCA
ArgA ArgB ArgC ArgD ArgE
OAT
ArgF ArgG ArgH
arginine
CarA CarB
LysC Asd
ThrA ThrB ThrC
threonine
lysine
DapA DapB DapD ArgD DapE DapF LysA
CysE CysK
cysteine
CGL
IlvN IlvB IlvC IlvD BCA
isoleucine
methionine
MetA MetB
CBL MetE
Translation
amino acyl-tRNA synthetases
release factors
initiation factors
elongation factors
ribosome recycling factor
peptide deformylase
Vitamins
AccD AccA AccC AccB FabD FabH BioC FabH FabG FabZ FabI FabB FabG FabZ FabI BioH BioF BioA BioD BioB
biotin
RibA RibD RibE RibC
riboflavin
Peptidoglycan
MurI
MurA MurB MurC MurD MurE MurF MraY MurG
peptidoglycan
MltD AmiD
hydrolyzed peptidoglycan
Alr DdlB
B Phenacoccus avenae
Essential amino acids
AroG AroB AroD AroE AroK AroA AroC
TrpE TrpG TrpD TrpF TrpC TrpA TrpB
tryptophan
phenylalanine
PheA AAT
HisG HisI HisA HisF HisH HisB HisC HisB HisD
histidine
IlvN IlvB IlvC IlvD
LeuA LeuC LeuD LeuB BCA
leucine
valine
BCA
ArgA ArgB ArgC ArgD ArgE
OAT
ArgF ArgG ArgH
arginine
CarA CarB
LysC Asd
ThrA ThrB ThrC
threonine
lysine
DapA DapB DapD ArgD DapE DapF LysA
CysE CysK
cysteine
CGL
IlvN IlvB IlvC IlvD BCA
isoleucine
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Translation
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ribosome recycling factor
peptide deformylase
Vitamins
AccD AccA AccC AccB FabD FabH BioC FabH FabG FabZ FabI FabB FabG FabZ FabI BioH BioF BioA BioD BioB
biotin
RibA RibD RibE RibC
riboflavin
Tremblaya
Moranella
Tremblaya and Moranella
Host genome, eukaryotic origin
Missing in the system
HGT from Alphaproteobacteria
HGT from Gammaproteobacteria
HGT from Bacteroidetes

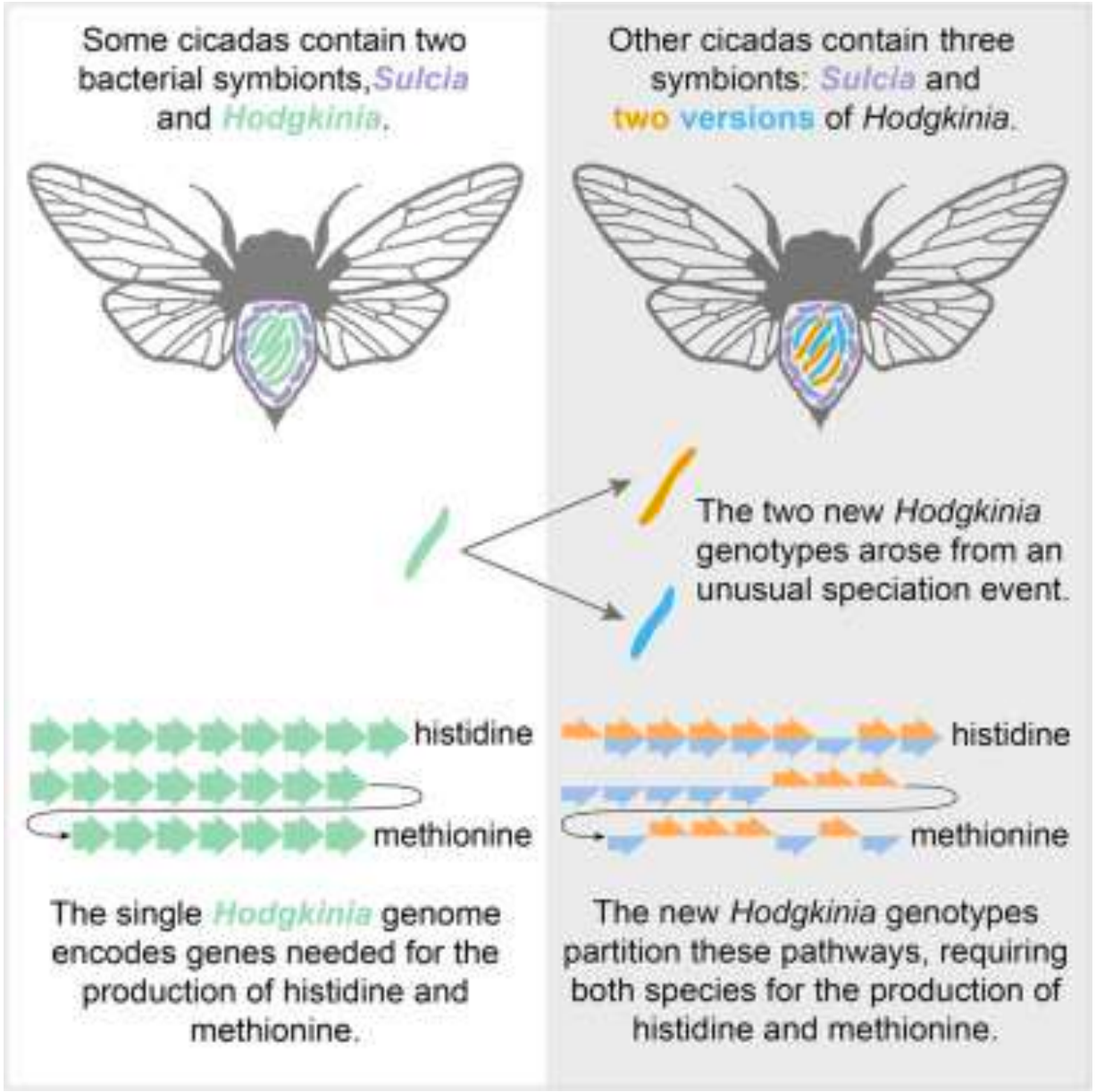
Even more fascinating case

Cell

Sympatric Speciation in a Bacterial Endosymbiont Results in Two Genomes with the Functionality of One

James T. Van Leuven,[1] Russell C. Meister,[2] Chris Simon,[2] and John P. McCutcheon[1,3,*]
[1]Division of Biological Sciences, University of Montana, Missoula, MT 59812, USA
[2]Department of Ecology and Evolutionary Biology, University of Connecticut, Storrs, CT 06269, USA
[3]Canadian Institute for Advanced Research, CIFAR Program in Integrated Microbial Biodiversity, Toronto, ON M5G 1Z8, Canada
*Correspondence: john.mccutcheon@umontana.edu
http://dx.doi.org/10.1016/j.cell.2014.07.047

https://www.youtube.com/watch?v=XRI2JxTzJ-0&list=UUlSV2Tk7x-wBBXP6-VCNbNw



More case studies:

nature plants

ARTICLES

https://doi.org/10.1038/s41477-018-0337-0

OPEN

Case study

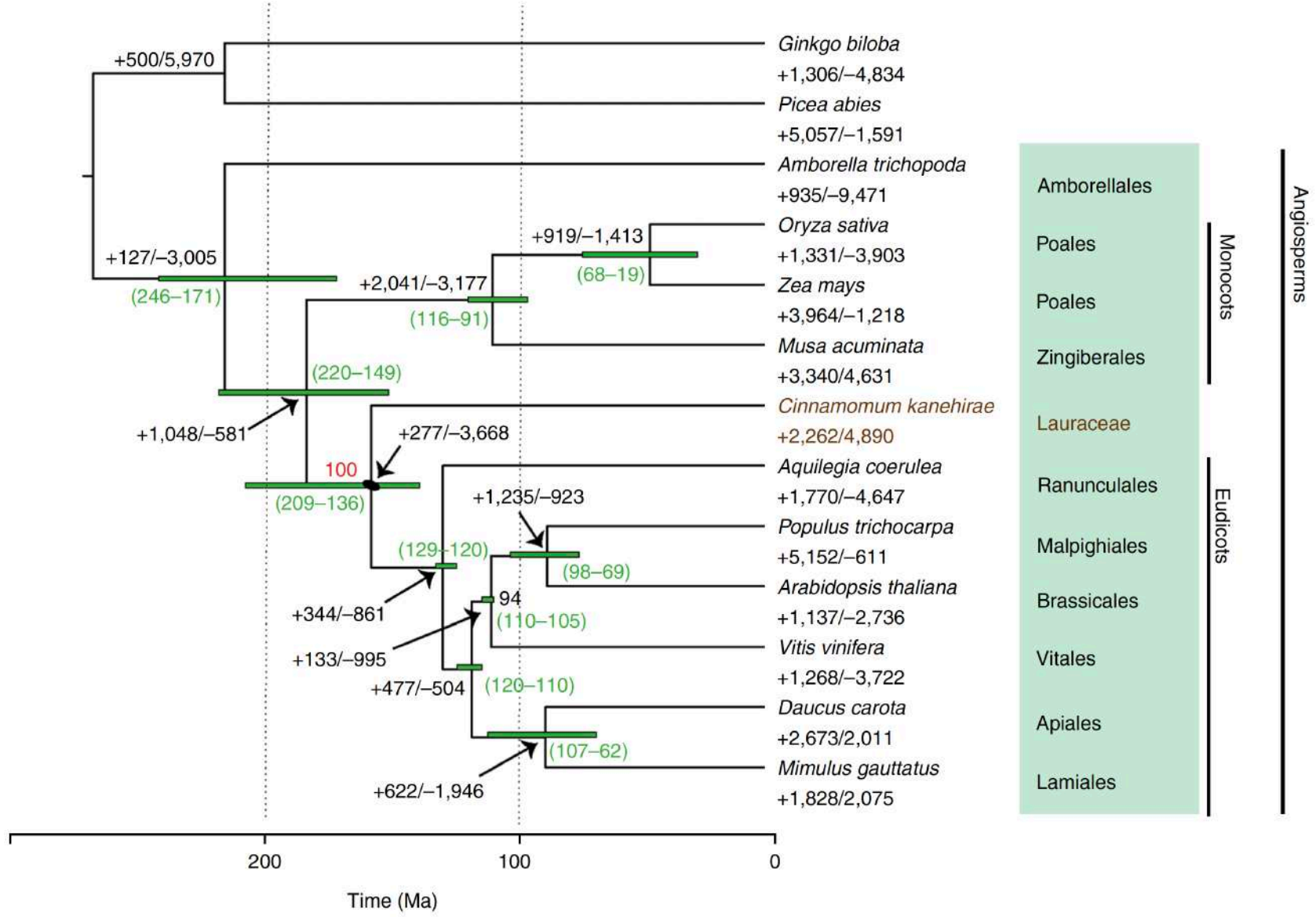
Stout camphor tree genome fills gaps in understanding of flowering plant genome evolution

Shu-Miaw Chaw[1,6*], Yu-Ching Liu[1], Yu-Wei Wu[2], Han-Yu Wang[1], Chan-Yi Ivy Lin[1], Chung-Shien Wu[1], Huei-Mien Ke[1], Lo-Yu Chang[1,3], Chih-Yao Hsu[1], Hui-Ting Yang[1], Edi Sudianto[1], Min-Hung Hsu[1,4], Kun-Pin Wu[4], Ling-Ni Wang[1], James H. Leebens-Mack[5] and Isheng J. Tsai[1,6*]

We present reference-quality genome assembly and annotation for the stout camphor tree (*Cinnamomum kanehirae* (Laurales, Lauraceae)), the first sequenced member of the Magnoliidae comprising four orders (Laurales, Magnoliales, Canellales and Piperales) and over 9,000 species. **Phylogenomic analysis of 13 representative seed plant genomes indicates that magnoliid and eudicot lineages share more recent common ancestry than monocots**. **Two whole-genome duplication events were inferred within the magnoliid lineage: one before divergence of Laurales and Magnoliales and the other within the Lauraceae**. Small-scale segmental duplications and tandem duplications also contributed to innovation in the evolutionary history of *Cinnamomum*. For example, expansion of the terpenoid synthase gene subfamilies within the Laurales spawned the diversity of *Cinnamomum* monoterpenes and sesquiterpenes.

Chaw et al (2018)

Stout camphor tree genome



Chaw et al (2018)

Stout camphor tree genome

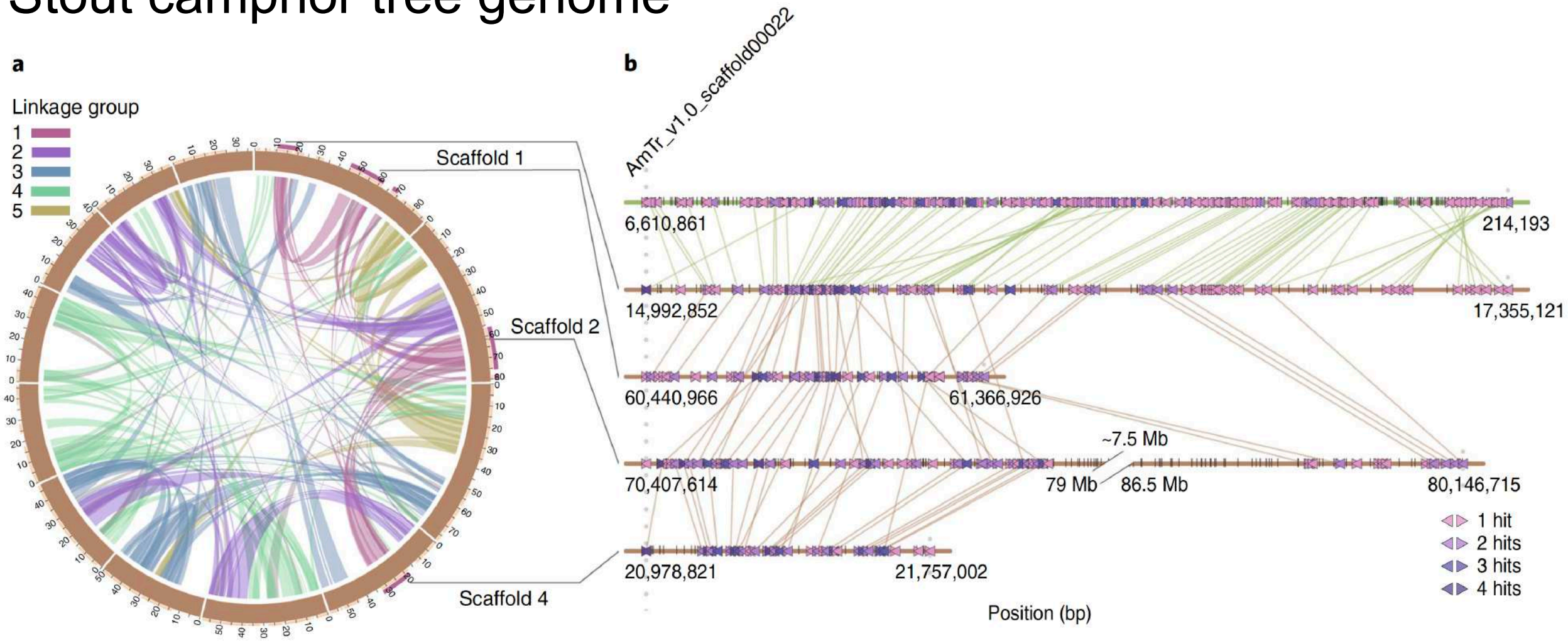


Fig. 3 | Evolutionary analysis of the SCT genome. a, Schematic representation of the intragenomic relationship among the 637 synteny blocks in the SCT genome. Synteny blocks (denoted by peach blocks) were assigned unambiguously into five linkage clusters representing ancient karyotypes and are colour coded. Purple blocks denote the synteny block assigned in the first linkage group (see also Supplementary Fig. 13). **b**, Schematic representation of the first linkage group within the SCT genome and their corresponding relationship in *A. trichopoda*.

Chaw et al (2018)

Stout camphor tree genome

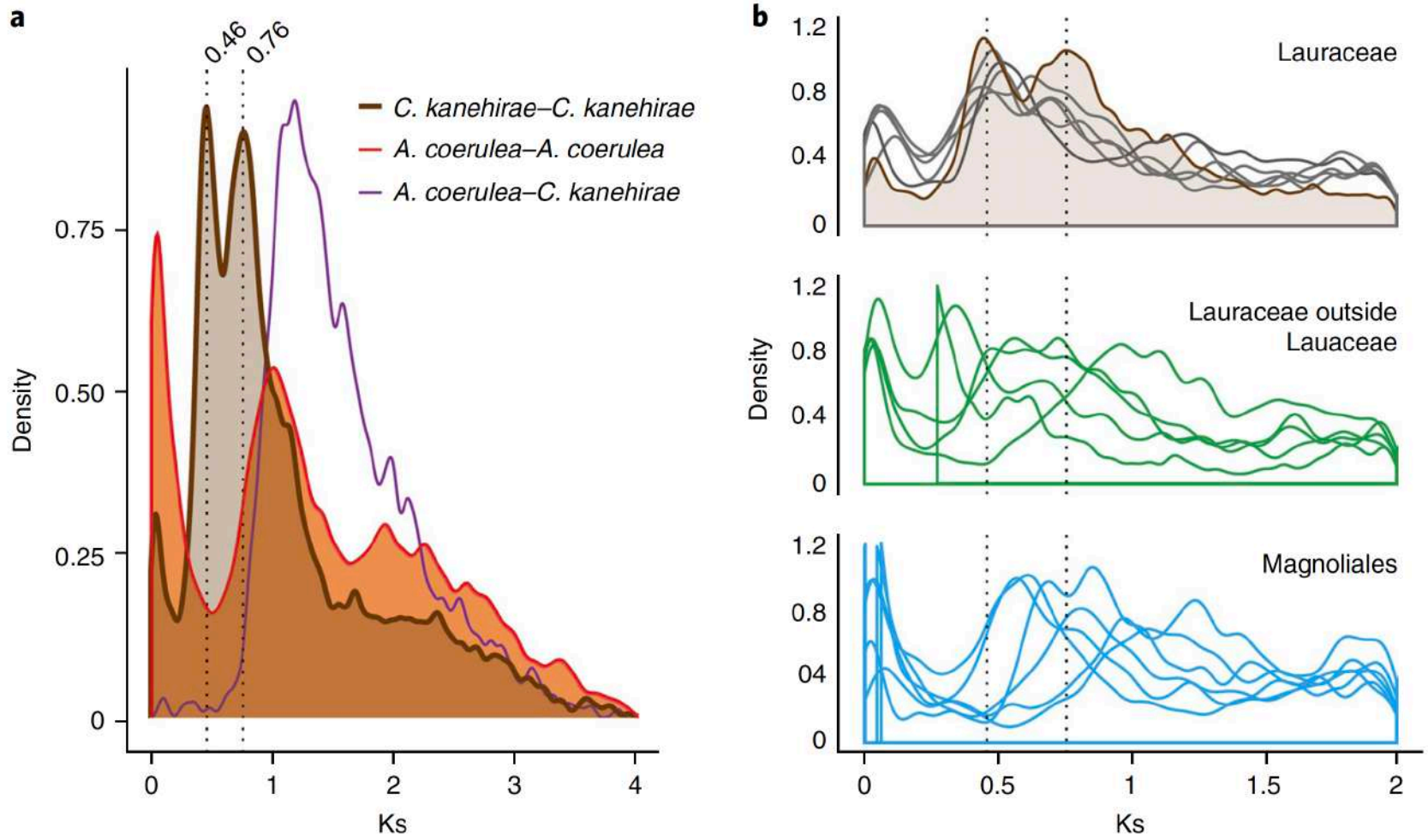
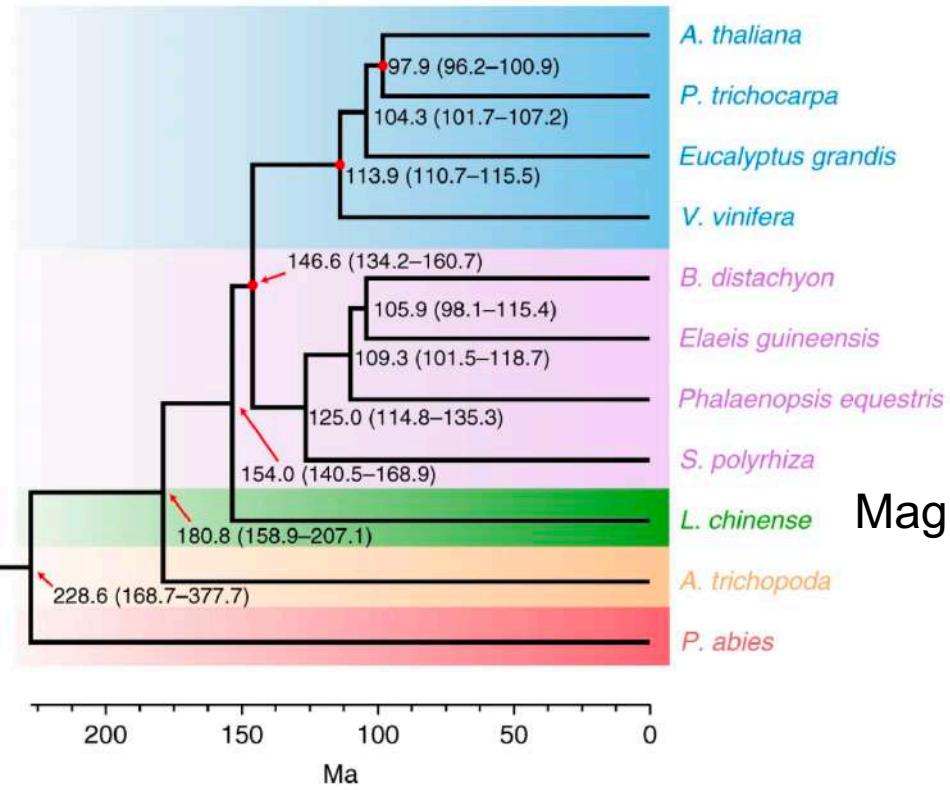


Fig. 4 | Density plots of synonymous substitutions (Ks) of the SCT genome and other plant species. a, Pairwise orthologue duplicates identified in synteny blocks within SCT, *A. coerulea* and between SCT and *A. coerulea*. **b**, Ks of intragenomic pairwise duplicates of the Lauraceae and the Magnoliales in the 1KP project[29]. Dashed lines denote the two Ks peaks observed in SCT. Brown and grey lines denote SCT and other Lauraceae's Ks distribution, respectively.

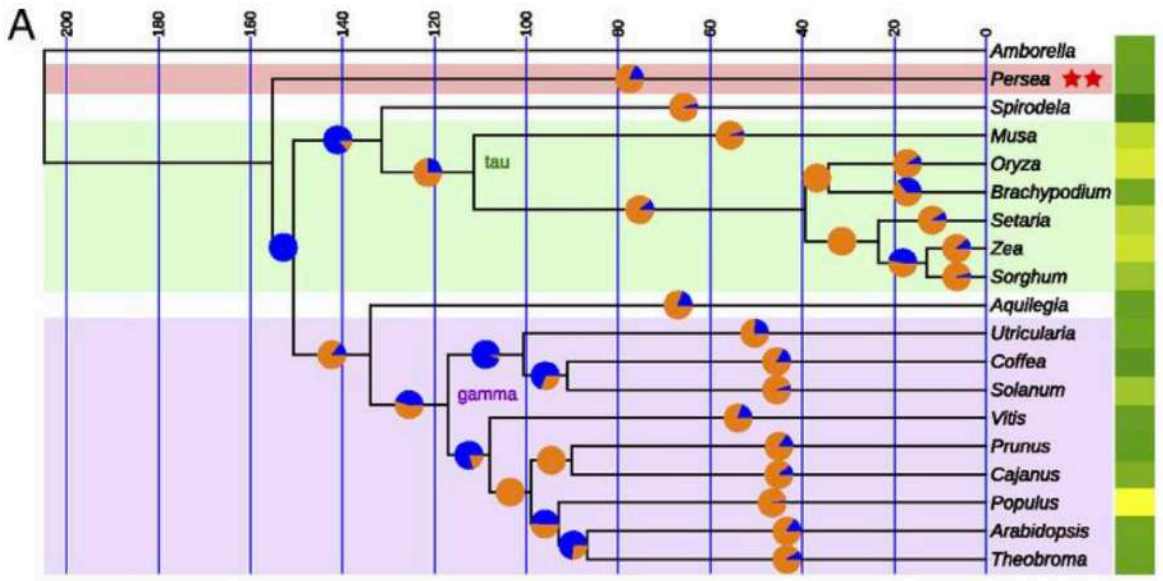
Chaw et al (2018)

Still unresolved…

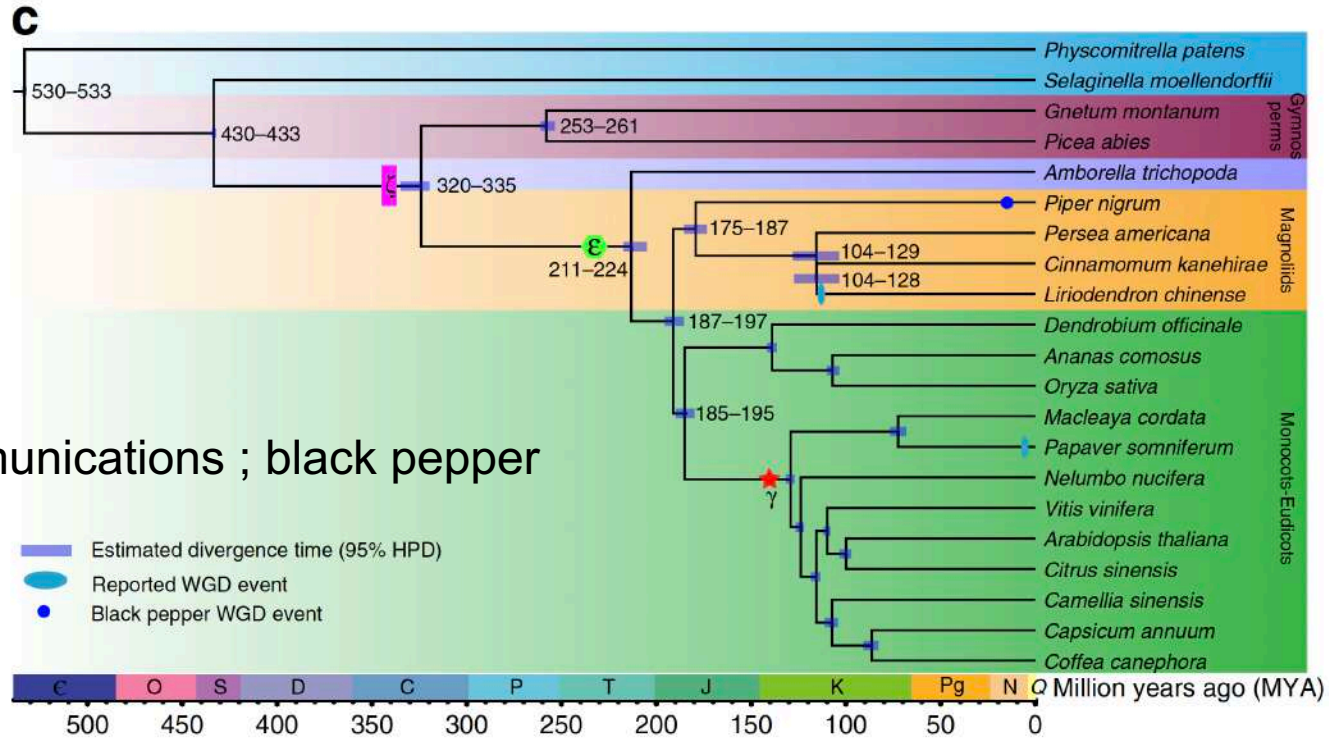


Chen et al (2018) Nature Plant

Magnollids



Rendón-Anaya et al (2019) PNAS ; avocado



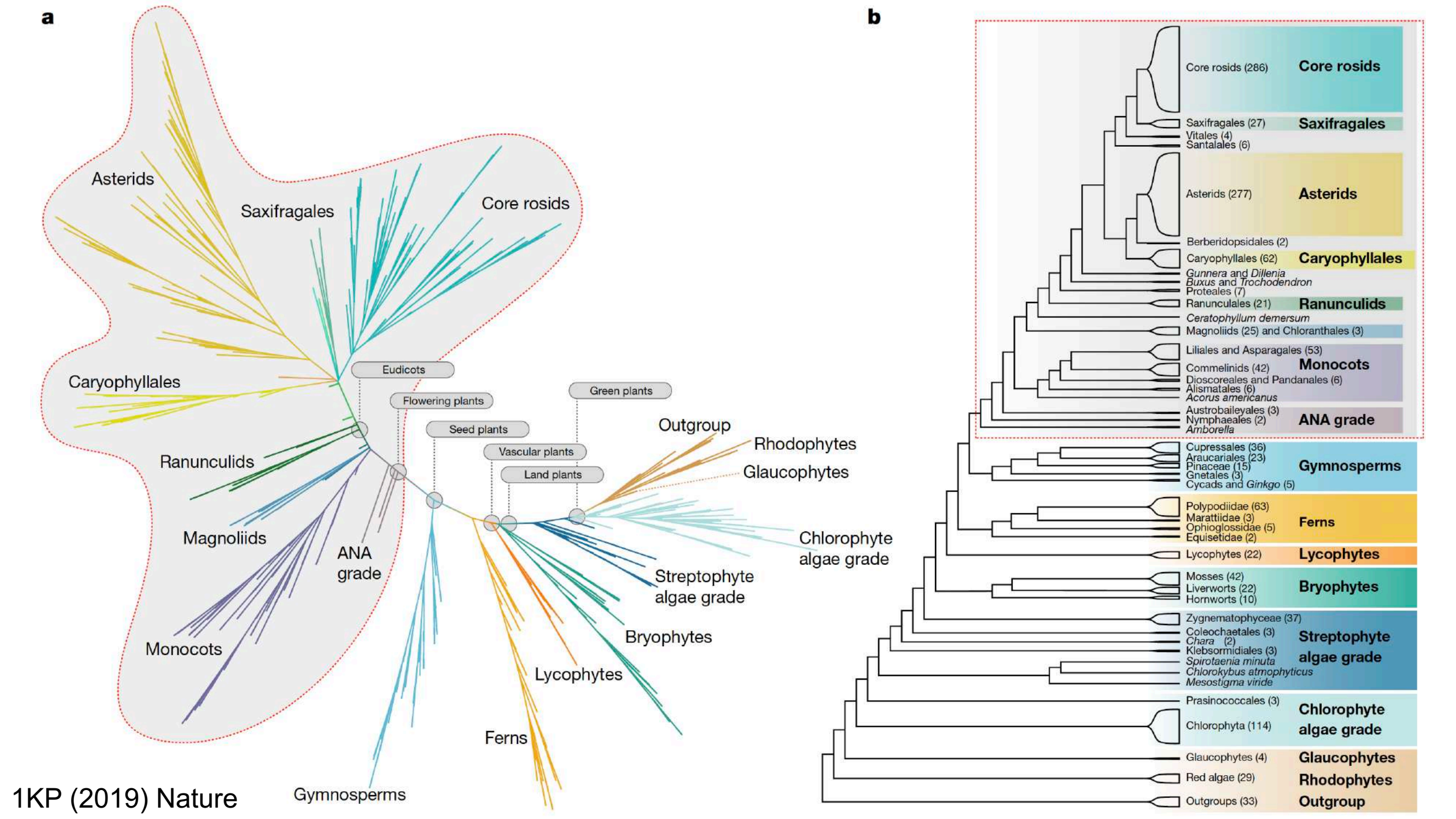
Hu et al (2019) Nature communications ; black pepper

One thousand plant transcriptomes and the phylogenomics of green plants

https://doi.org/10.1038/s41586-019-1693-2

One Thousand Plant Transcriptomes Initiative

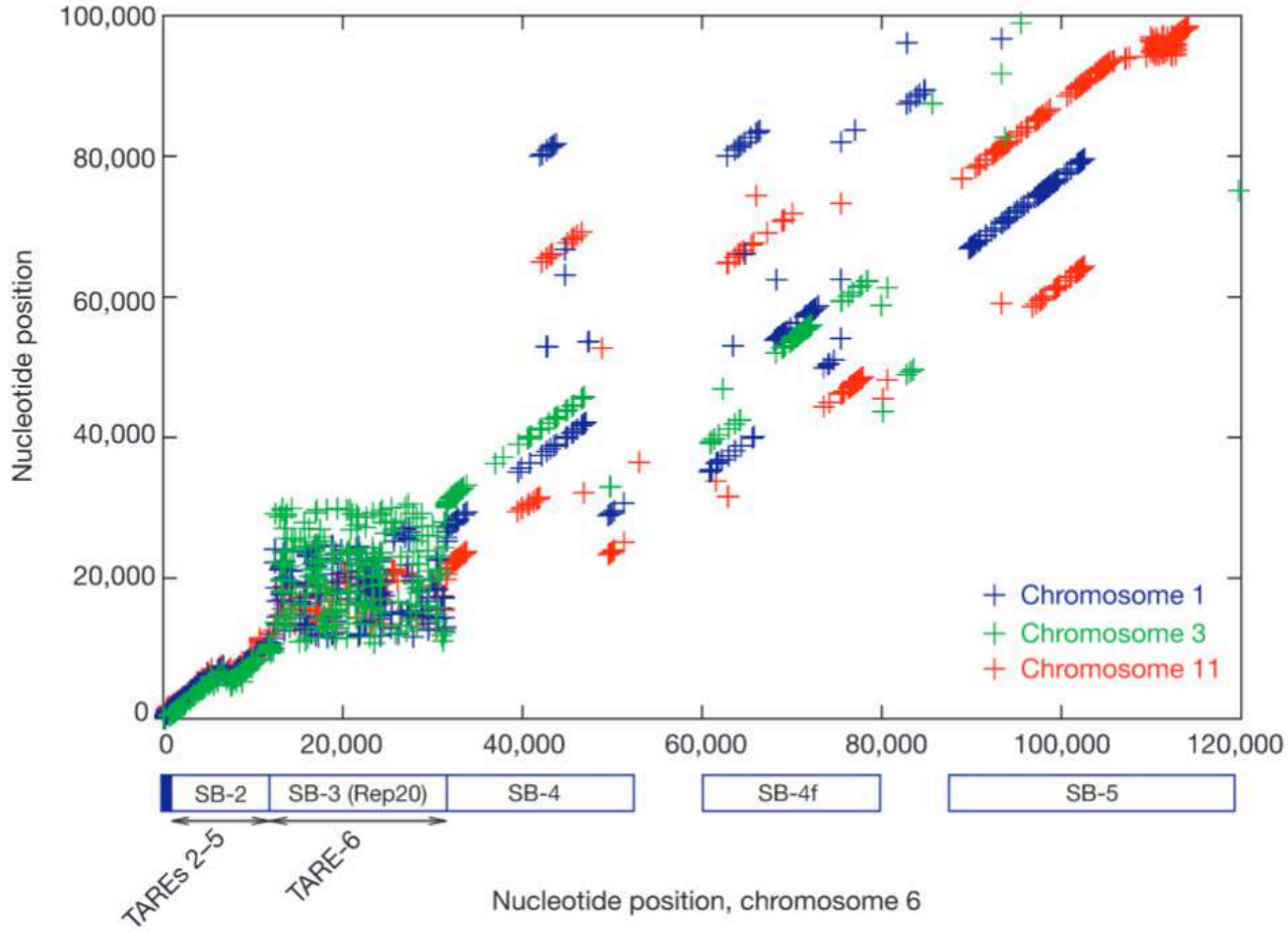
Green plants (Viridiplantae) include around 450,000–500,000 species[1,2] of great diversity and have important roles in terrestrial and aquatic ecosystems. **Here, as part of the One Thousand Plant Transcriptomes Initiative, we sequenced the vegetative transcriptomes of 1,124 species that span the diversity of plants in a broad sense (Archaeplastida), including green plants (Viridiplantae), glaucophytes (Glaucophyta) and red algae (Rhodophyta)**. Our analysis provides a robust phylogenomic framework for examining the evolution of green plants. Most inferred species relationships are well supported across multiple species tree and supermatrix analyses, but discordance among plastid and nuclear gene trees at a few important nodes highlights the complexity of plant genome evolution, including polyploidy, periods of rapid speciation, and extinction. Incomplete sorting of ancestral variation, polyploidization and massive expansions of gene families punctuate the evolutionary history of green plants. Notably, we find that large expansions of gene families preceded the origins of green plants, land plants and vascular plants, whereas whole-genome duplications are inferred to have occurred repeatedly throughout the evolution of flowering plants and ferns. The increasing availability of high-quality plant genome sequences and advances in functional genomics are enabling research on genome evolution across the green tree of life.



1KP (2019) Nature

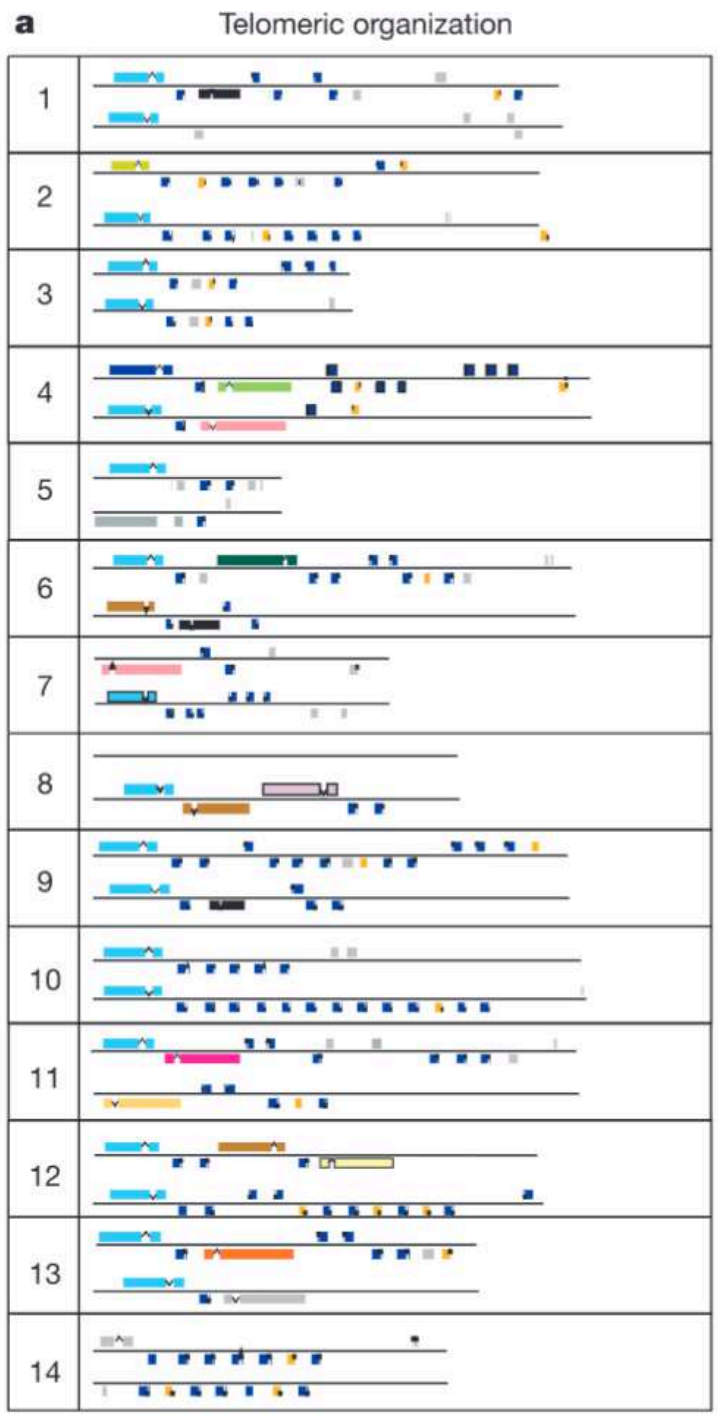
Genome sequence of the human malaria parasite *Plasmodium falciparum*

Malcolm J. Gardner[1], Neil Hall[2], Eula Fung[3], Owen White[1], Matthew Berriman[2], Richard W. Hyman[3], Jane M. Carlton[1], Arnab Pain[2], Karen E. Nelson[1], Sharen Bowman[2]*, Ian T. Paulsen[1], Keith James[2], Jonathan A. Eisen[1], Kim Rutherford[2], Steven L. Salzberg[1], Alister Craig[4], Sue Kyes[5], Man-Suen Chan[5], Vishvanath Nene[1], Shamira J. Shallom[1], Bernard Suh[1], Jeremy Peterson[1], Sam Angiuoli[1], Mihaela Pertea[1], Jonathan Allen[1], Jeremy Selengut[1], Daniel Haft[1], Michael W. Mather[6], Akhil B. Vaidya[6], David M. A. Martin[7], Alan H. Fairlamb[7], Martin J. Fraunholz[8], David S. Roos[8], Stuart A. Ralph[9], Geoffrey I. McFadden[9], Leda M. Cummings[1], G. Mani Subramanian[10], Chris Mungall[11], J. Craig Venter[12], Daniel J. Carucci[13], Stephen L. Hoffman[13]*, Chris Newbold[5], Ronald W. Davis[3], Claire M. Fraser[1] & Bart Barrell[2]



….The conserved regions fall into five large subtelomeric, contains the 7-bp telomeric repeat in a variable number of near-exact copies

NATURE | VOL 419 | 2002 | www.nature.com/nature



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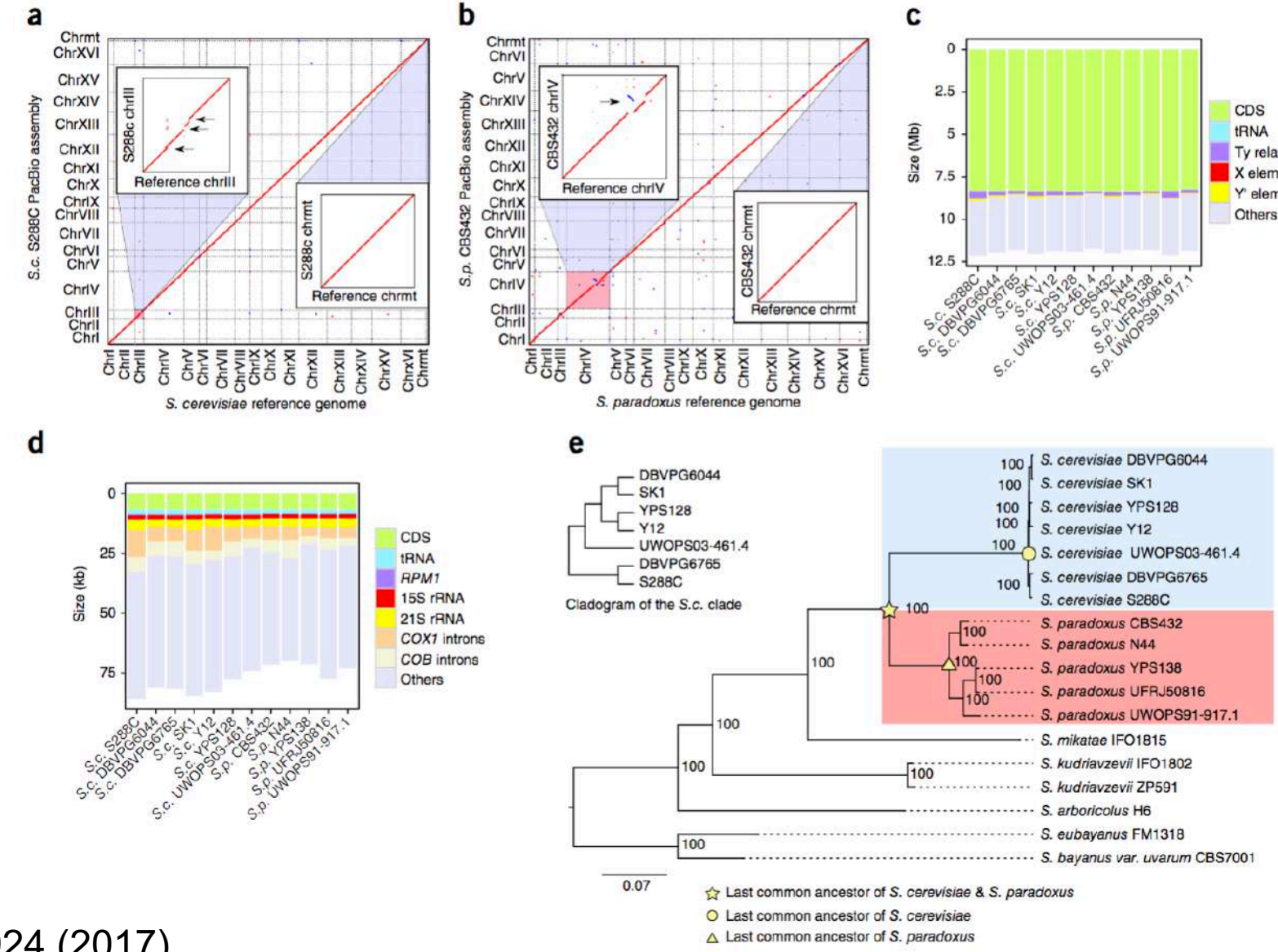
The var genes code for proteins which are exported to the surface of infected red blood cells where they mediate adherence to host endothelial receptors, resulting in the sequestration of infected cells in a variety of organs. These and other adherence properties are important virulence factors that contribute to the development of severe disease

NATURE | VOL 419 | 2002 | www.nature.com/nature

Contrasting evolutionary genome dynamics between domesticated and wild yeasts

Jia-Xing Yue[1], Jing Li[1], Louise Aigrain[2], Johan Hallin[1], Karl Persson[3], Karen Oliver[2], Anders Bergström[2], Paul Coupland[2,5], Jonas Warringer[3], Marco Cosentino Lagomarsino[4], Gilles Fischer[4], Richard Durbin[2] & Gianni Liti[1]

- long-read sequencing to generate **end-to-end genome assemblies** for **12 strains** representing major subpopulations of the partially domesticated yeast *Saccharomyces cerevisiae* and its wild relative *S. paradoxus*.



Nature Genetics **volume 49**, pages 913–924 (2017)

Contrasting evolutionary genome dynamics between domesticated and wild yeasts

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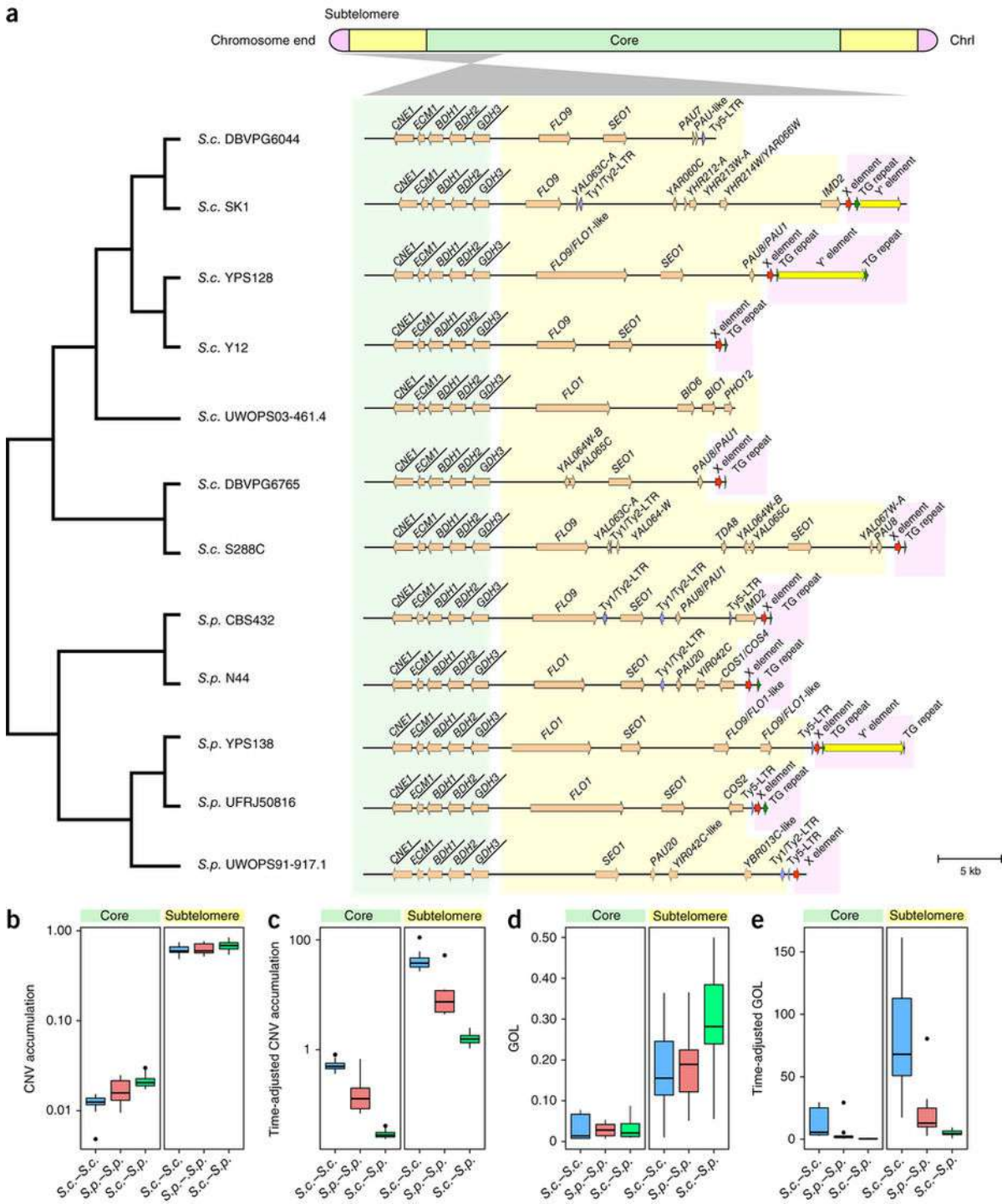
- enable precise definition of chromosomal boundaries between cores and subtelomeres
- *S. paradoxus* shows faster accumulation of balanced rearrangements (inversions, reciprocal translocations and transpositions), *S. cerevisiae* accumulates unbalanced rearrangements (novel insertions, deletions and duplications) more rapidly.

- Such striking contrasts between wild and domesticated yeasts are likely to reflect the influence of human activities on structural genome evolution.

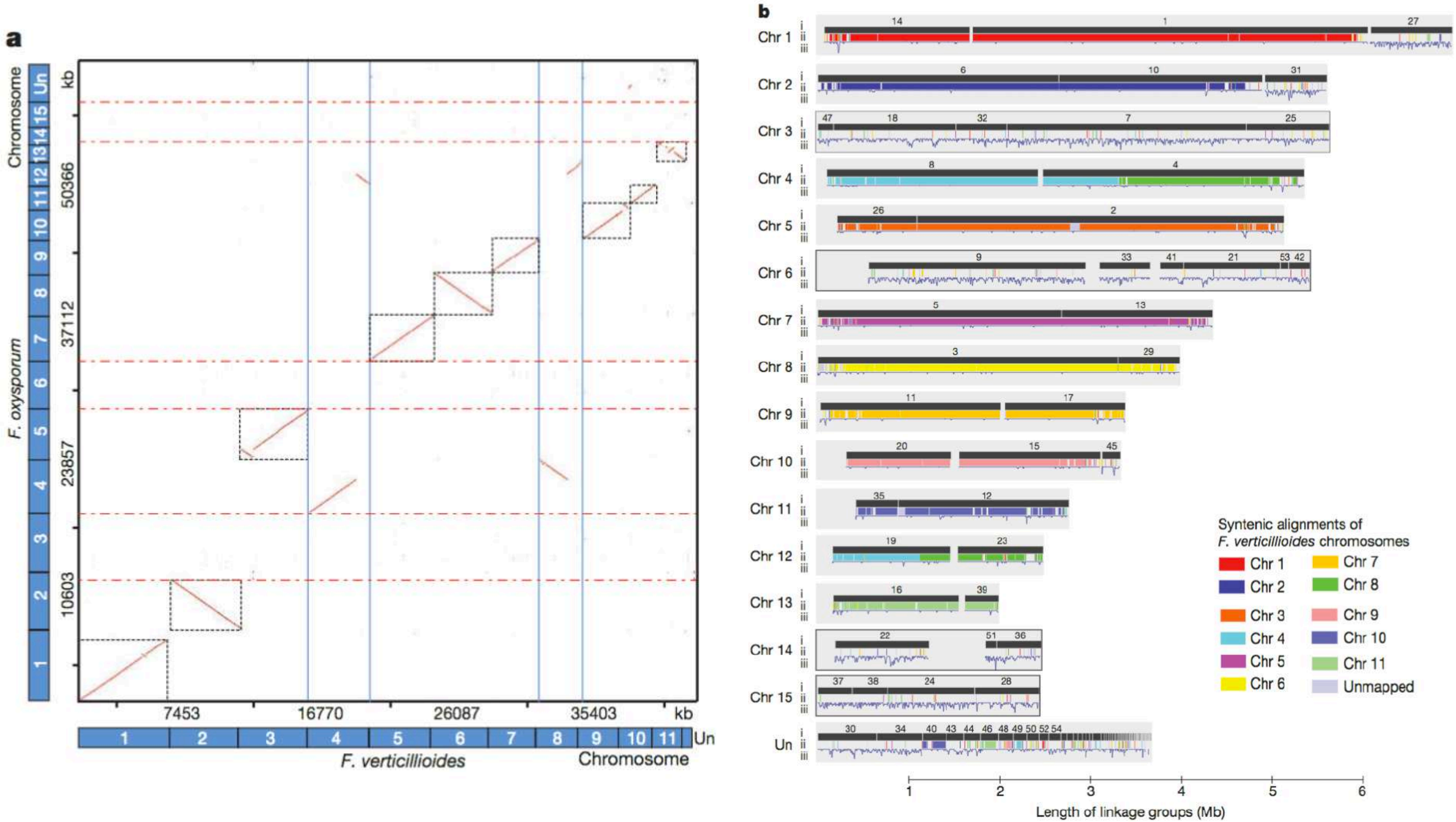
Nature Genetics **volume 49**, pages 913–924 (2017)



Comparative genomics reveals mobile pathogenicity chromosomes in *Fusarium*

Li-Jun Ma[1]*, H. Charlotte van der Does[2]*, Katherine A. Borkovich[3], Jeffrey J. Coleman[4], Marie-Josée Daboussi[5], Antonio Di Pietro[6], Marie Dufresne[5], Michael Freitag[7], Manfred Grabherr[1], Bernard Henrissat[8], Petra M. Houterman[2], Seogchan Kang[9], Won-Bo Shim[10], Charles Woloshuk[11], Xiaohui Xie[12], Jin-Rong Xu[11], John Antoniw[13], Scott E. Baker[14], Burton H. Bluhm[11], Andrew Breakspear[15], Daren W. Brown[16], Robert A. E. Butchko[16], Sinead Chapman[1], Richard Coulson[17], Pedro M. Coutinho[8], Etienne G. J. Danchin[8]†, Andrew Diener[18], Liane R. Gale[15], Donald M. Gardiner[19], Stephen Goff[20], Kim E. Hammond-Kosack[13], Karen Hilburn[15], Aurélie Hua-Van[5], Wilfried Jonkers[2], Kemal Kazan[19], Chinnappa D. Kodira[1]†, Michael Koehrsen[1], Lokesh Kumar[1], Yong-Hwan Lee[21], Liande Li[3], John M. Manners[19], Diego Miranda-Saavedra[22], Mala Mukherjee[10], Gyungsoon Park[3], Jongsun Park[21], Sook-Young Park[9]†, Robert H. Proctor[16], Aviv Regev[1], M. Carmen Ruiz-Roldan[6], Divya Sain[3], Sharadha Sakthikumar[1], Sean Sykes[1], David C. Schwartz[23], B. Gillian Turgeon[24], Ilan Wapinski[1], Olen Yoder[25], Sarah Young[1], Qiandong Zeng[1], Shiguo Zhou[23], James Galagan[1], Christina A. Cuomo[1], H. Corby Kistler[15] & Martijn Rep[2]

Our analysis revealed **lineage-specific (LS) genomic regions in *F. oxysporum* that include four entire chromosomes and account for more than one-quarter of the genome**. LS regions are **rich in transposons and genes with distinct evolutionary profiles but related to pathogenicity**, indicative of horizontal acquisition. Experimentally, **we demonstrate the transfer of two LS chromosomes between strains of *F. oxysporum*, converting a non-pathogenic strain into a pathogen**.


a
Chromosome
F. oxysporum
kb
50366
37112
23857
10603
7453
16770
26087
35403
kb
F. verticillioides
Chromosome
b
Chr 1
Chr 2
Chr 3
Chr 4
Chr 5
Chr 6
Chr 7
Chr 8
Chr 9
Chr 10
Chr 11
Chr 12
Chr 13
Chr 14
Chr 15
Un
Syntenic alignments of
F. verticillioides chromosomes
Chr 1
Chr 2
Chr 3
Chr 4
Chr 5
Chr 6
Chr 7
Chr 8
Chr 9
Chr 10
Chr 11
Unmapped
Length of linkage groups (Mb)

LETTER

doi:10.1038/nature12235

Reversal of an ancient sex chromosome to an autosome in *Drosophila*

Beatriz Vicoso[1] & Doris Bachtrog[1]

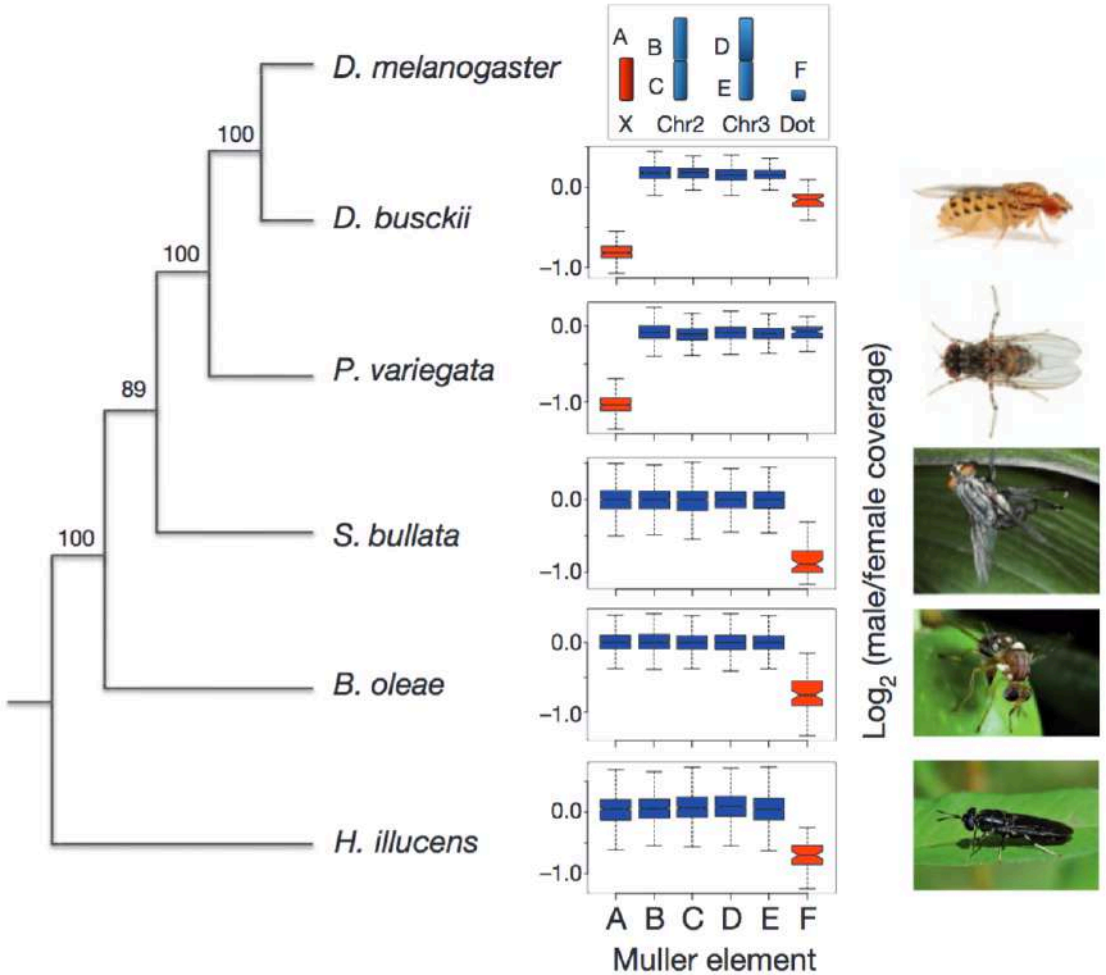


Figure 1 | Sex chromosomes in higher Diptera revealed by genome analysis. Evolutionary relationship inferred from 185 conserved protein-coding genes (93,134 amino acids) using PhyML (with bootstrap values indicated at the nodes), and male-to-female coverage ratio across chromosome elements (Muller elements A–F) in the Diptera species studied. X chromosomes (red) have only half the read coverage in males versus females. Boxes extend from the first to the third quartile and whiskers to the most extreme data point within 1.5 times the interquantile range.

Looking back in 2003

Group	Species	Common	Size (Mb)	Chromosome (1N)	Gene no.	Repeat %
Mammal	*Homo sapiens*	Human	2900	23	30,000	46
Mammal	*Mus musculus*	House mouse	2500	20	30,000	38
Fish	*Takifugu rubripes*	Tiger pufferfish	400	22 (?)	30,000	<10
Urochordate	*Ciona intestinales*	Sea squirt	155	14	16,000	~10
Insect	*Anopheles gambiae*	Malaria mosquito	280	3	14,000	16
Insect	*Drosophila melanogaster*	Fruit fly	137	4	13,600	2
Nematode	*Caenorhabditis elegans*	Nematode worm	97	6	19,100	<1
Apicomplexa	*Plasmodium falciparum*	Human malaria parasite	23	14	5,300	<1
Apicomplexa	*Plasmodium yoelli*	Rodent malaria parasite	25	14	5,300	<1
Dictyosteliida	*Dictyostelium discoideum**	Social amoeba	34	6	2,800	<1
Protozoan	*Leishmania major**	Intracellular parasite	34	36	9,800	<1
Fungi	*Saccharomyces cerevisiae*	Brewer's yeast	12	16	5,700	2.4
Fungi	*Schizosaccharomyces pombe*	Fission yeast	13.8	3	4,900	0.35
Microsporidium	*Encephalitozoon cuniculi*	Intracellular parasite	2.5	11	2,000	<0.1
Angisoperm	*Arabidopsis thaliana*	Mustard weed	125	5	25,500	14
Angiosperm	*Oryza sativa*	Rice	400	12	32000–50000	?

Chromosomal Rearrangements and Repeats: Cause or Consequence?

Centromeric and Telomeric Regions—Sites of Rapid Genomic Change

Duplications: Engines of Gene and Genome Evolution?

Synteny: Fragile Versus Random Breakage Model?

http://science.sciencemag.org/content/sci/301/5634/793.full.pdf

Why comparative genomics? – A summary

- Duplication (genes, chromosomes, whole genomes)
- Conservation
- Specificity
- Inferring Paralogs, orthologs
- Families (clusters) of paralogs, of orthologs
- Gene Transfer, introgression between species
- Origin of genes

How genome evolved;
How genome functions

Why comparative genomics? – A summary

Compare multiple genomes now a norm

Similarity and differences between genomes

Use genomes to study evolution of these species:

- At various resolution (whole genome, chromosomes, regions, genes, base pairs)
- Identify the genomic basis of key phenotypes

Reference

https://www.notion.so/References-papers-links-in-start-learning-genomics-b7e57b28e9194bb29a02f483e0b894ad