# Gene duplication and loss

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How many genes does a human have:

a. <1
b. 1-10,000
c. 10,000-100,000
d. >100,000

How many genes does a human have:

a. <1
b. 1-10,000
c. 10,000-100,000 (~23,000)
d. >100,000

How many genes does a fruitfly have:

a. <1
b. 1-10,000
c. 10,000-100,000
d. >100,000

How many genes does a fruitfly have:

a. <1
b. 1-10,000
c. 10,000-100,000 (~15,000)
d. >100,000

# Gene Number Variation

| | |
|---|---|
| Corn | 40,000 genes |
| Rice | 33,000 |
| Thale cress | 28,000 |
| Mouse | 23,000 |
| Human | 23,000 |
| Worm | 19,000 |
| Fruitfly | 15,000 |
| Yeast | 6,000 |
| *M. genitalium* | 500 |

# Gene duplication and loss result in genome size variation

| | *S. cerevisiae* | *C. elegans* | *D. melanogaster* | *H. sapiens* | *A. thaliana* |
|---|---|---|---|---|---|
| Homeodomain | 9 | 109 | 148 | 267 | 118 |
| Zinc-finger | 121 | 437 | 357 | 706 | 1049 |
| Nuclear receptor | 1 | 183 | 25 | 59 | 4 |

from Venter et al. (2001)

# Similar genomes have similar numbers of genes

Insects: ~15,000
Mammals: ~23,000
Worms: ~19,000
Fungi: 6,000-10,000

Despite this, lots of variation in individual genes.

# Gene duplication and loss

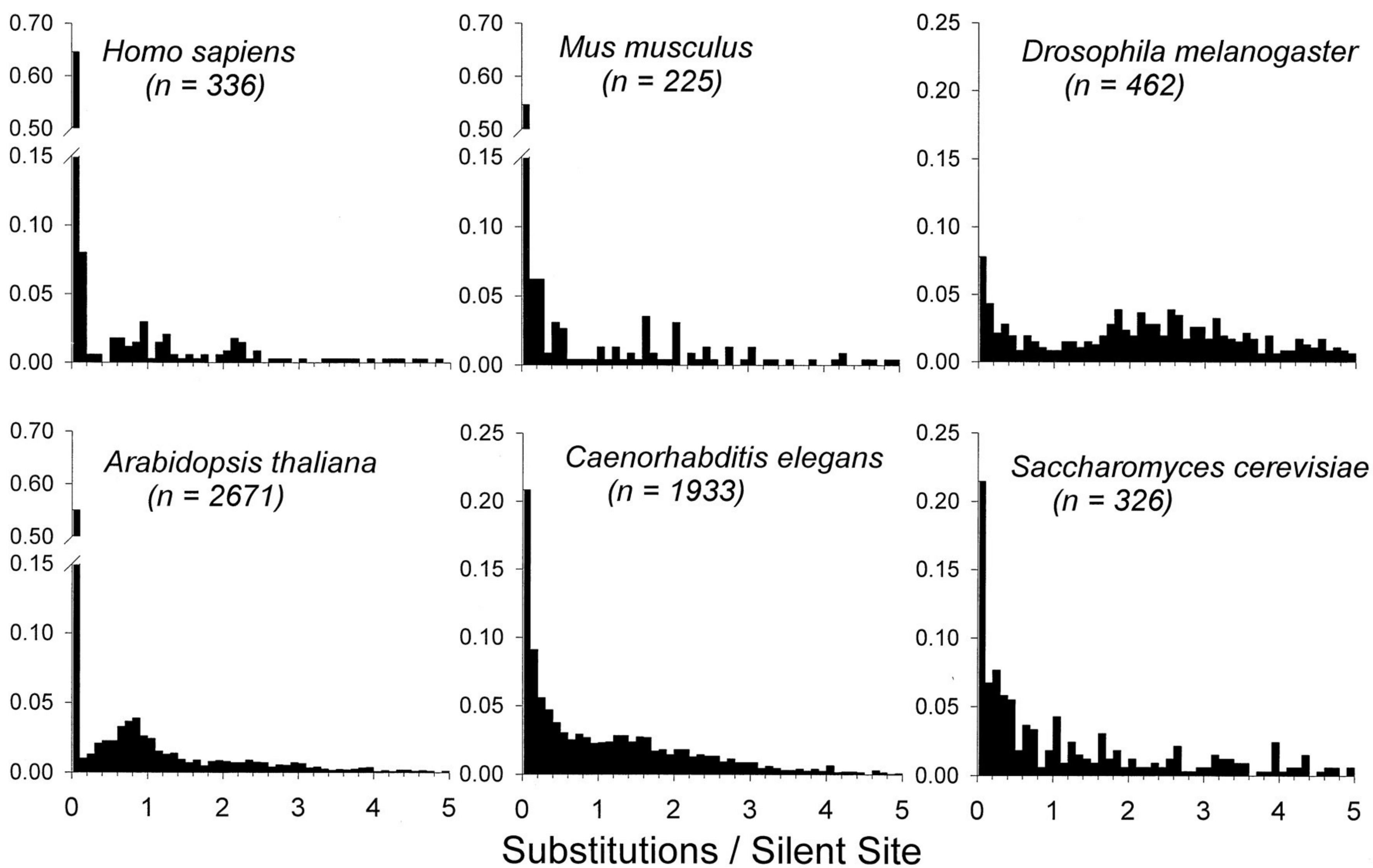
**Table 1. Prevalence of gene duplication in all three domains of life[a]**

| | Total number of genes | Number of duplicate genes (% of duplicate genes) | Refs |
|---|---|---|---|
| **Bacteria** | | | |
| *Mycoplasma pneumoniae* | 677 | 298 (44) | [65] |
| *Helicobacter pylori* | 1590 | 266 (17) | [66] |
| *Haemophilus influenzae* | 1709 | 284 (17) | [67] |
| **Archaea** | | | |
| *Archaeoglobus fulgidus* | 2436 | 719 (30) | [68] |
| **Eukarya** | | | |
| *Saccharomyces cerevisiae* | 6241 | 1858 (30) | [67] |
| *Caenorhabditis elegans* | 18 424 | 8971 (49) | [67] |
| *Drosophila melanogaster* | 13 601 | 5536 (41) | [67] |
| *Arabidopsis thaliana* | 25 498 | 16 574 (65) | [69] |
| *Homo sapiens* | 40 580[b] | 15 343 (38) | [11] |

[a]Use of different computational methods or criteria results in slightly different estimates of the number of duplicated genes [12].
[b]The most recent estimate is ~30 000 [61].

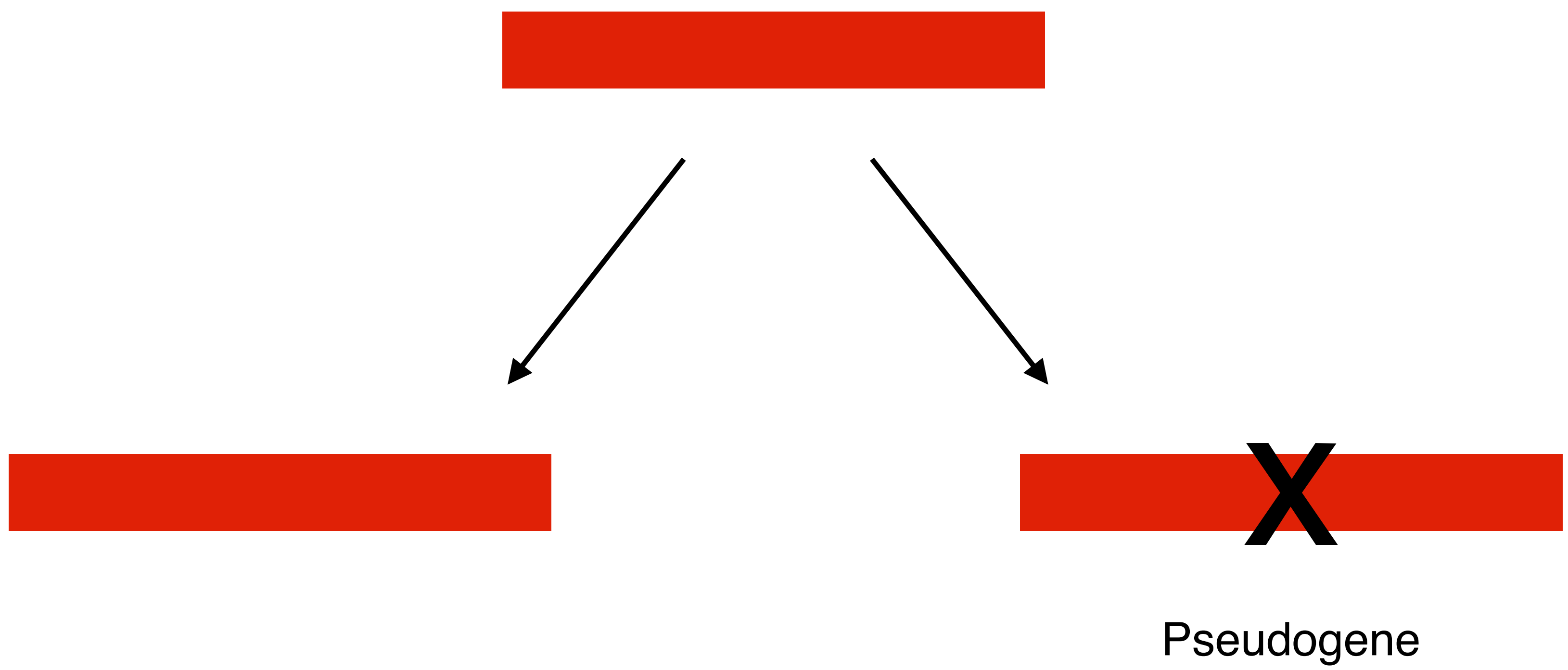
Zhang (2003)

# Gene duplication and loss



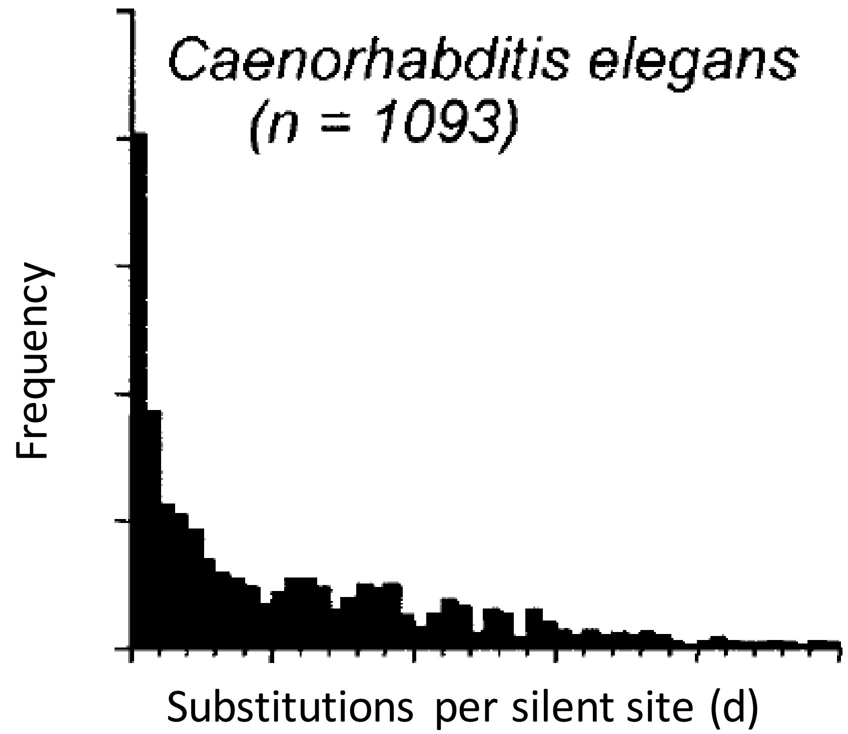

Lynch and Conery (2003)

# Gene duplication and loss




The most common outcome of duplication is loss

# Gene duplication and loss




The most common outcome of duplication is loss

# Big questions in gene duplication

“The main interest in duplications lay in ... identical genes which could subsequently mutate separately and diversify their effects.”

--Bridges 1918

# Big questions in gene duplication



## SPECIAL ARTICLES

### THE BAR "GENE" A DUPLICATION

THE nature of the Bar gene has been the subject of extensive investigation and speculation since February, 1913, when Tice[1] found this reduced-eye mutant as a single male in the progeny of normal-eyed parents. The eye-reduction behaves as a sex-linked dominant, with a locus at 57.0, and has been one of the most important of all the sex-linked characters of *D. melanogaster*. A remarkable peculiarity of the mutant is that occasionally the homozygous stock gives rise to a fly indistinguishable in appearance and genetic behavior from wild-type.[2] More rarely the stock gives rise to an even more extreme reduction in eye-size, a type which was called Ultra-Bar by Zeleny,[3] who found it.

Sturtevant and Morgan[4] and Sturtevant[5] found that these two-way changes were the result of a novel type of "'unequal" crossing-over, by which the two genes originally present in the two parental chromosomes both emerged in the same chromosome (Bar-double) while the other resultant chromosome was without Bar

The exact point of the insertion is ambiguous, for a reason which will appear below. The normal X in this region (see revised map in Fig. 1) shows in sub-sec-

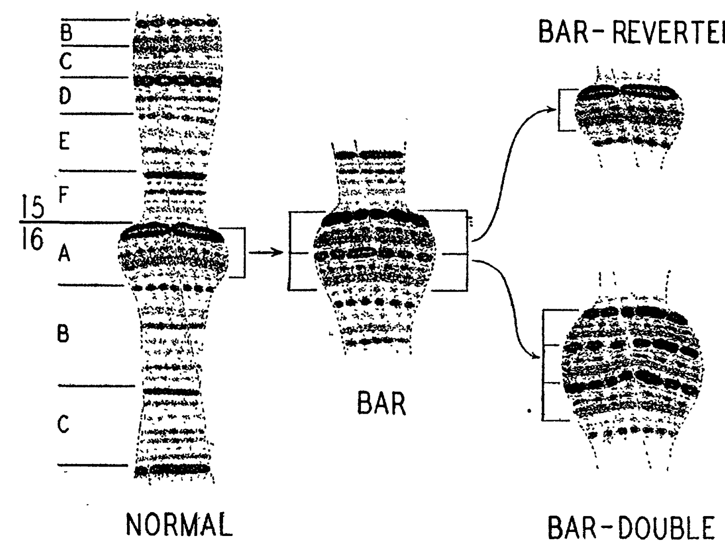
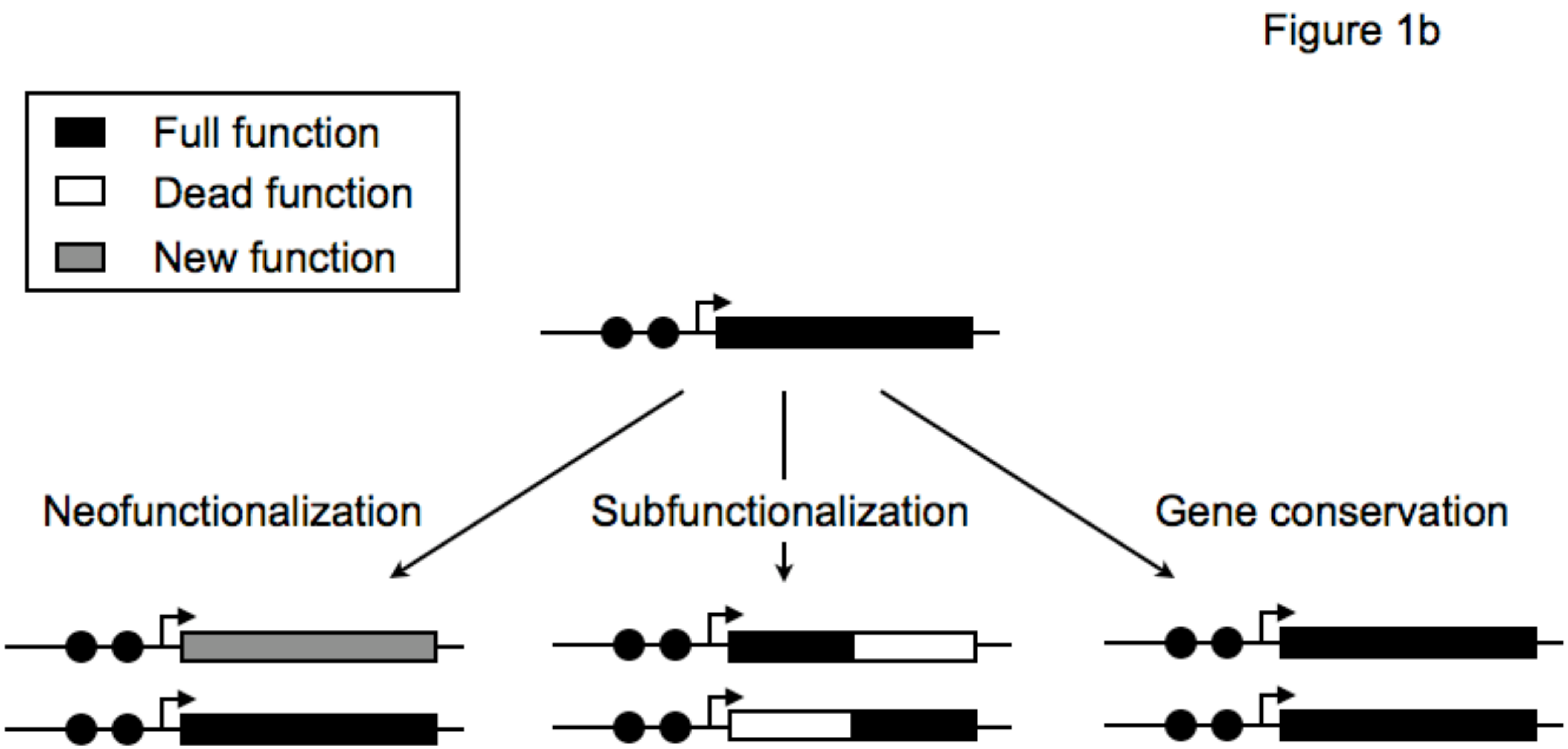



FIG. 1

tion 16A a heavy band, which in well-stretched chro-

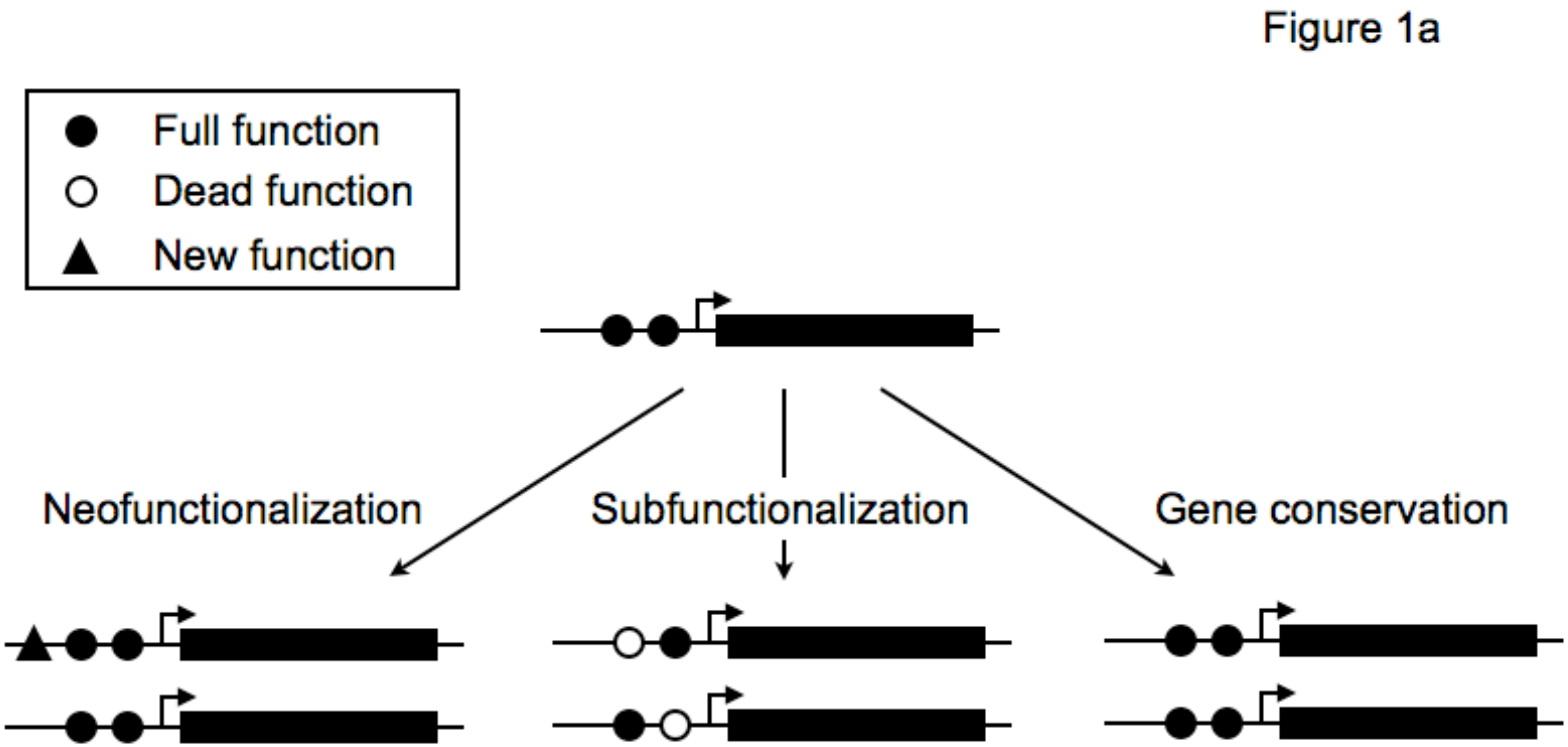
Bridges (1935)

# Big questions in gene duplication



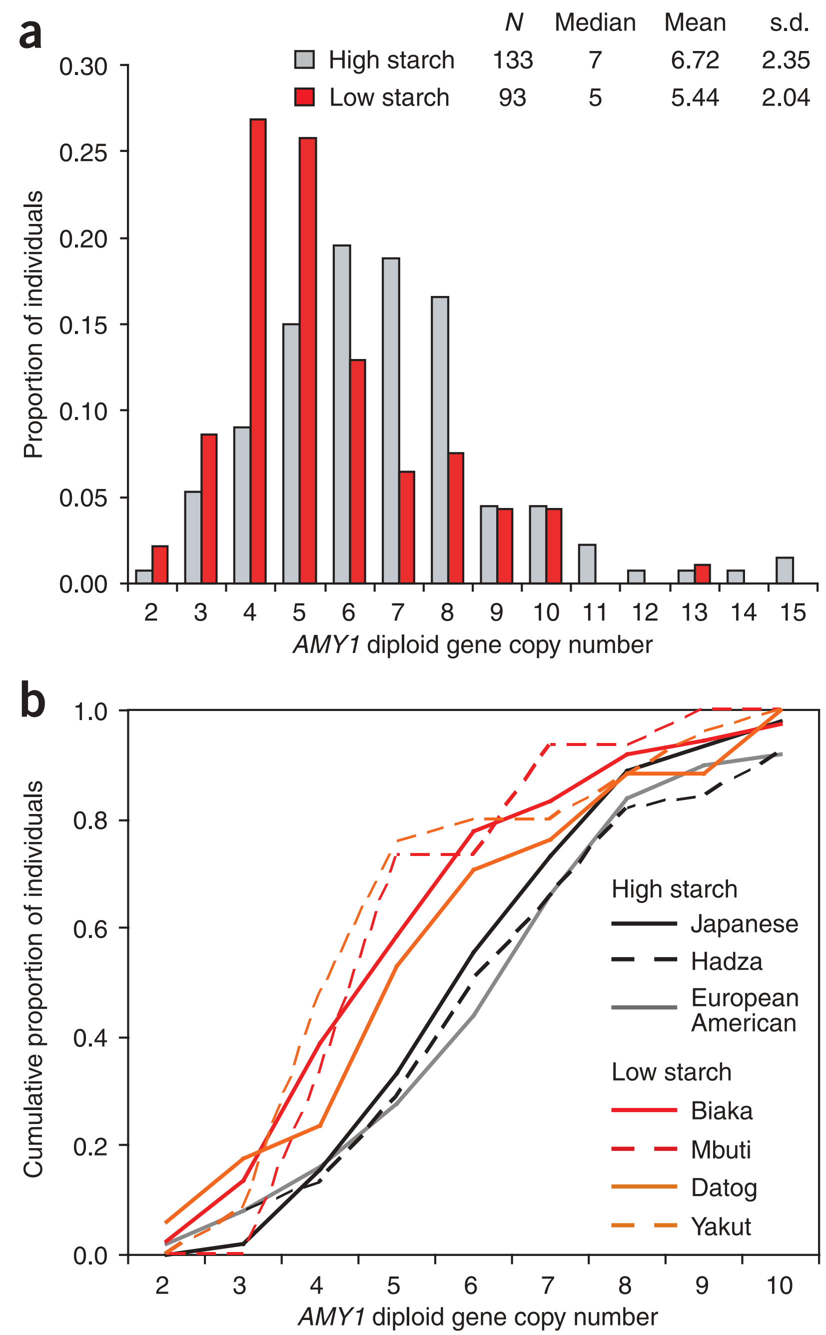

Hahn (2009)

# Big questions in gene duplication




Hahn (2009)

# Gene conservation




Perry et al. (2007)

# Subfunctionalization

*Proc. Natl. Acad. Sci. USA*
Vol. 85, pp. 3479–3483, May 1988
Evolution

## Gene sharing by δ-crystallin and argininosuccinate lyase

**(lens proteins/evolution/gene expression/enzymes/urea cycle)**

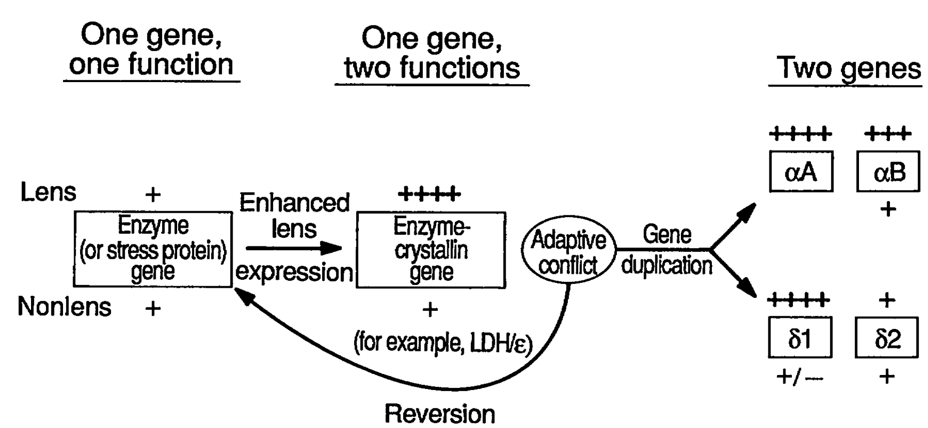
JORAM PIATIGORSKY*, WILLIAM E. O'BRIEN†, BARBARA L. NORMAN*, KAREN KALUMUCK†, GRAEME J. WISTOW*, TERESA BORRAS*, JOHN M. NICKERSON*, AND ERIC F. WAWROUSEK*

*Laboratory of Molecular and Developmental Biology, National Eye Institute, National Institutes of Health, Bethesda, MD 20892; and †Baylor College of Medicine, and Institute for Molecular Genetics, the Howard Hughes Medical Institute, Houston, TX 77030

*Communicated by Donald D. Brown, February 1, 1988*

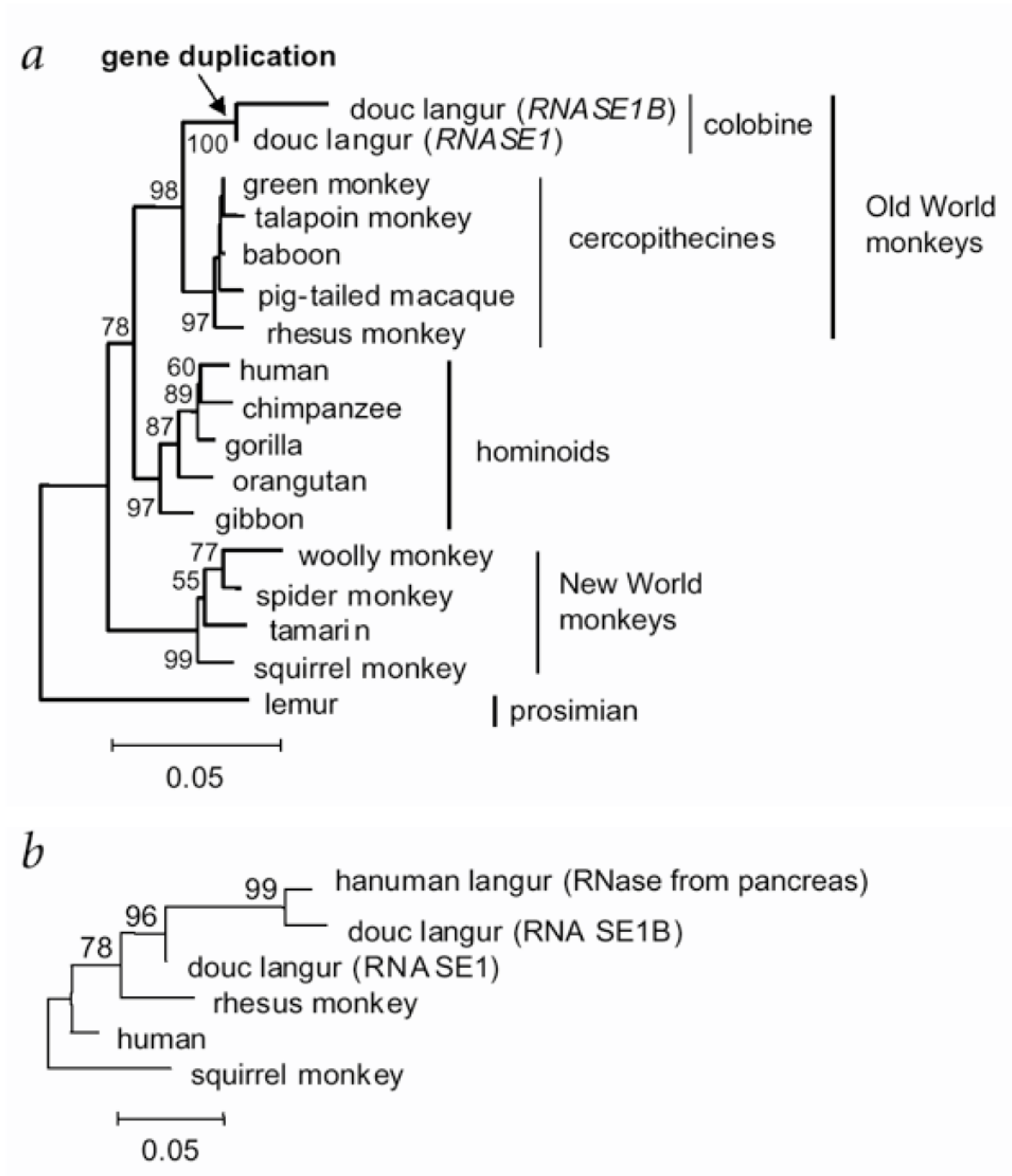
**ABSTRACT** The lens structural protein δ-crystallin and the metabolic enzyme argininosuccinate lyase (ASL; L-argininosuccinate arginine-lyase, EC 4.3.2.1) have striking

Although uricotelic, birds have some activity for ASL as well as for other enzymes of the urea cycle. δ-Crystallin is the dominant crystallin in lenses of birds and reptiles, but it is




Piatigorsky and Wistow (1991)

# Neofunctionalization



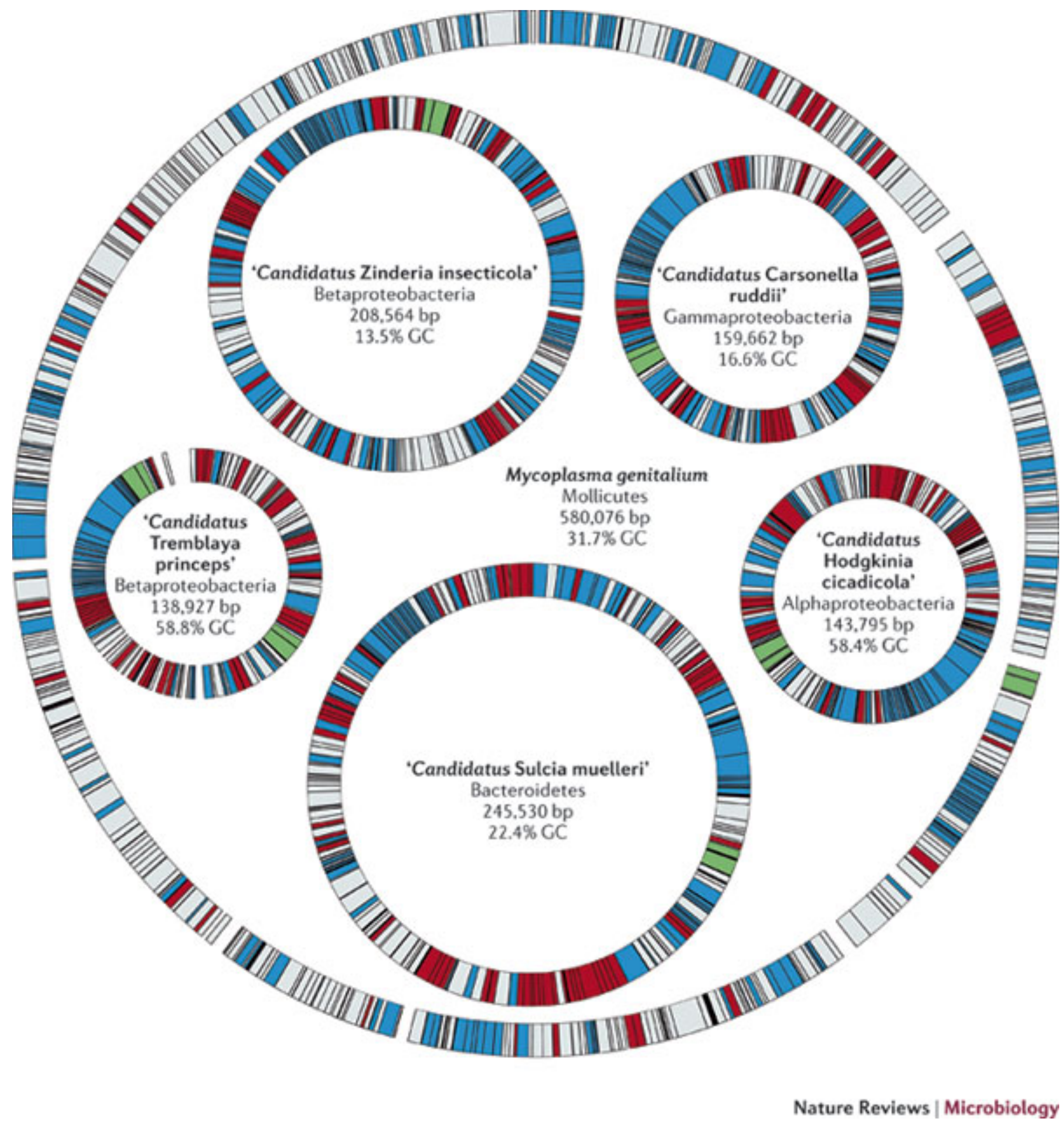

Zhang et al. (2002)

# Big questions in gene duplication

Neofunctionalization, subfunctionalization, or conservation?

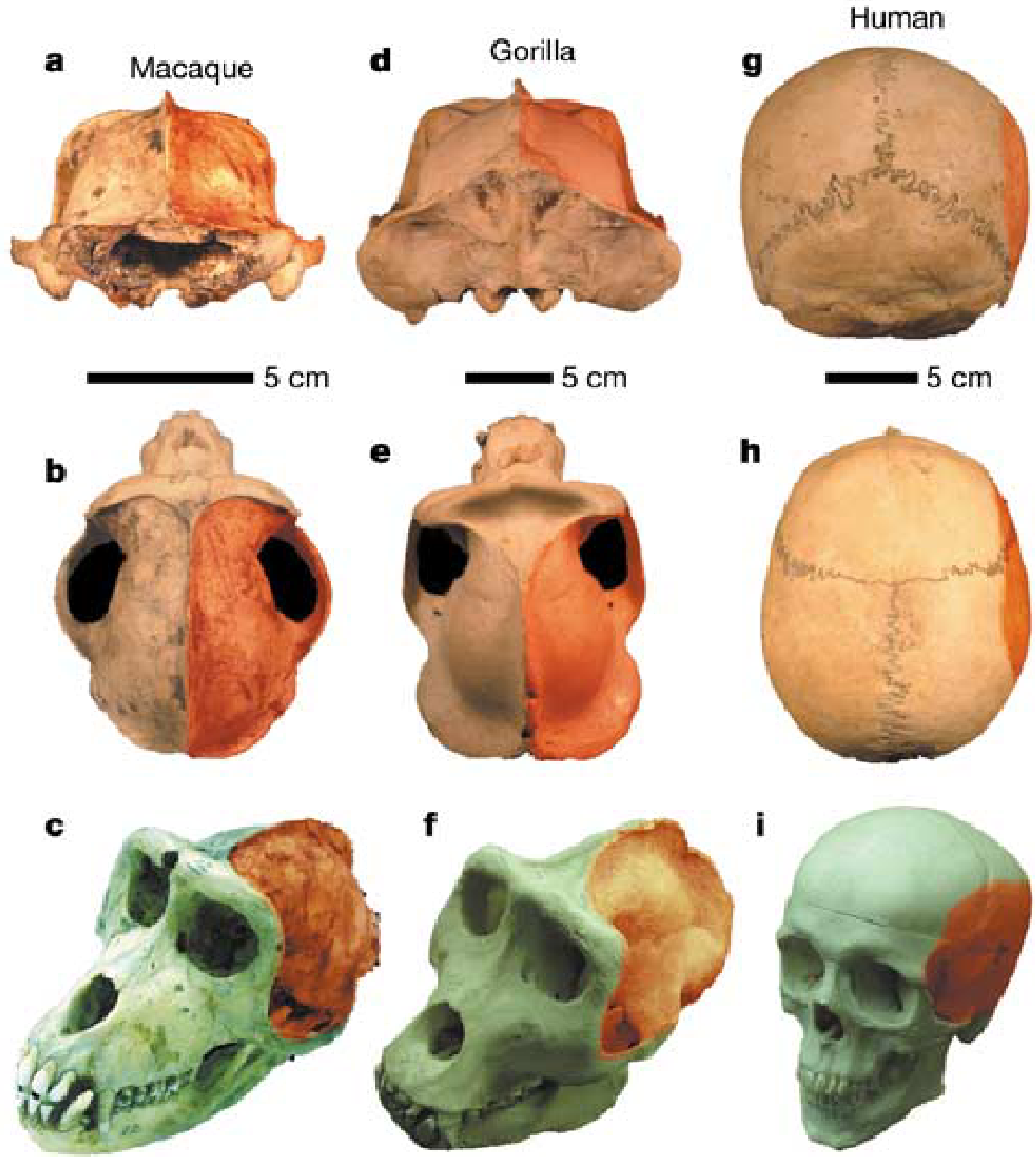
Positive selection or genetic drift?

# Big questions in gene loss




McCutcheon and Moran (2012)

# Loss of *Myh16* associated with cranial enlargement




Stedman et al. (2004)

# Molecular mechanisms of gene duplication

DNA- or RNA-based

Multiple genes, single genes, partial genes

# Molecular mechanisms of gene duplication

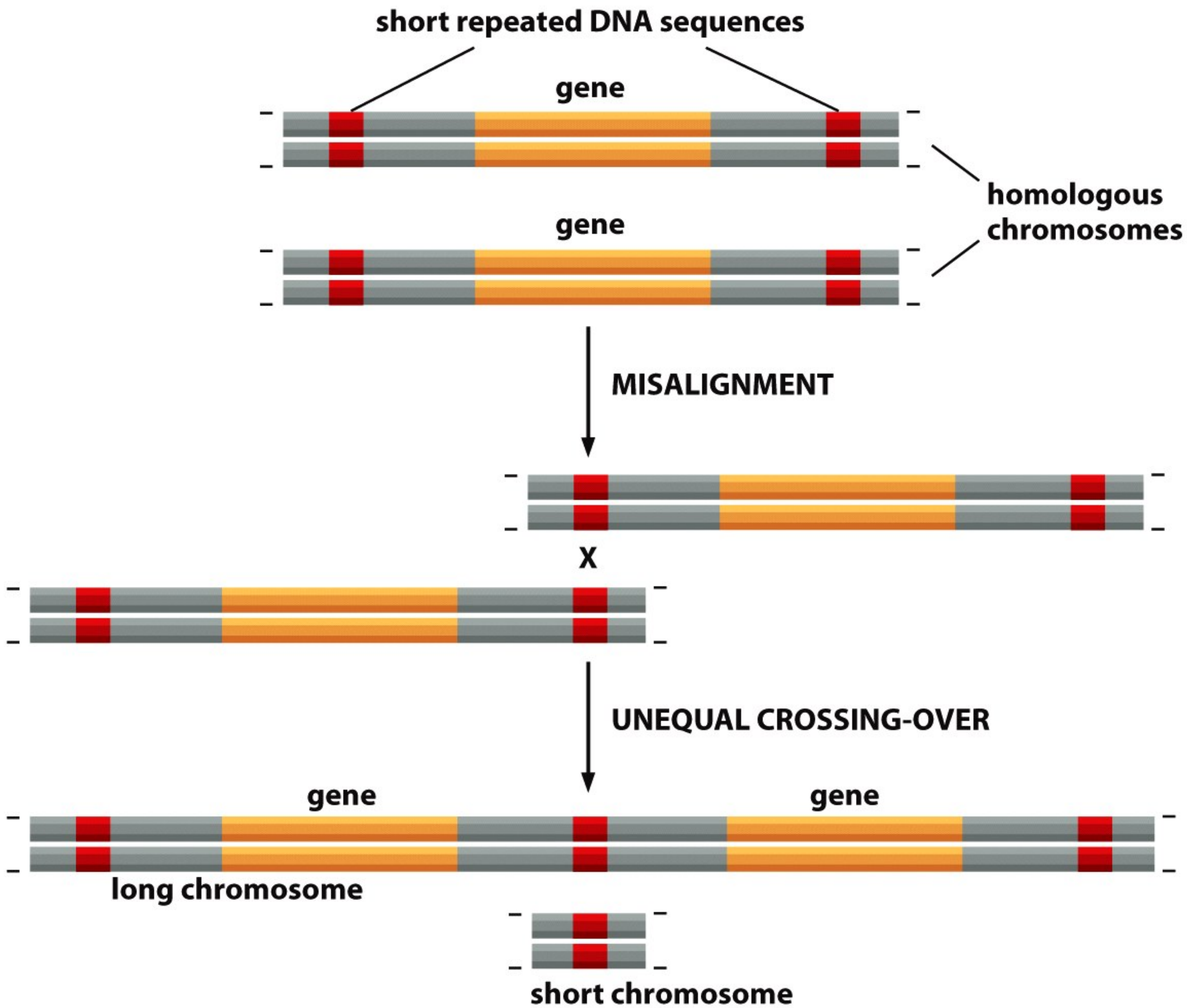



Figure 9-9 Essential Cell Biology 3/e (© Garland Science 2010)

“Unequal crossing-over”

# Molecular mechanisms of gene duplication

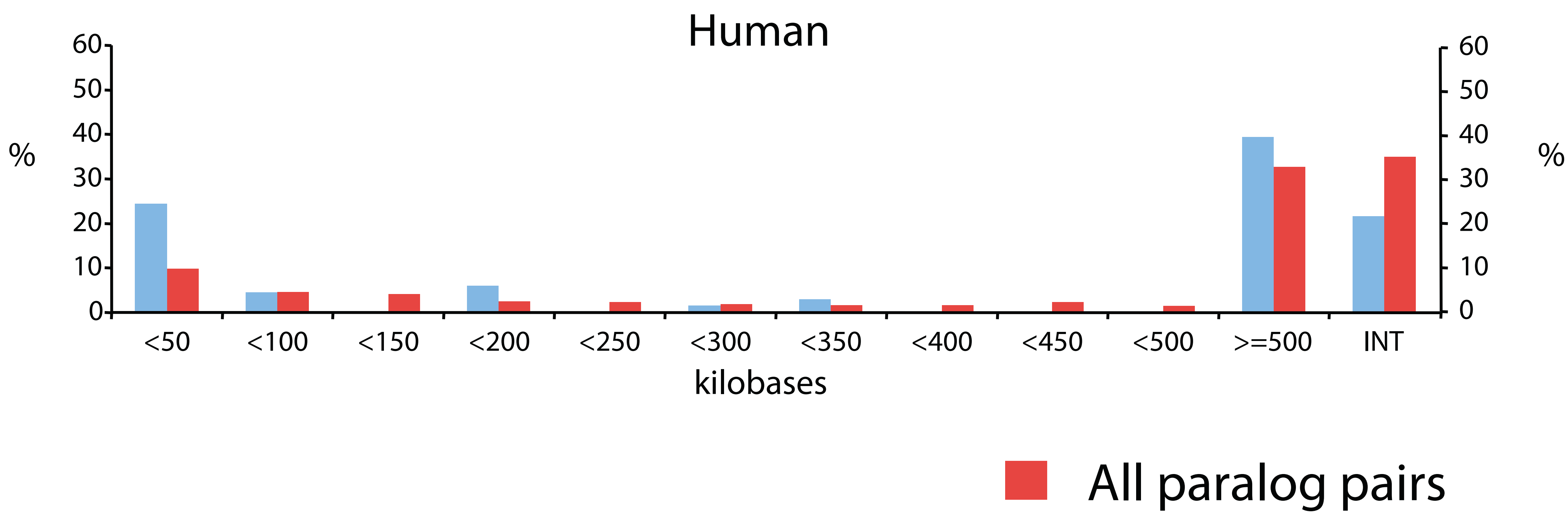
"Unequal crossing-over":

-Requires repeated elements to be present

-Is generally due to NAHR

-Does not always result in tandem duplicates

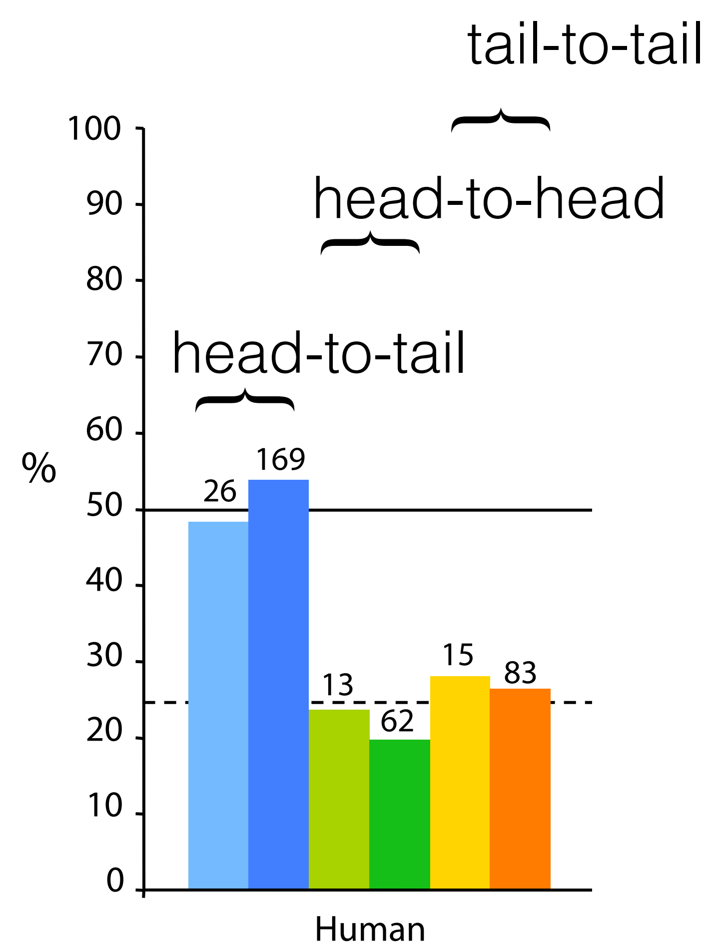
# Molecular mechanisms of gene duplication

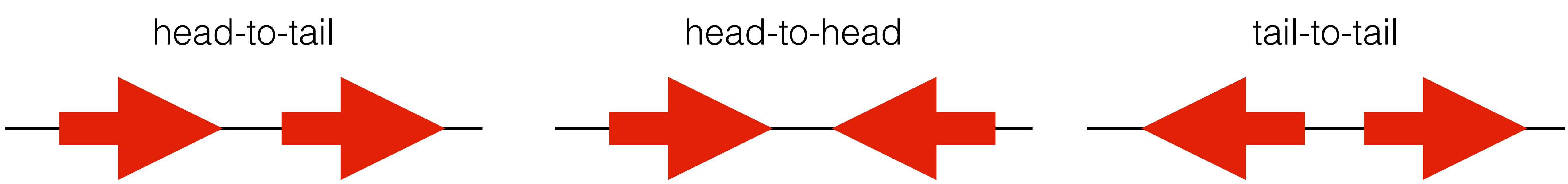



Hypothesis: the more TEs there are in a genome, the farther apart the duplicates are

McGrath et al. (2009)

# Molecular mechanisms of gene duplication

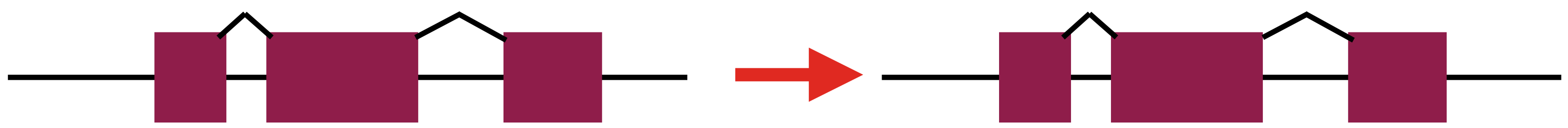


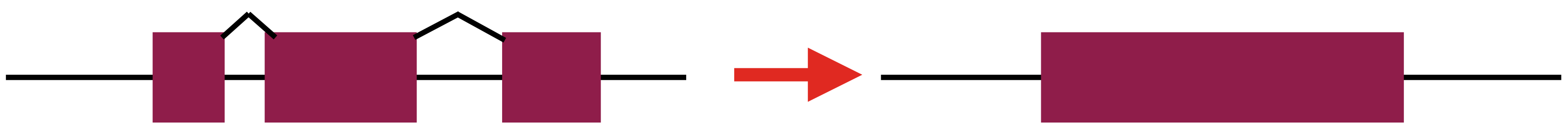

McGrath et al. (2009)

# Molecular mechanisms of gene duplication

DNA-based mechanisms



RNA-based mechanisms



“Retrotransposition”

# Molecular mechanisms of gene duplication

Retrotransposition:

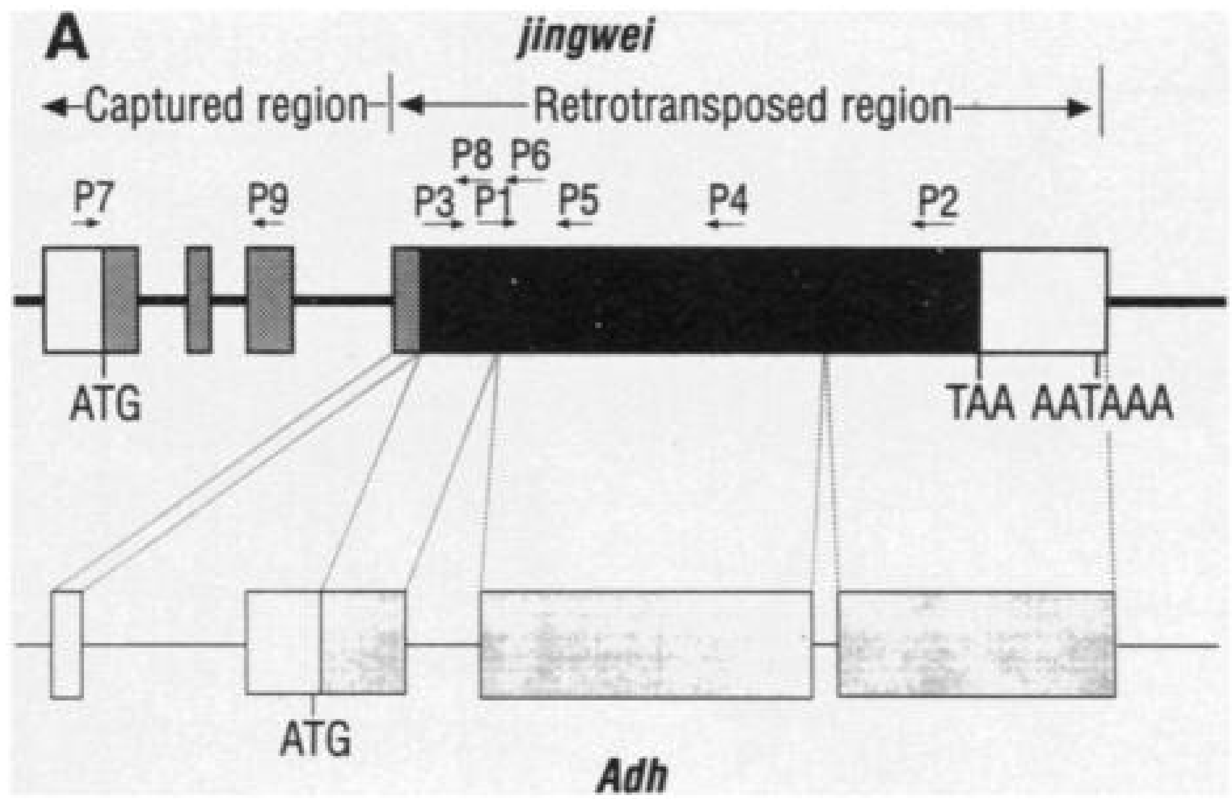
-Results in a daughter copy without introns

-Brings along (almost) no flanking sequence

-Can only copy one gene at a time

# Molecular mechanisms of gene duplication

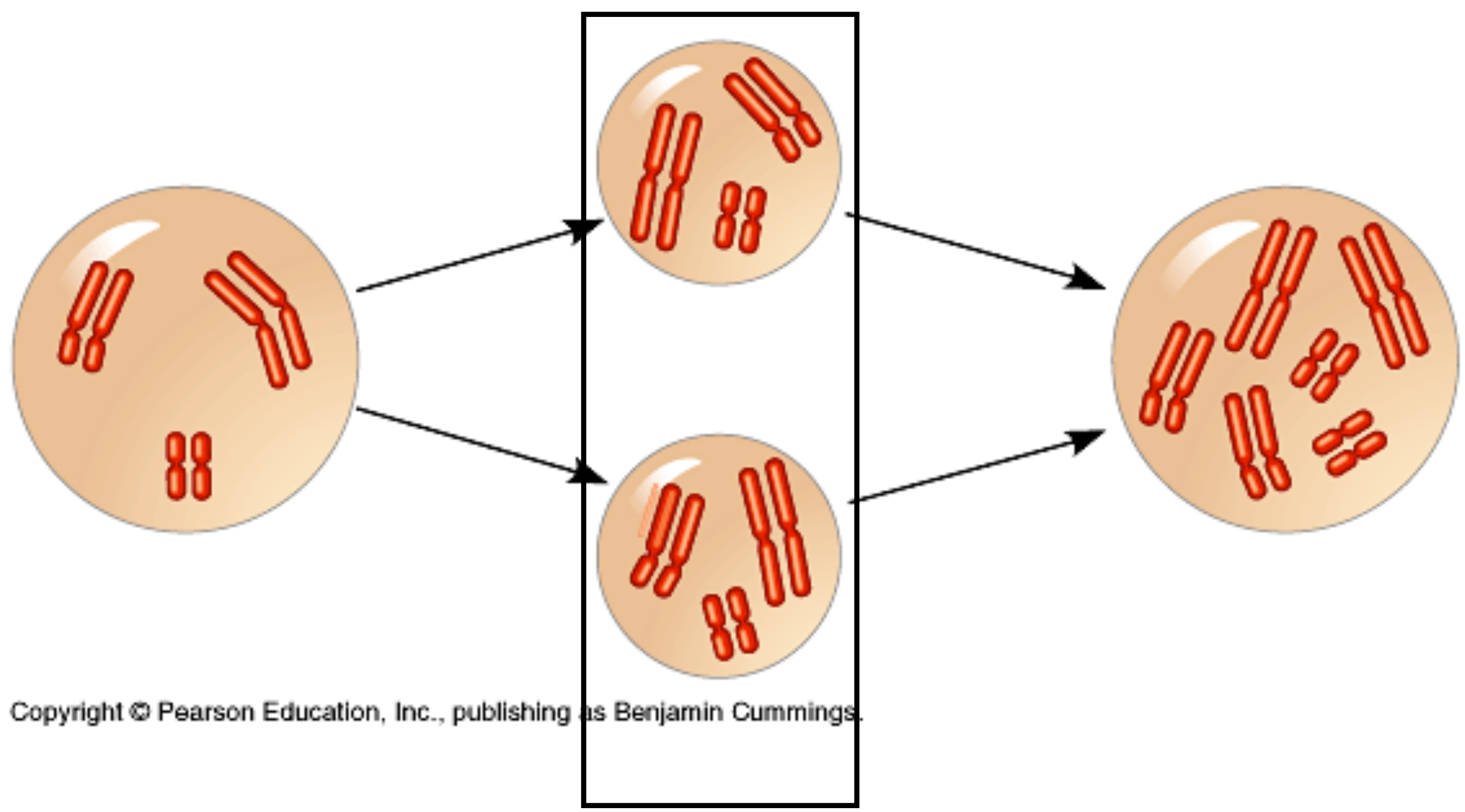
Weird hybrid case: “chimeric” gene duplicates




Long and Langley (1993)

# Molecular mechanisms of gene duplication

Polyploidy




Unreduced gametes

# Molecular mechanisms of gene duplication

Polyploidy:

-Doubles the entire content of the genome

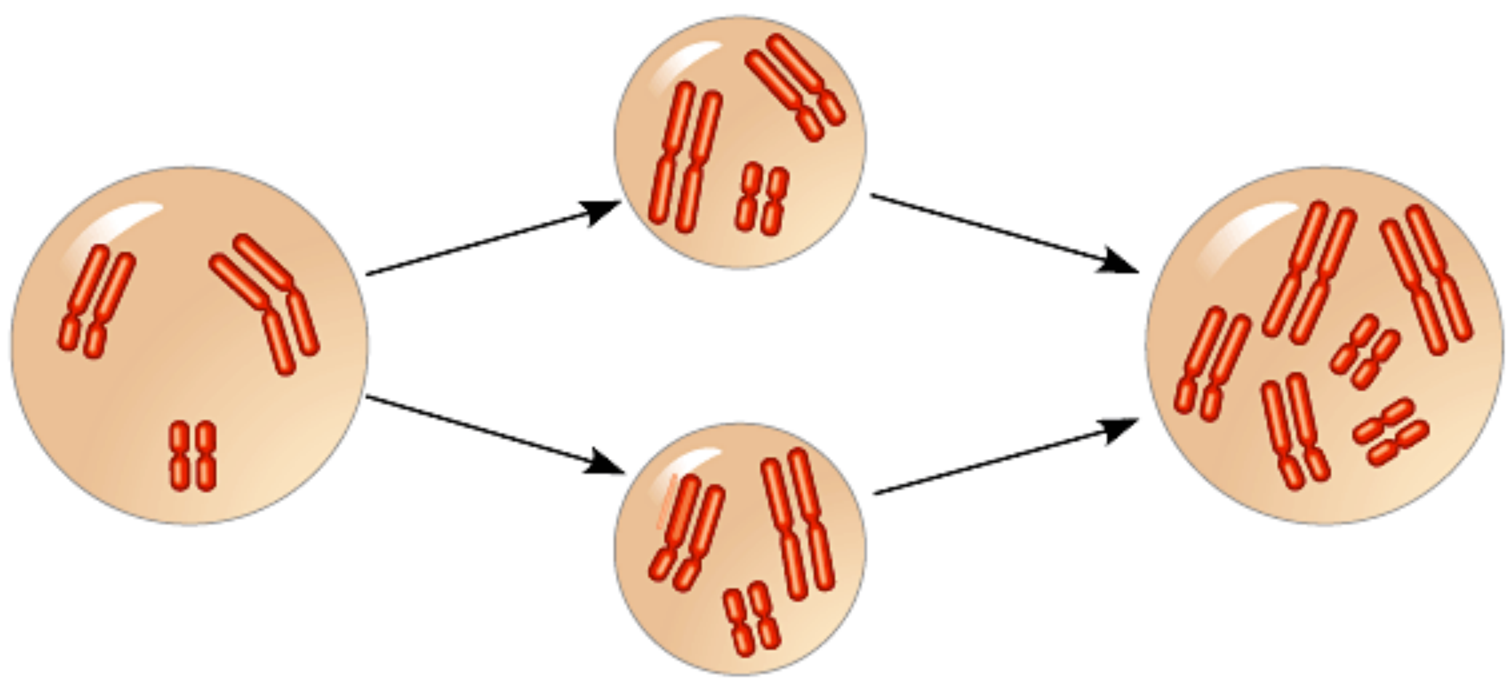
-Most genes subsequently return to single-copy

-Two types (at approximately equal frequency in nature):
Autopolyploidy and allopolyploidy

# Molecular mechanisms of gene duplication

Autopolyploidy:

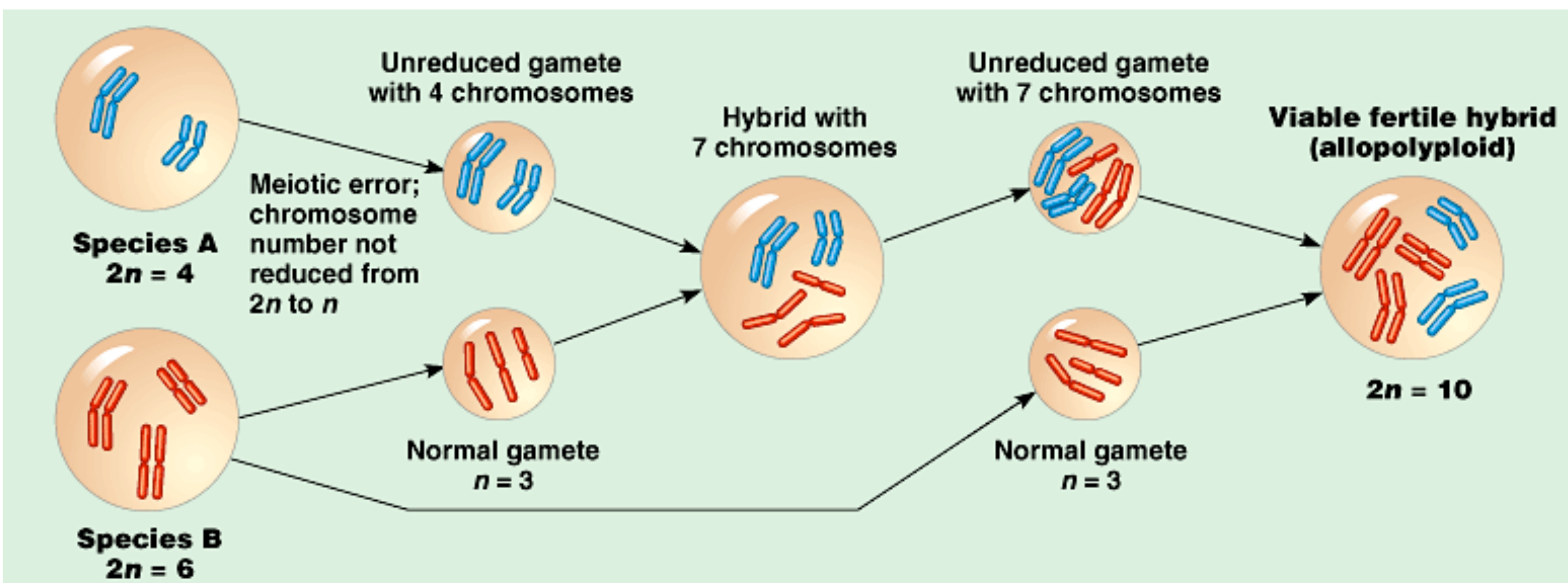
Doubling the number of chromosomes, where both parents are from the same species (or same individual)



# Molecular mechanisms of gene duplication

Allopolyploidy:

Doubling the number of chromosomes, where the parents are from *different* species



# Molecular mechanisms of gene loss

Nonsense mutation

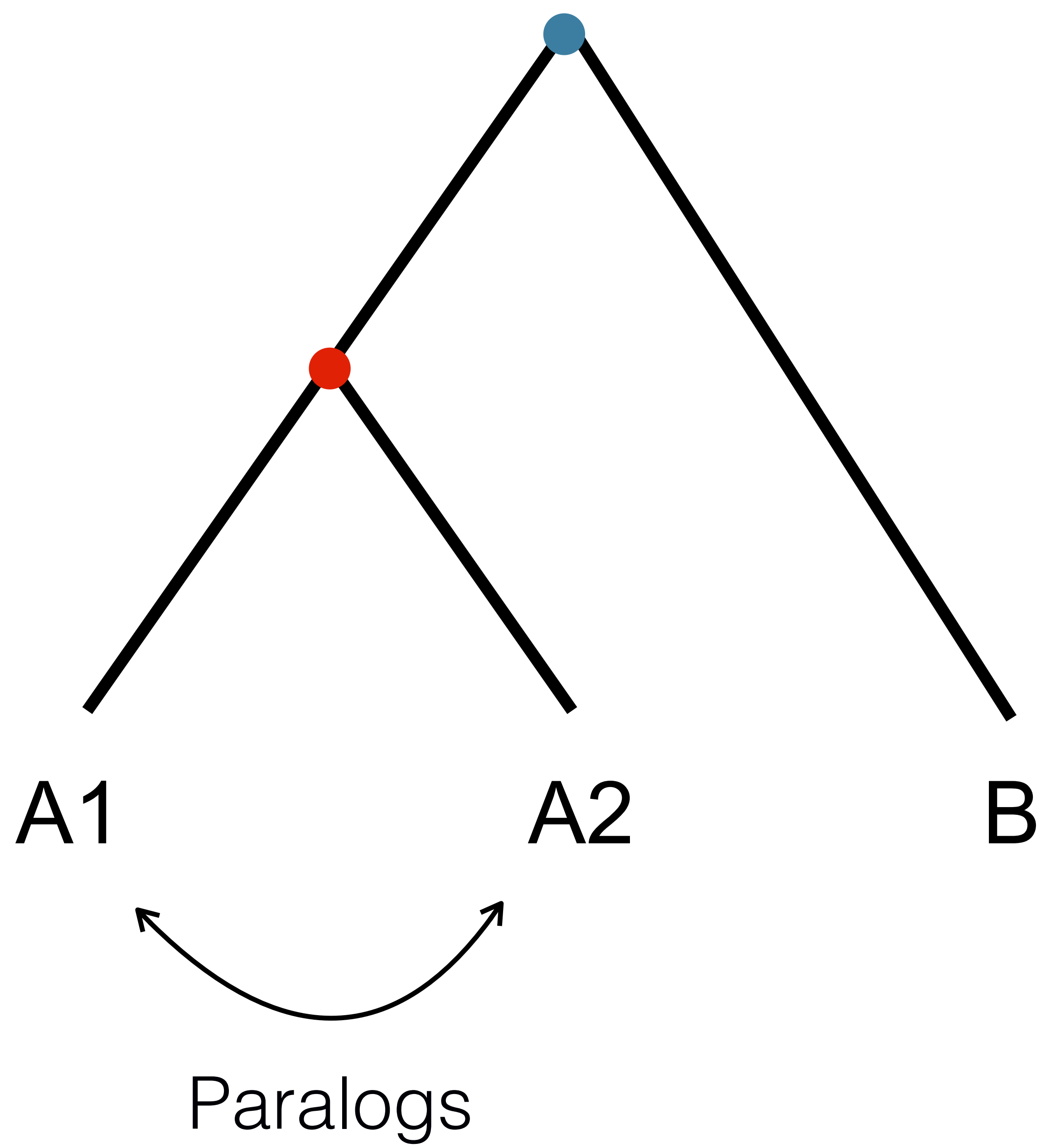
Frame shifting indel

Complete deletion (often due to NAHR)

# Genealogical relationships among genes

Paralogs: genes (loci) whose most recent common ancestor is a duplication node

# Genealogical relationships among genes

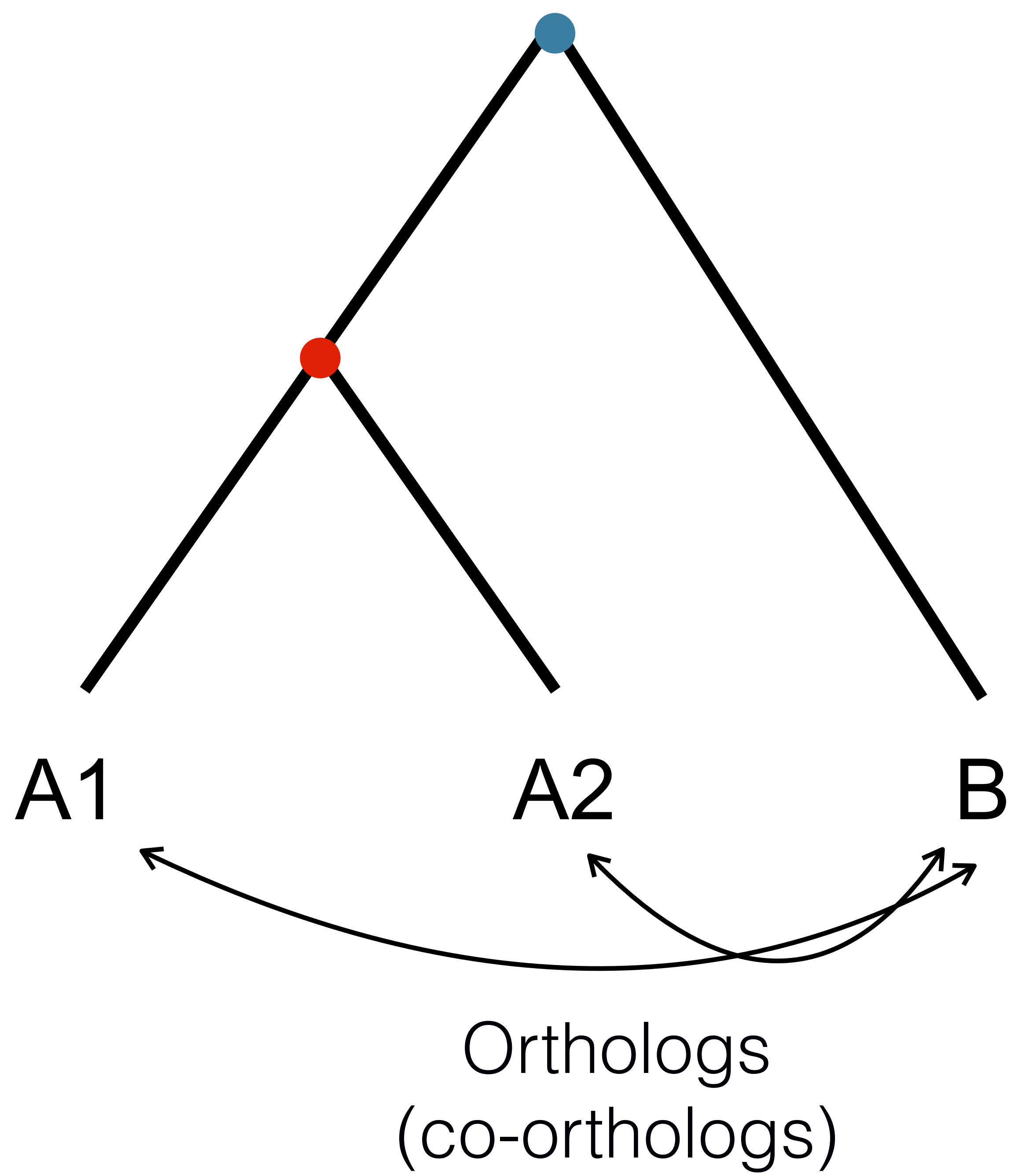


# Genealogical relationships among genes

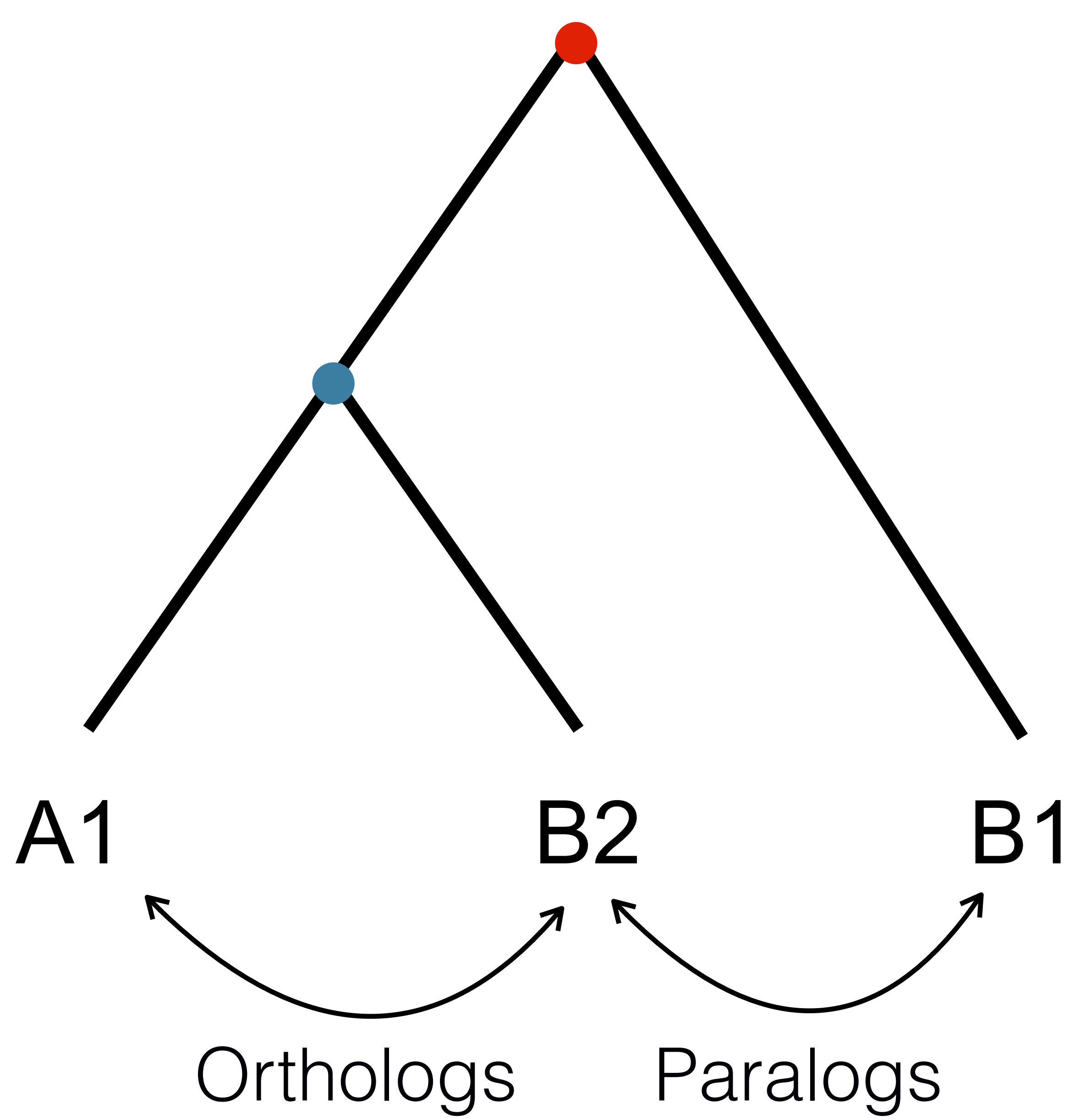
Paralogs: genes (loci) whose most recent common ancestor is a duplication node

Orthologs: genes (loci) whose most recent common ancestor is a speciation node

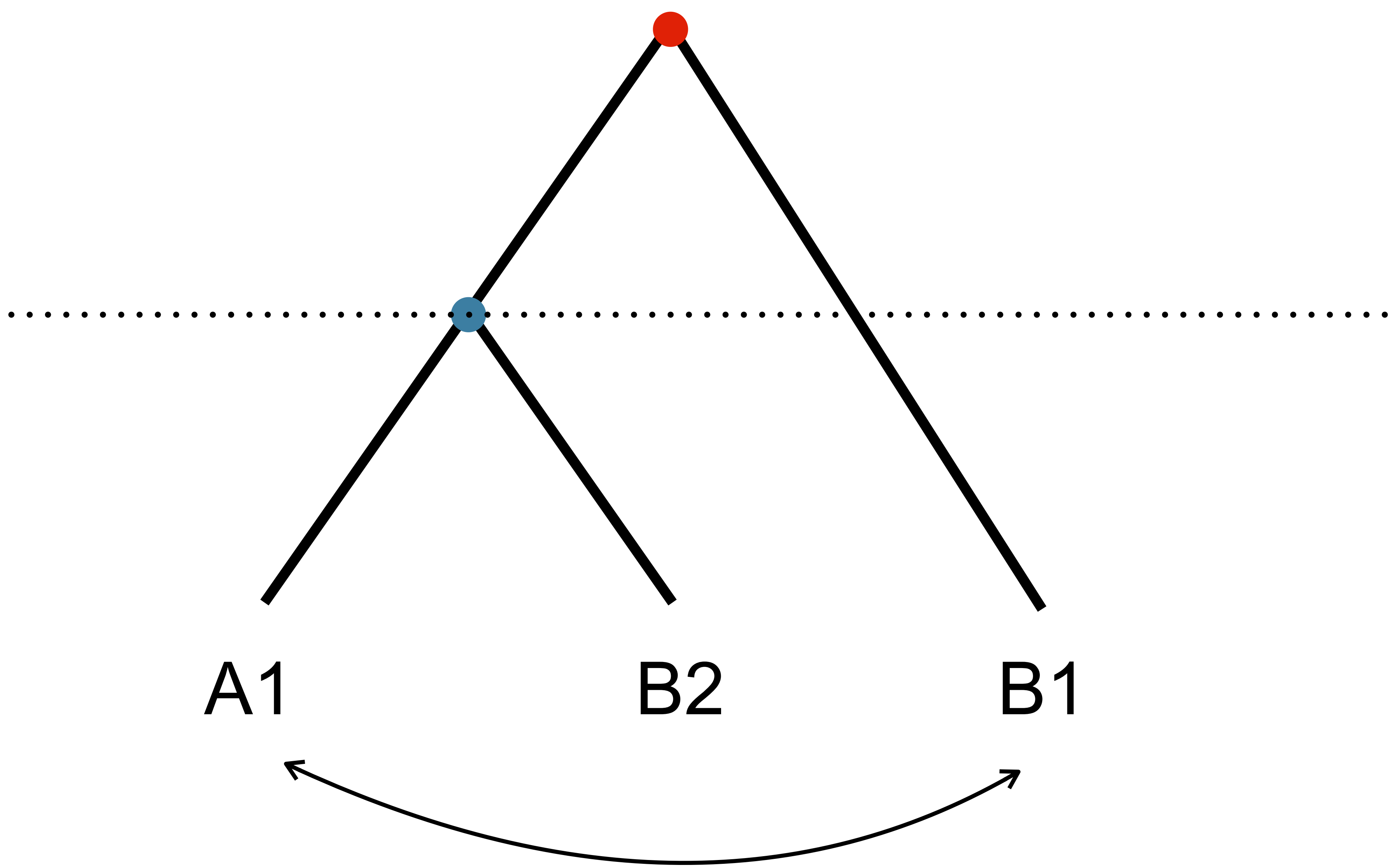
# Genealogical relationships among genes



# Genealogical relationships among genes

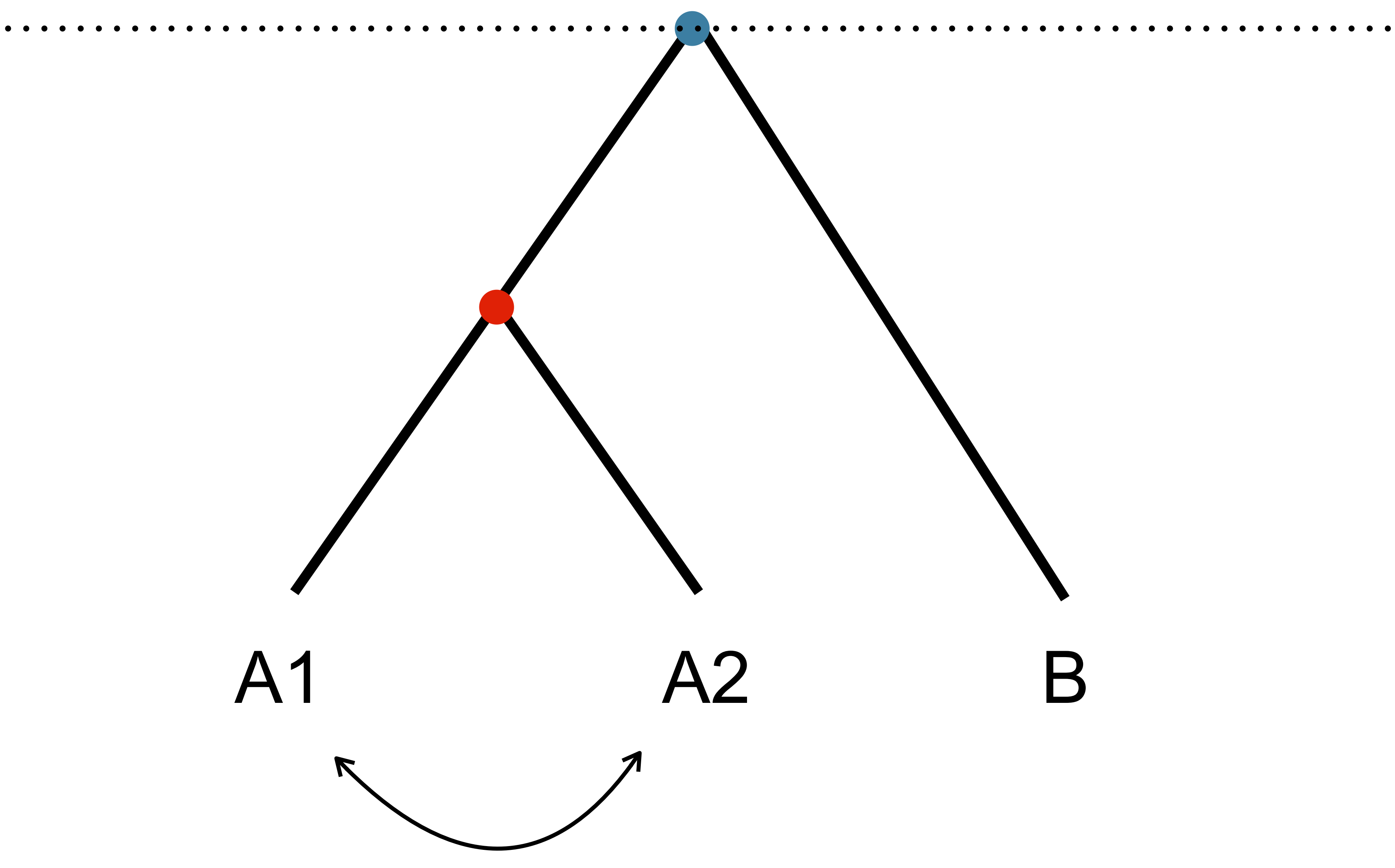


# Genealogical relationships among genes




Paralogs
(out-paralogs wrt the A-B speciation event)

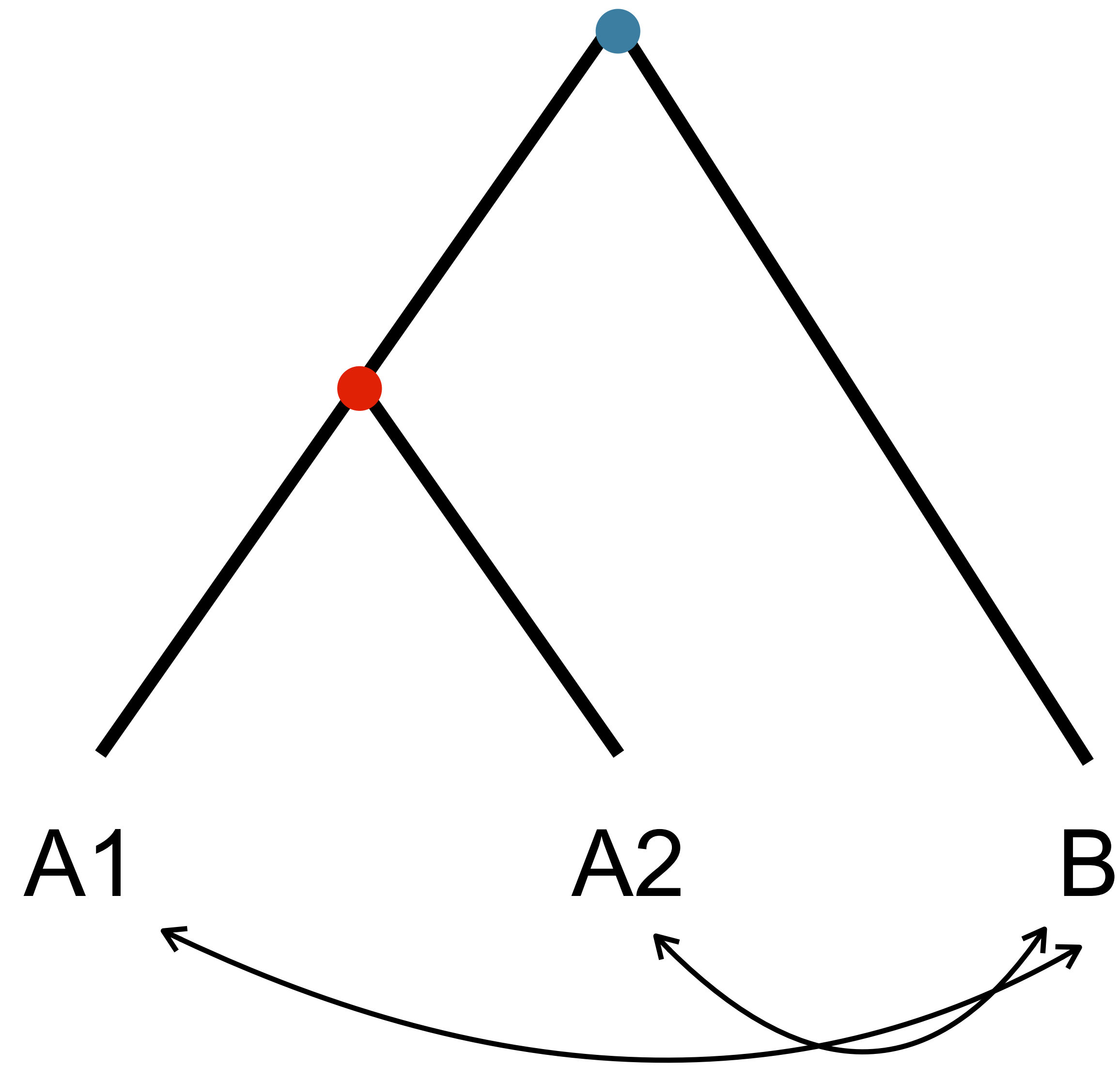
# Genealogical relationships among genes



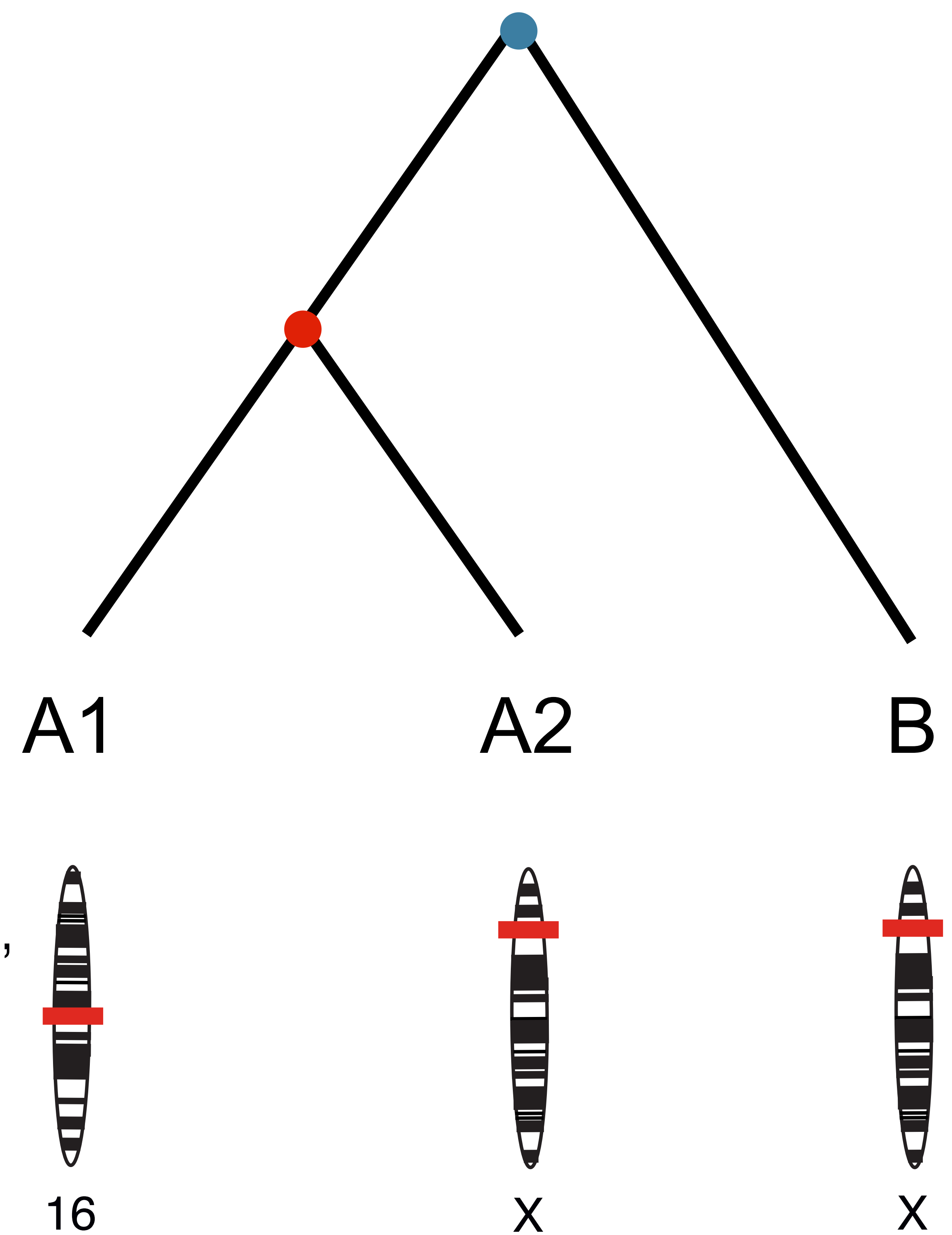

In-paralogs wrt the A-B speciation event

# More genealogical relationships among genes

Co-orthologs

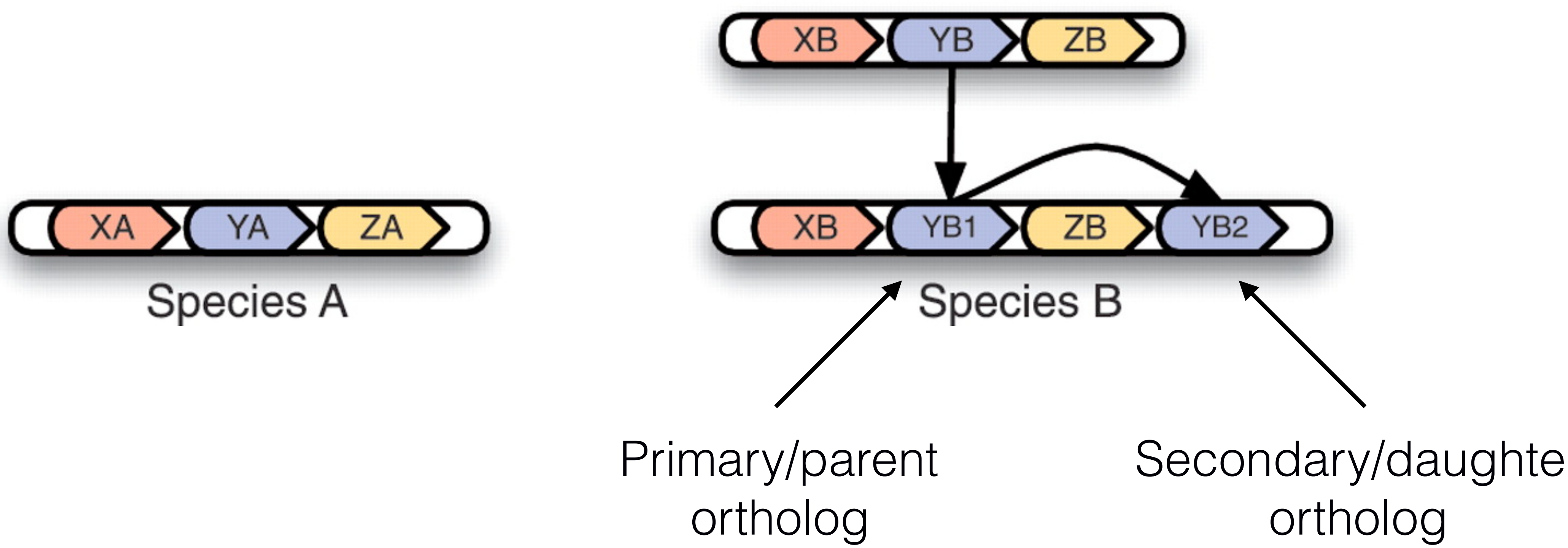


# More genealogical relationships among genes




“Positional orthologs”
(Dewey 2011)

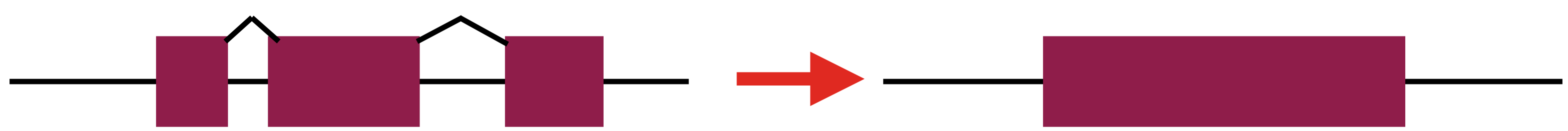
# More genealogical relationships among genes




"Positional orthologs"
(Dewey 2011)

# More genealogical relationships among genes

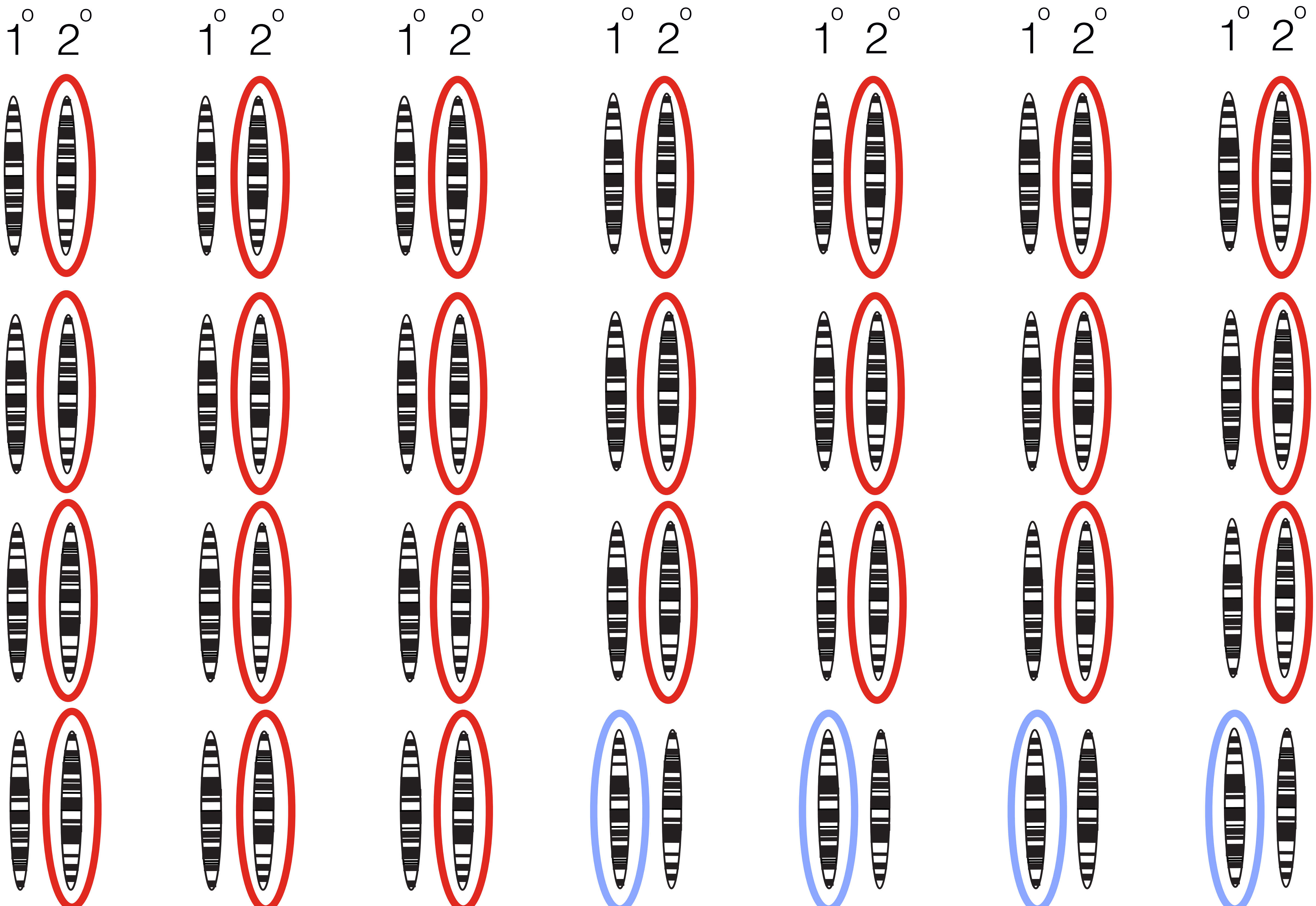
Retrotransposition



Primary/parent ortholog

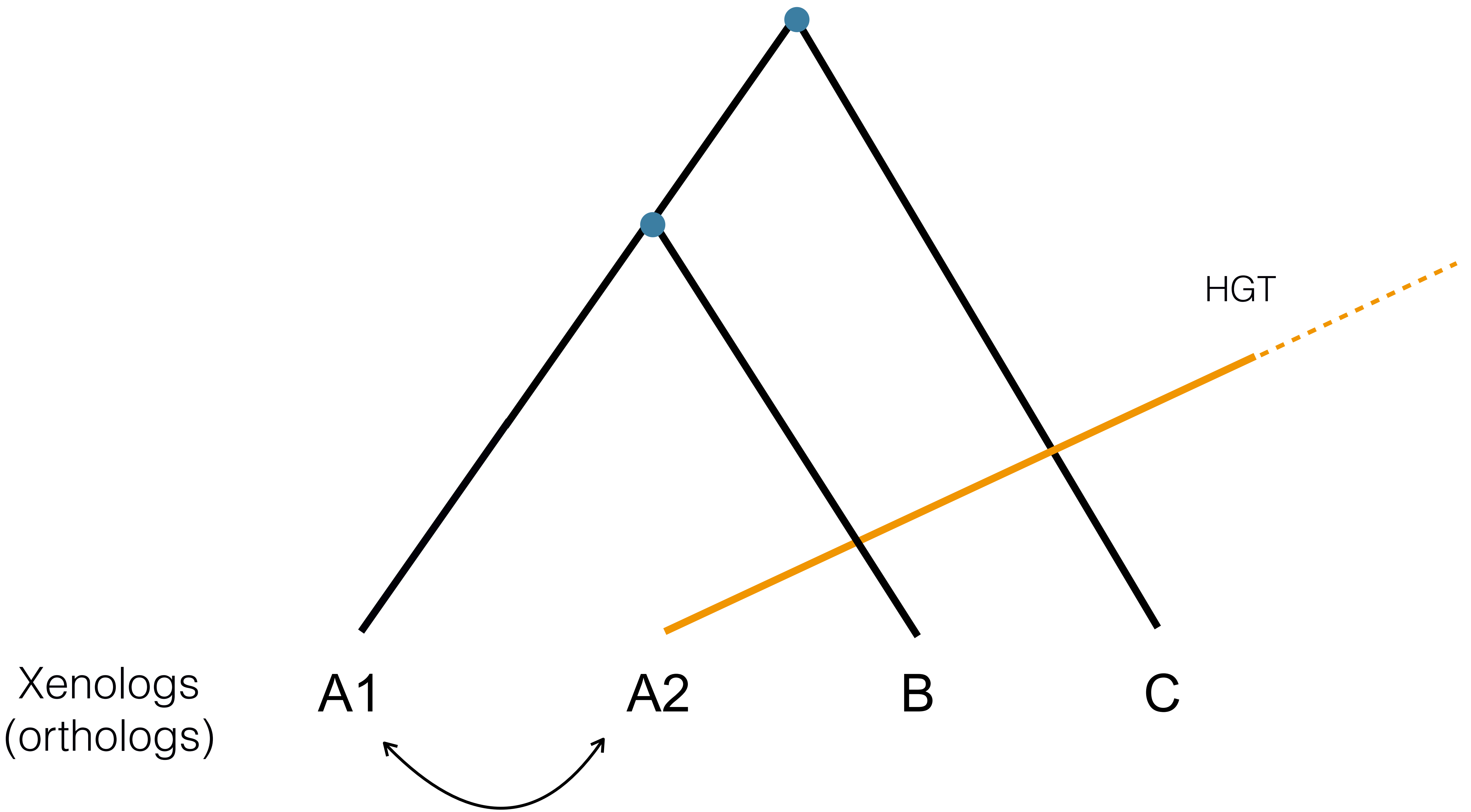
Secondary/daughter ortholog

# Polarized duplicates and adaptation




Han et al. (2009)

# More genealogical relationships among genes



# More genealogical relationships among genes



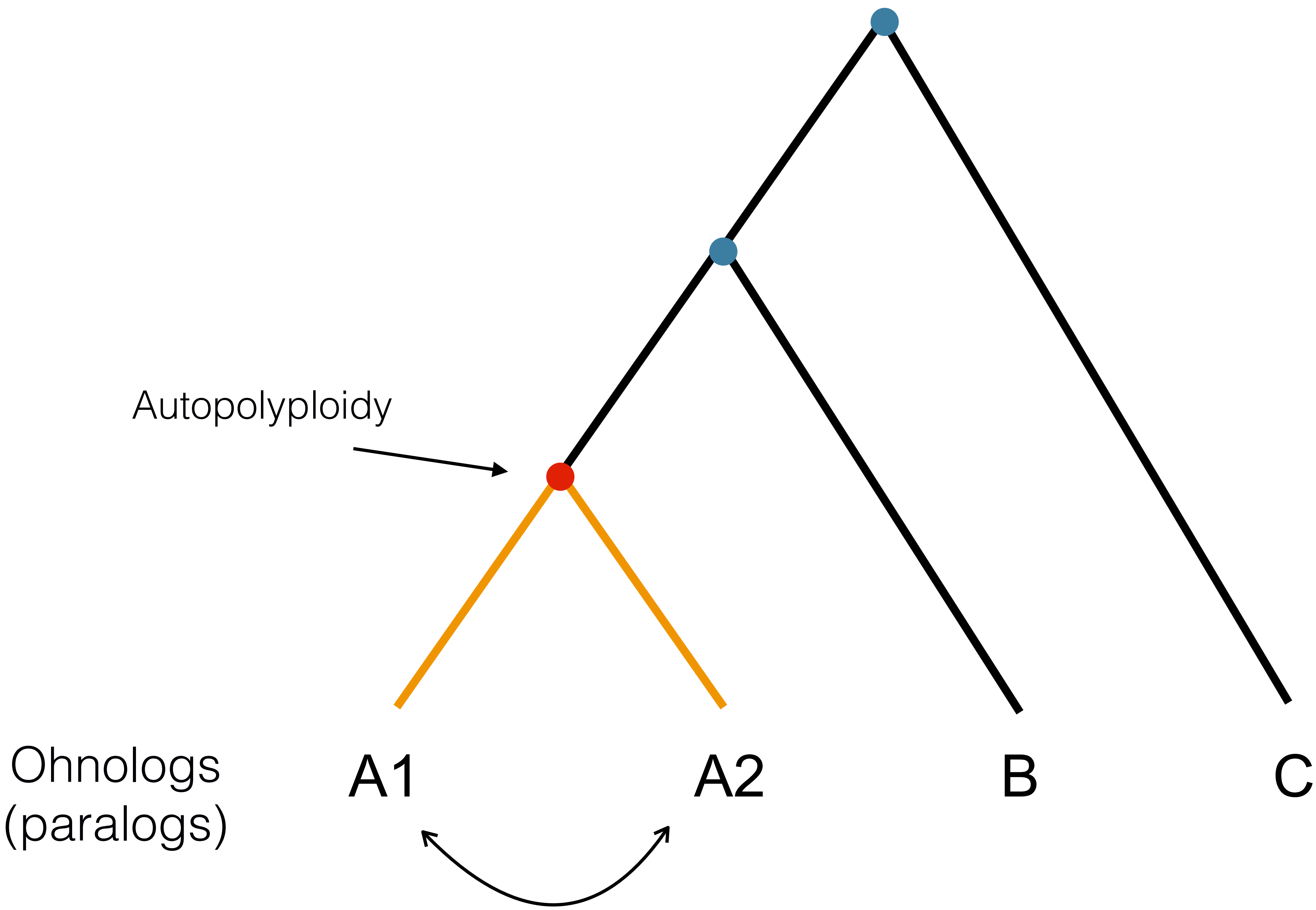
RESEARCH ARTICLE

## Horizontal Transfer, Not Duplication, Drives the Expansion of Protein Families in Prokaryotes

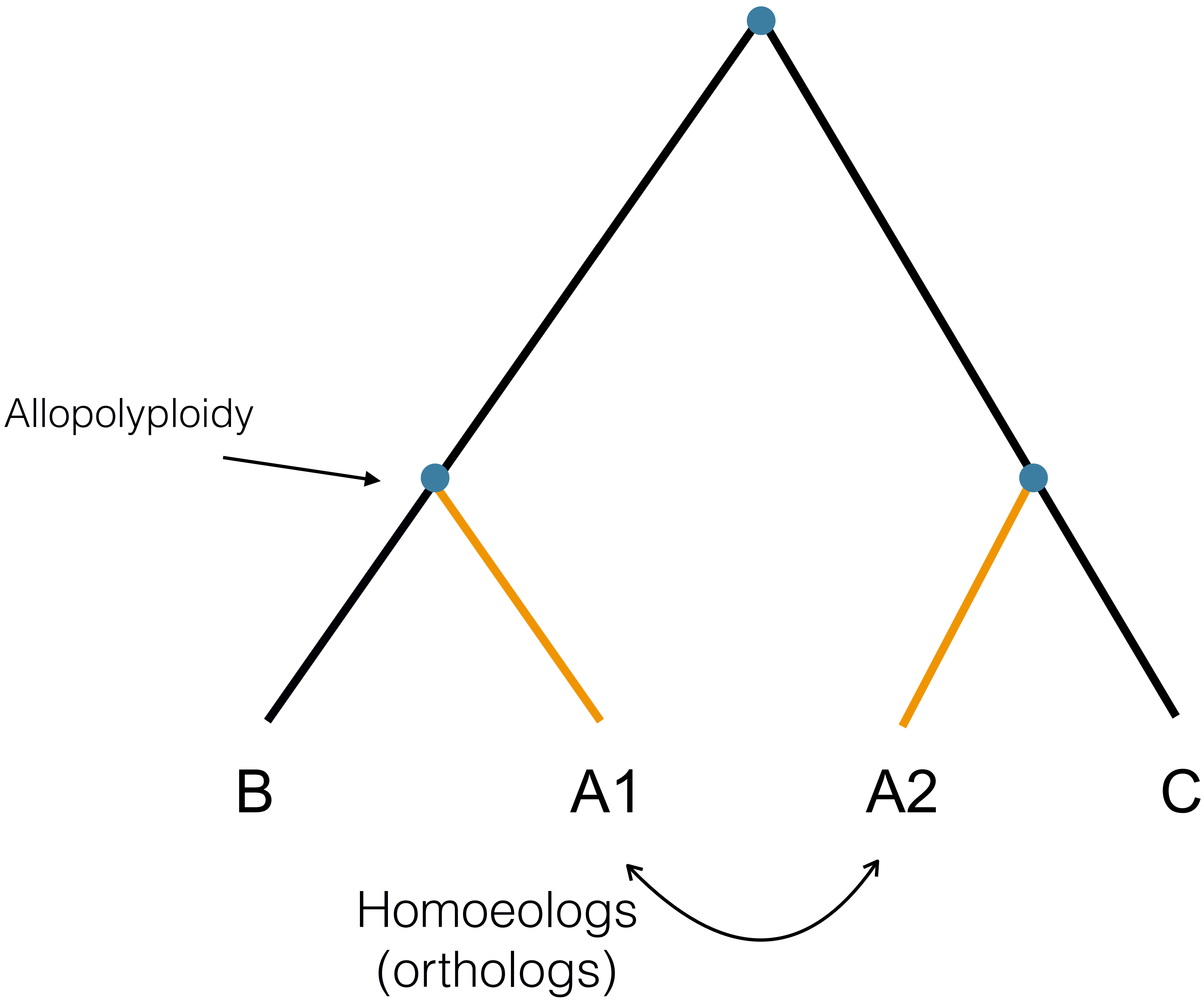
Todd J. Treangen, Eduardo P. C. Rocha

Published: January 27, 2011 • http://dx.doi.org/10.1371/journal.pgen.1001284

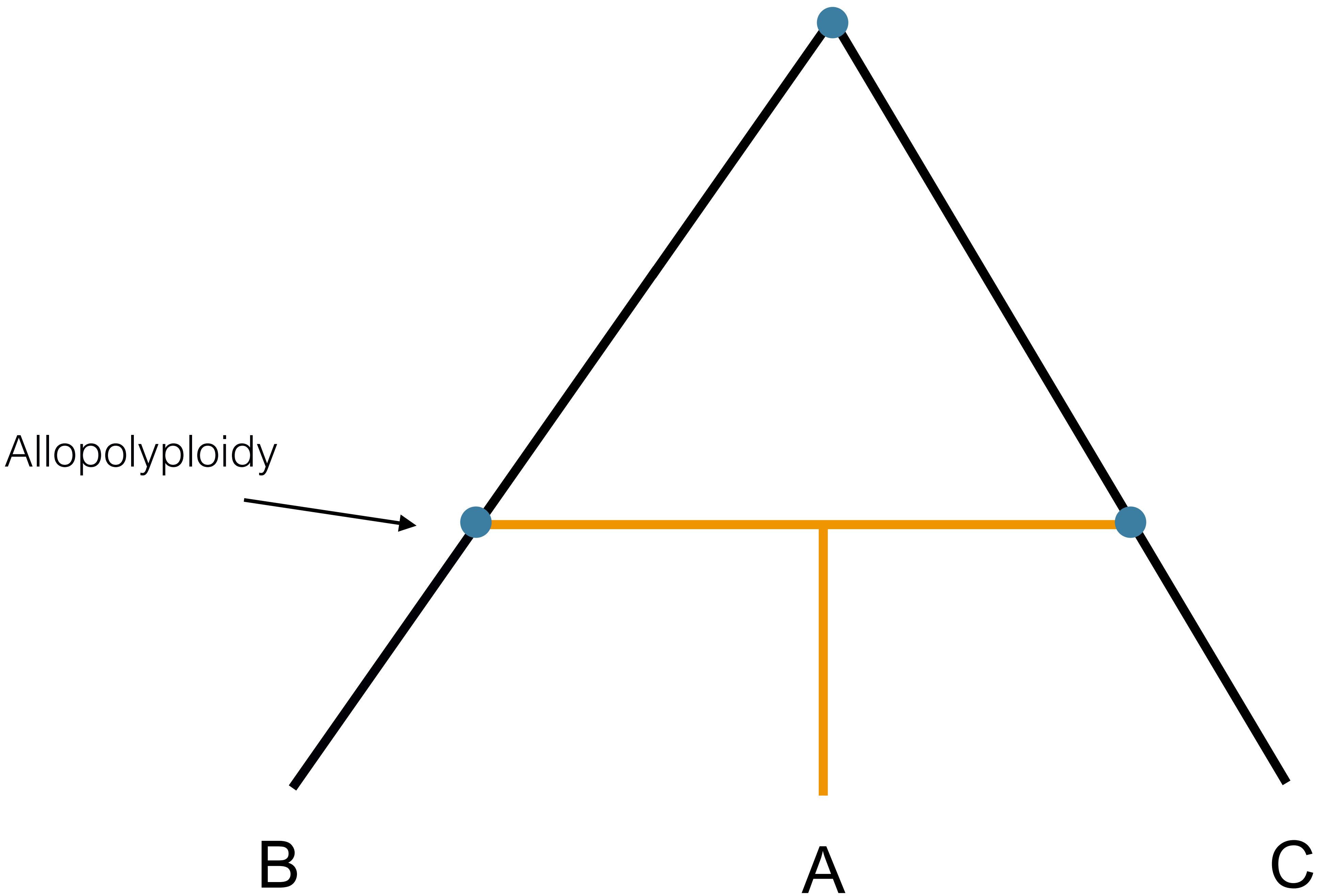
# More genealogical relationships among genes



# More genealogical relationships among genes



# More genealogical relationships among genes



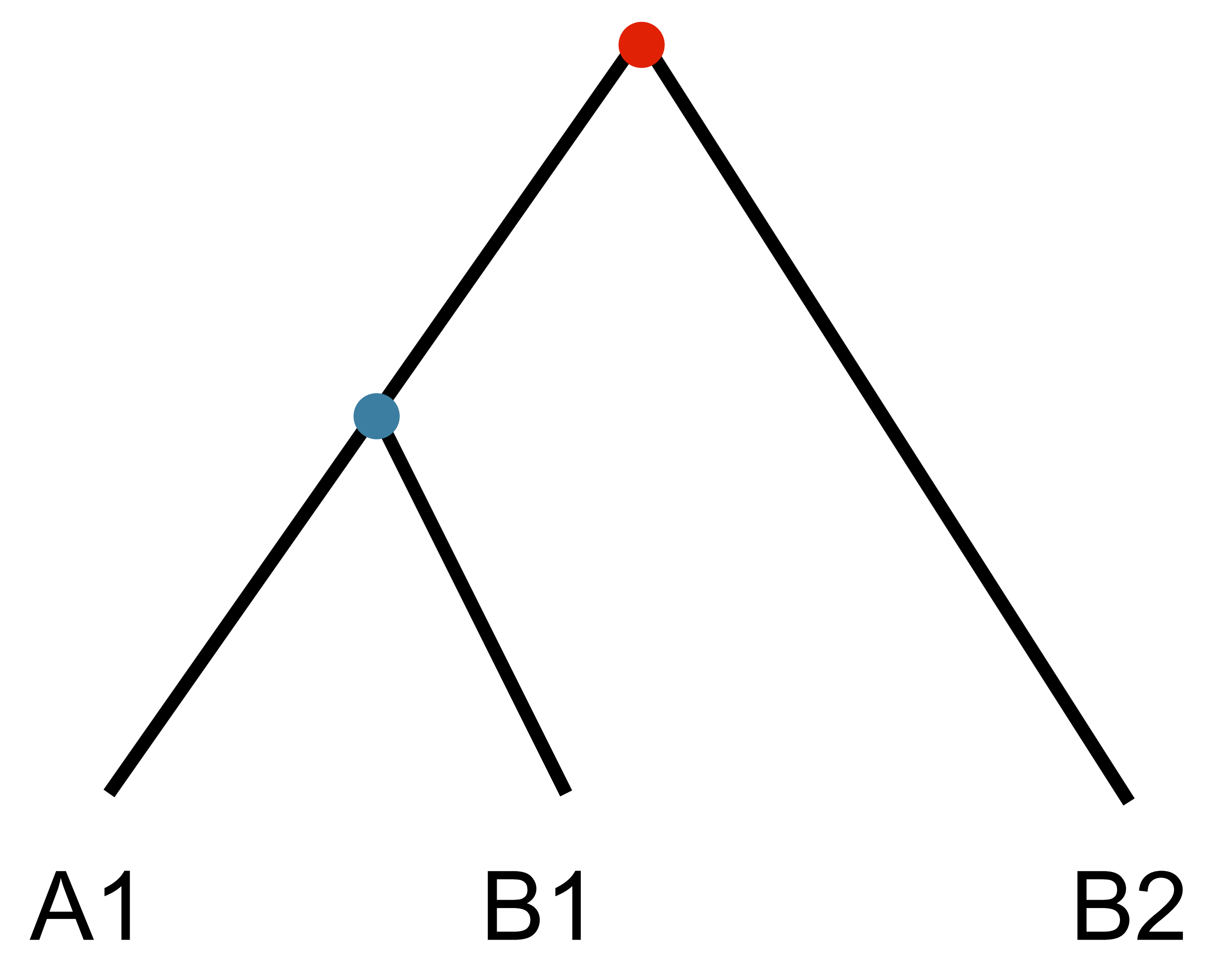
# More genealogical relationships among genes

| | Pairs of genes found in the same species | Pairs of genes found in different species |
|---|---|---|
| Genes that originated by a speciation event | **Homoeologs** | **Orthologs** |
| Genes that originated by a duplication event | Whole genome duplication: **Ohnologs**<br>Small scale duplication: **Paralogs** | **Paralogs** |

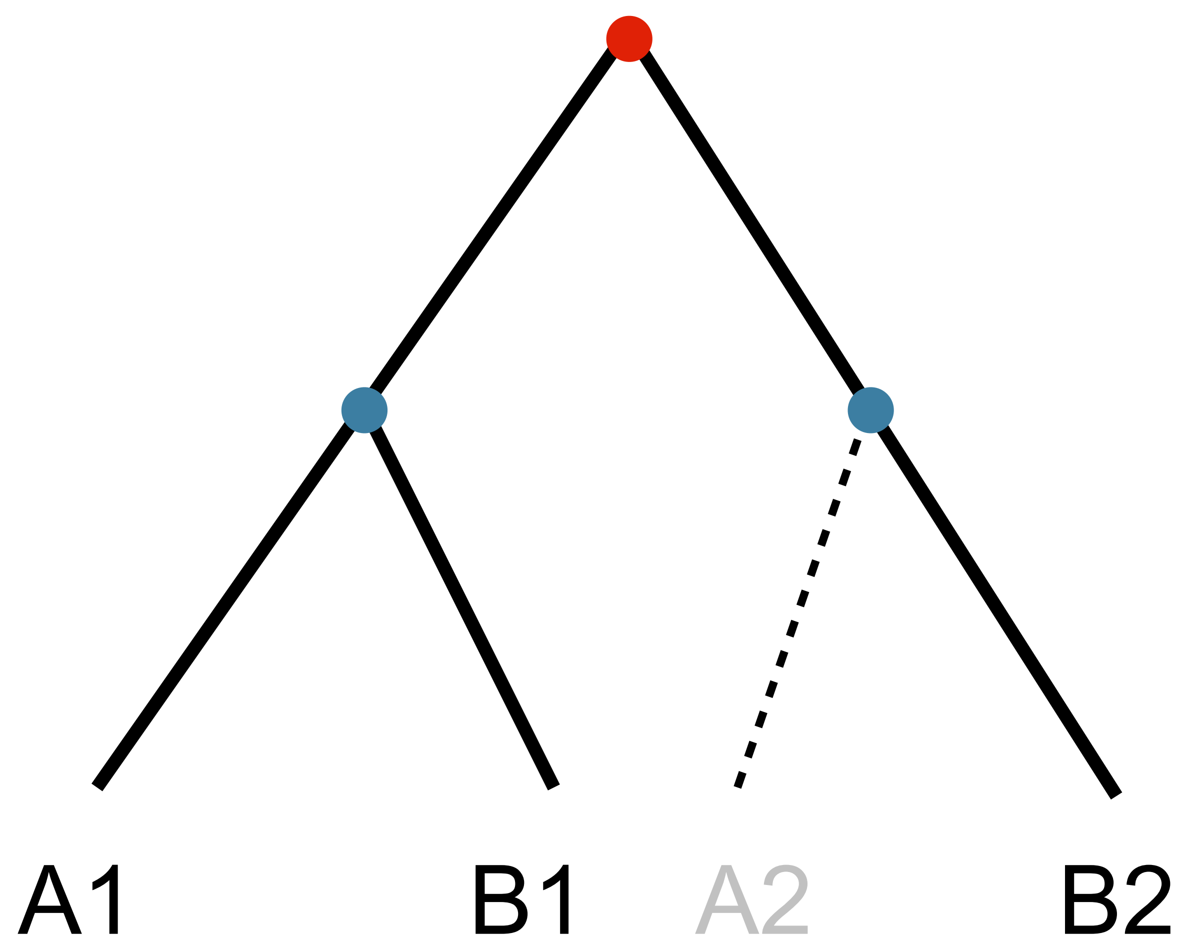
**Trends in Plant Science**

Glover et al. (2016)

# More genealogical relationships among genes

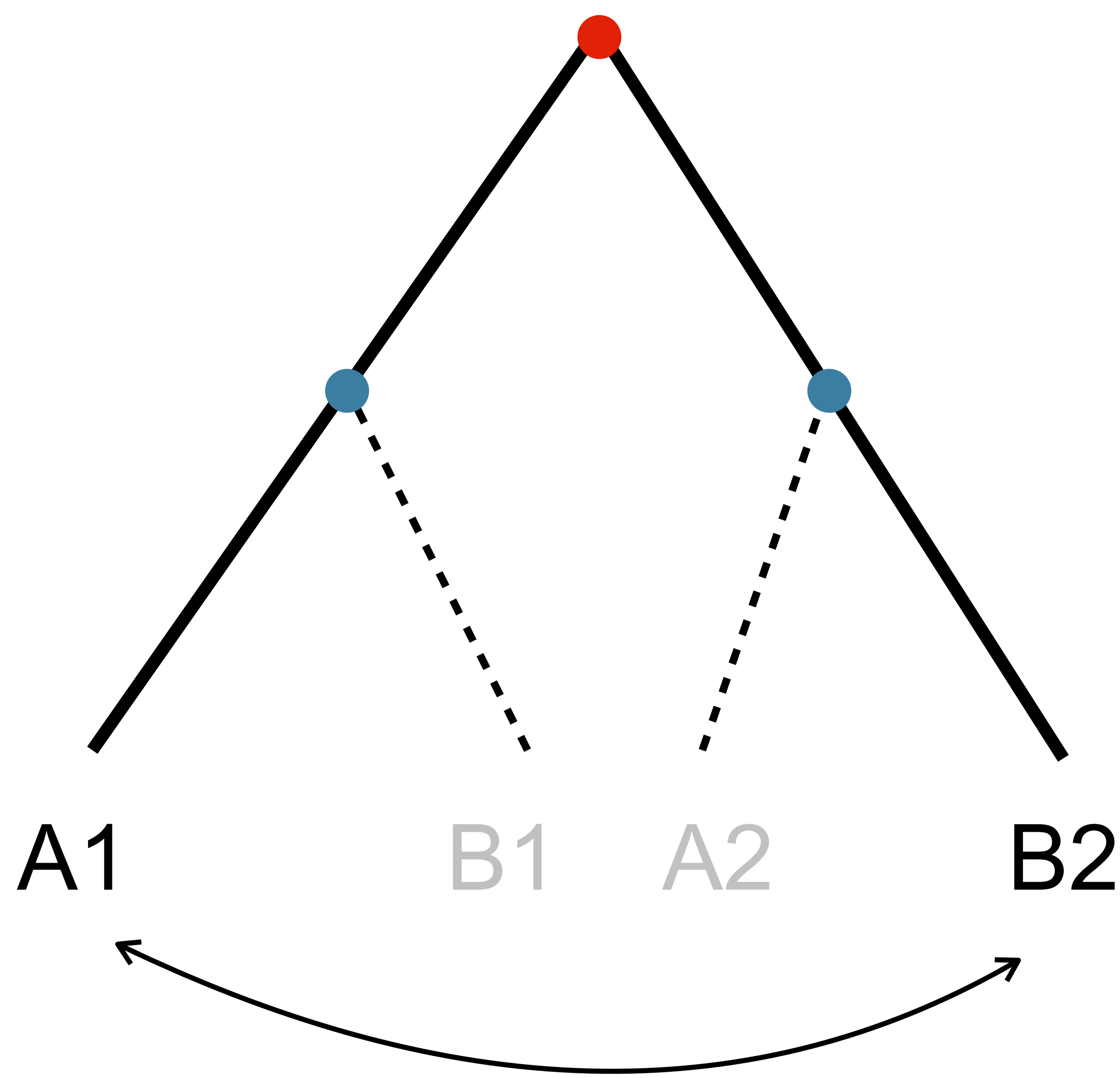


# More genealogical relationships among genes




“Reconciled” gene tree

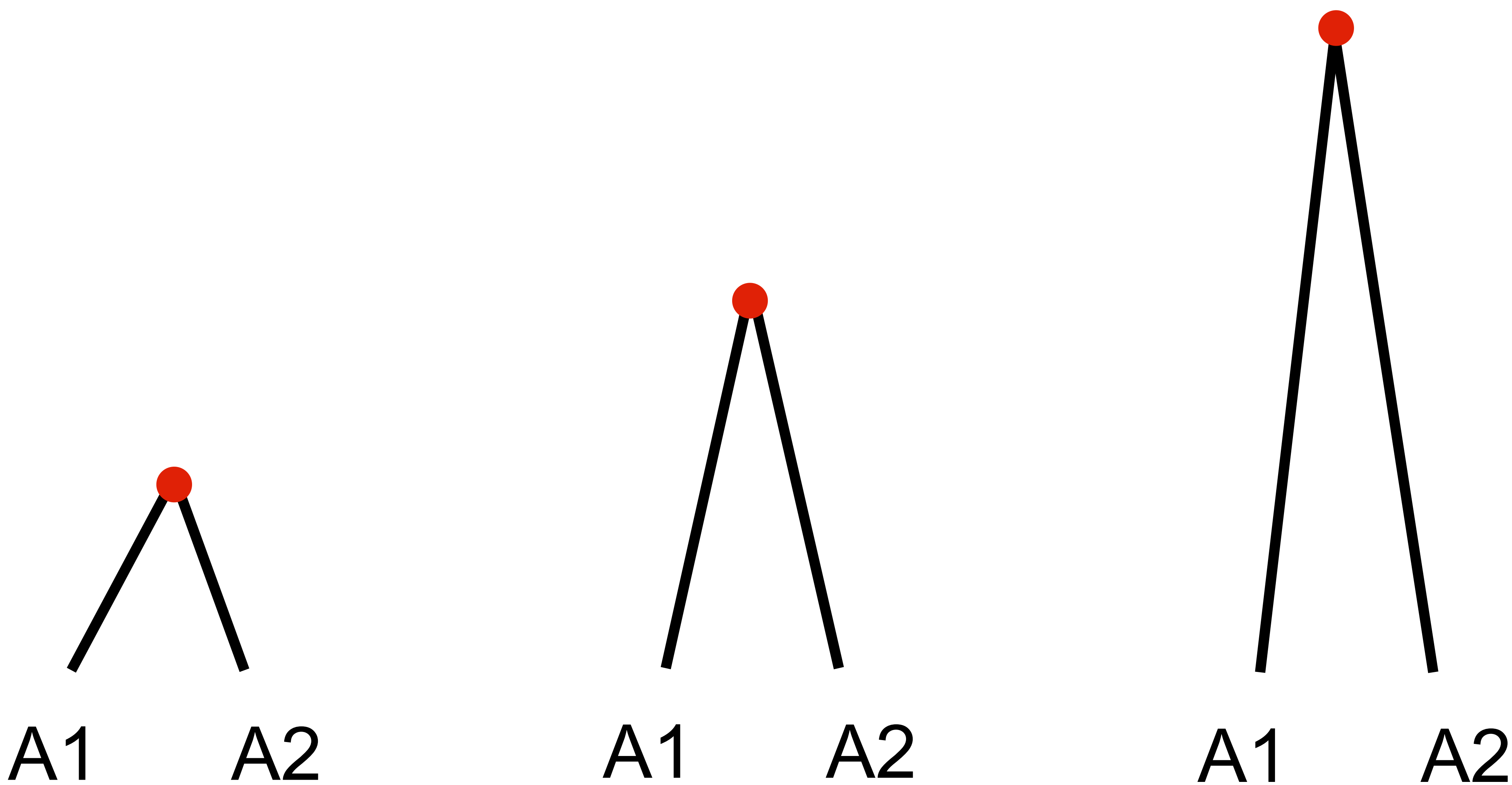
# More genealogical relationships among genes



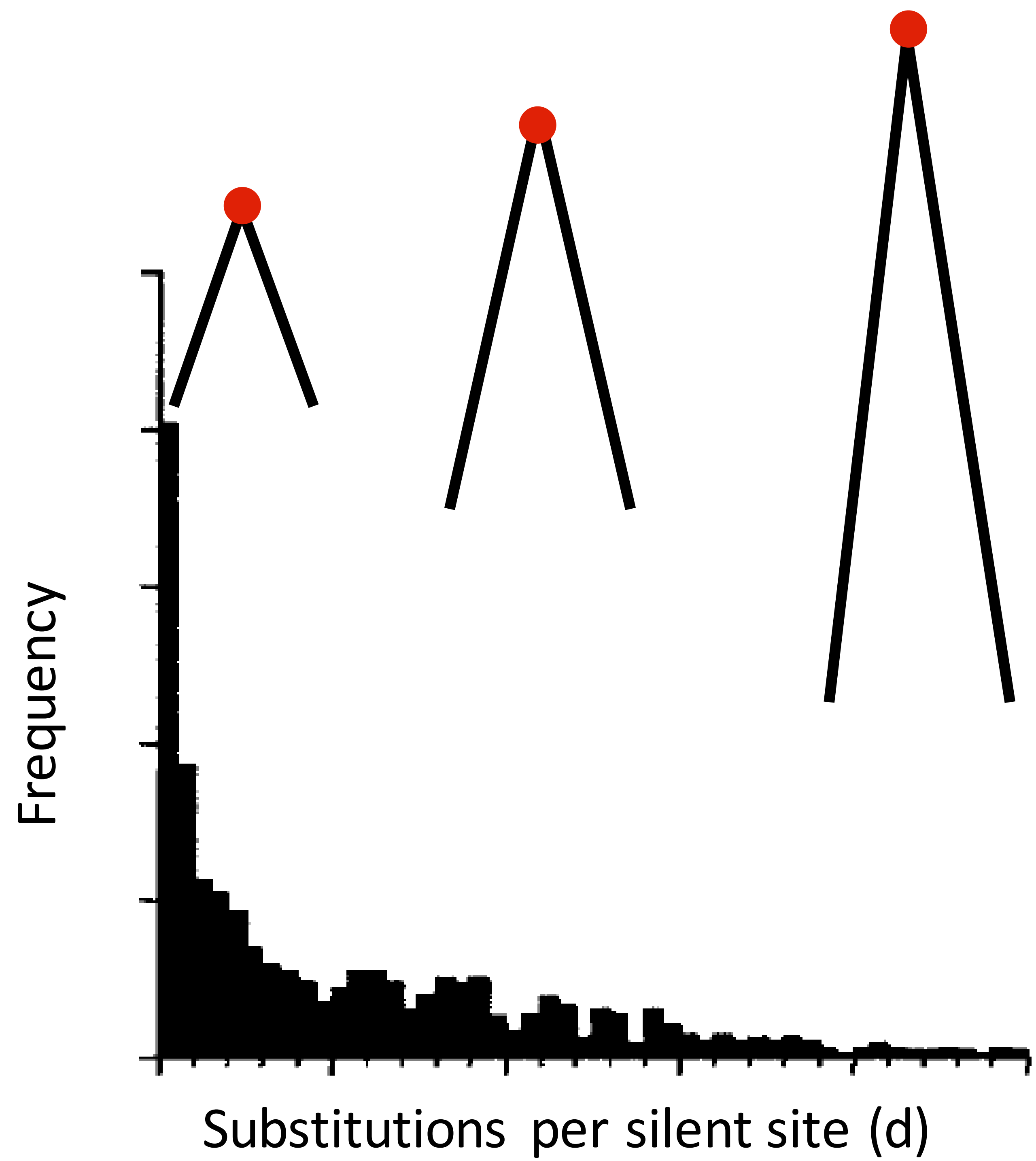

pseudo-orthologs

("hidden paralogy")

# Divergence between paralogs



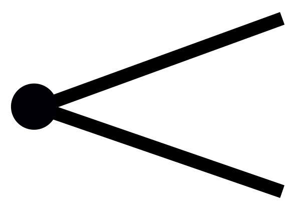
# Divergence between paralogs



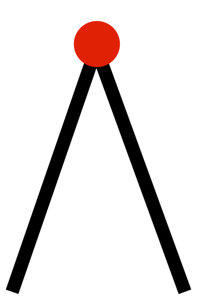
# Divergence between paralogs

How divergent are new paralogs?

$=4N_e\mu$



$=4N_e\mu$



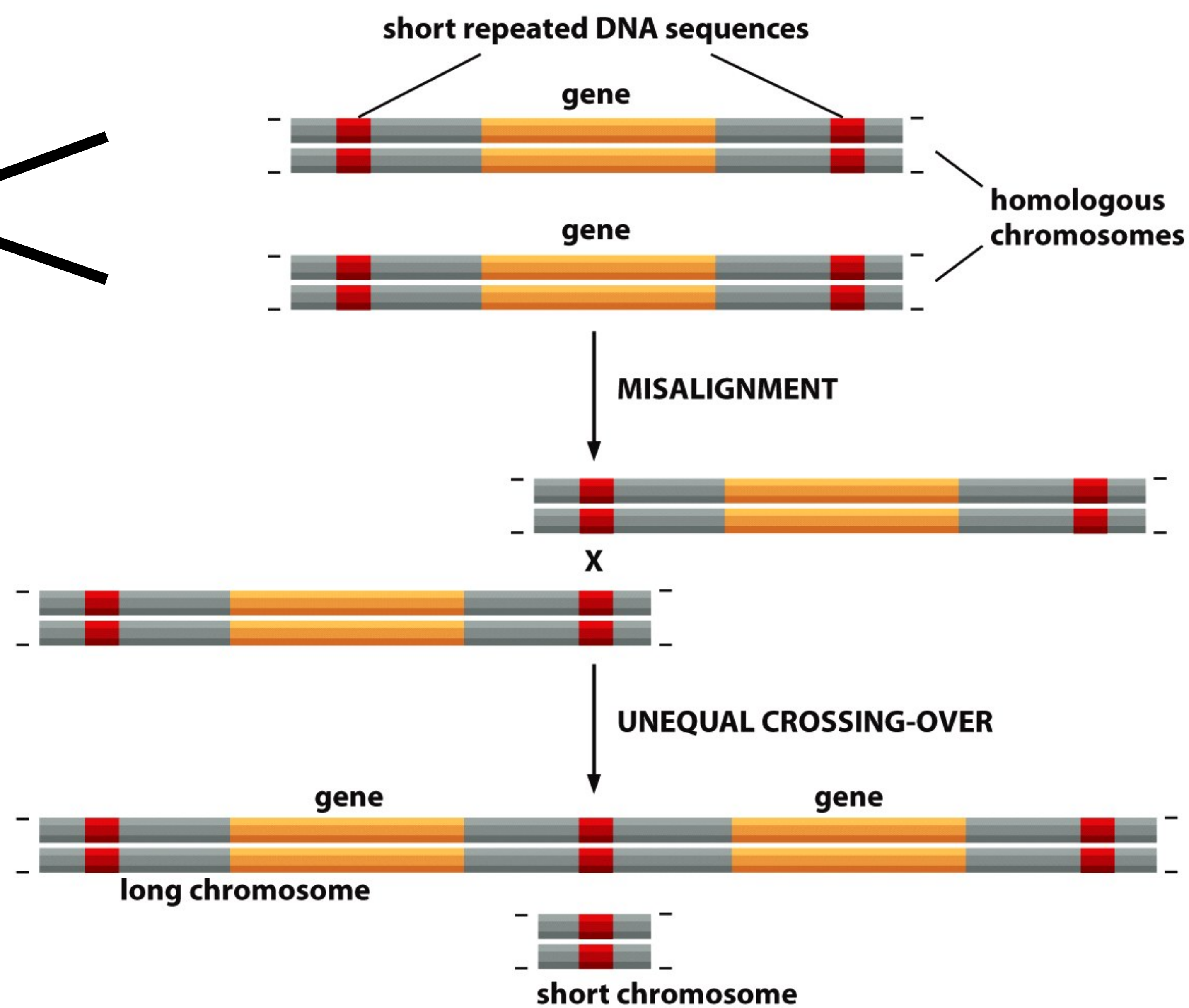



Figure 9-9 Essential Cell Biology 3/e (© Garland Science 2010)