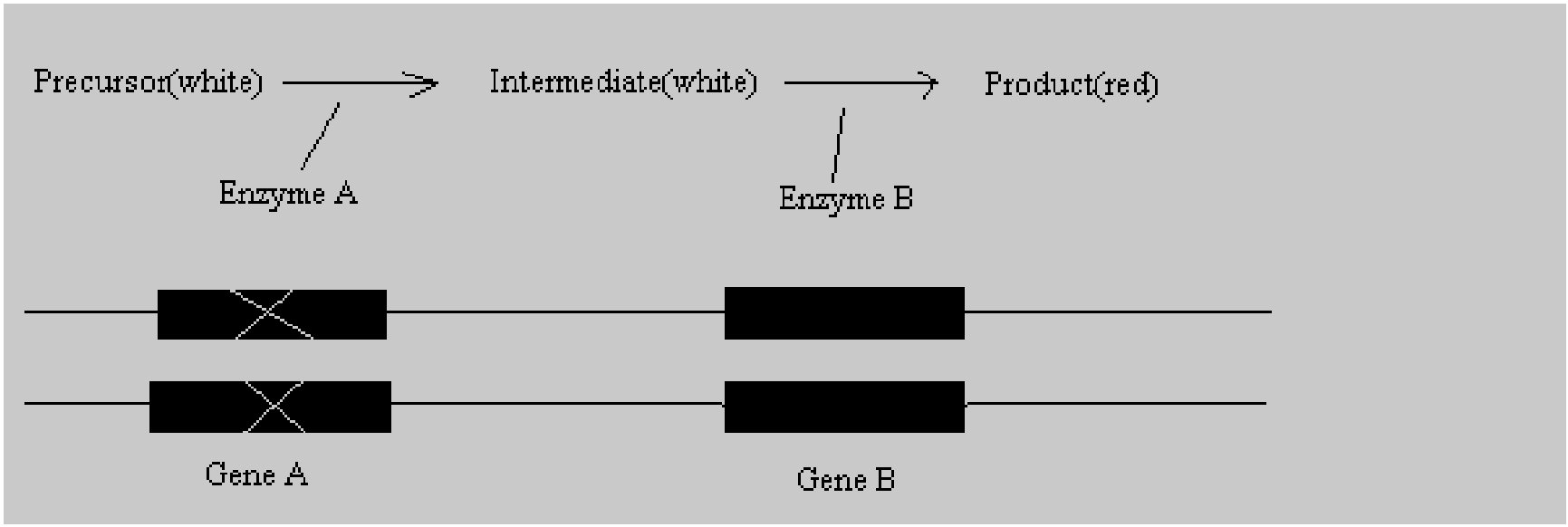
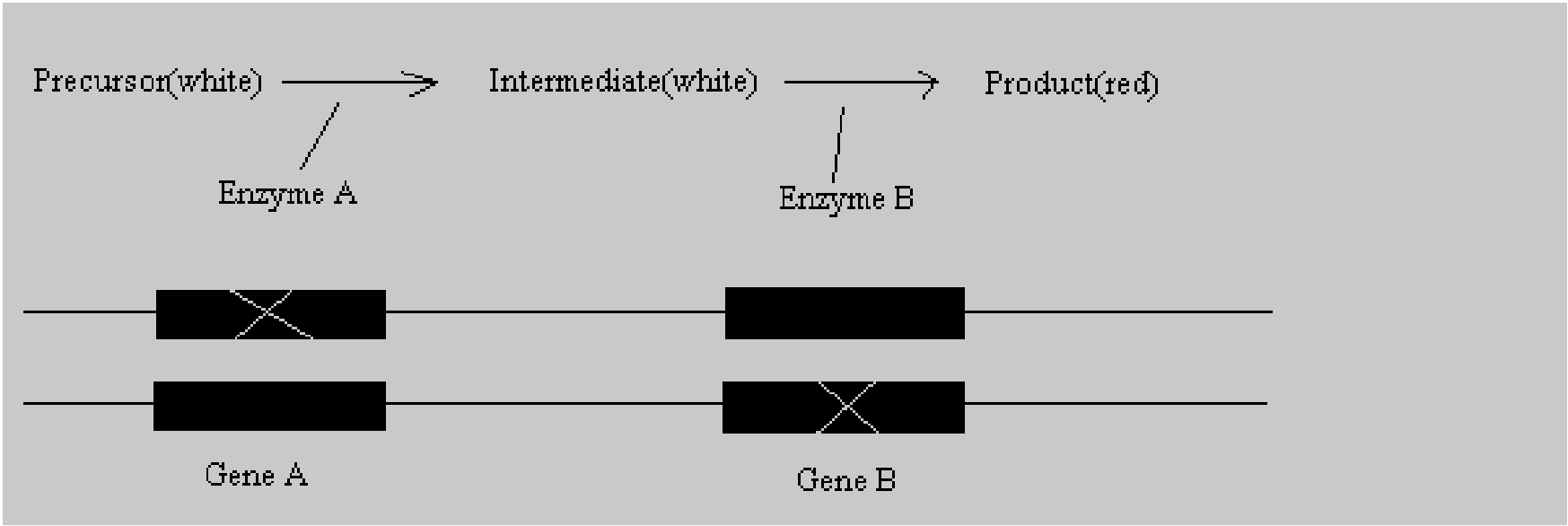
Complementation tests





"Complementation group" equals "Gene"

If two mutations failed to complement,

they are alleles of the same gene

they are allelic to each other

they belong to the same complementation group

If two mutations complements each other,

they are alleles of different genes

they are not allelic to each other

they belong to different complementation groups

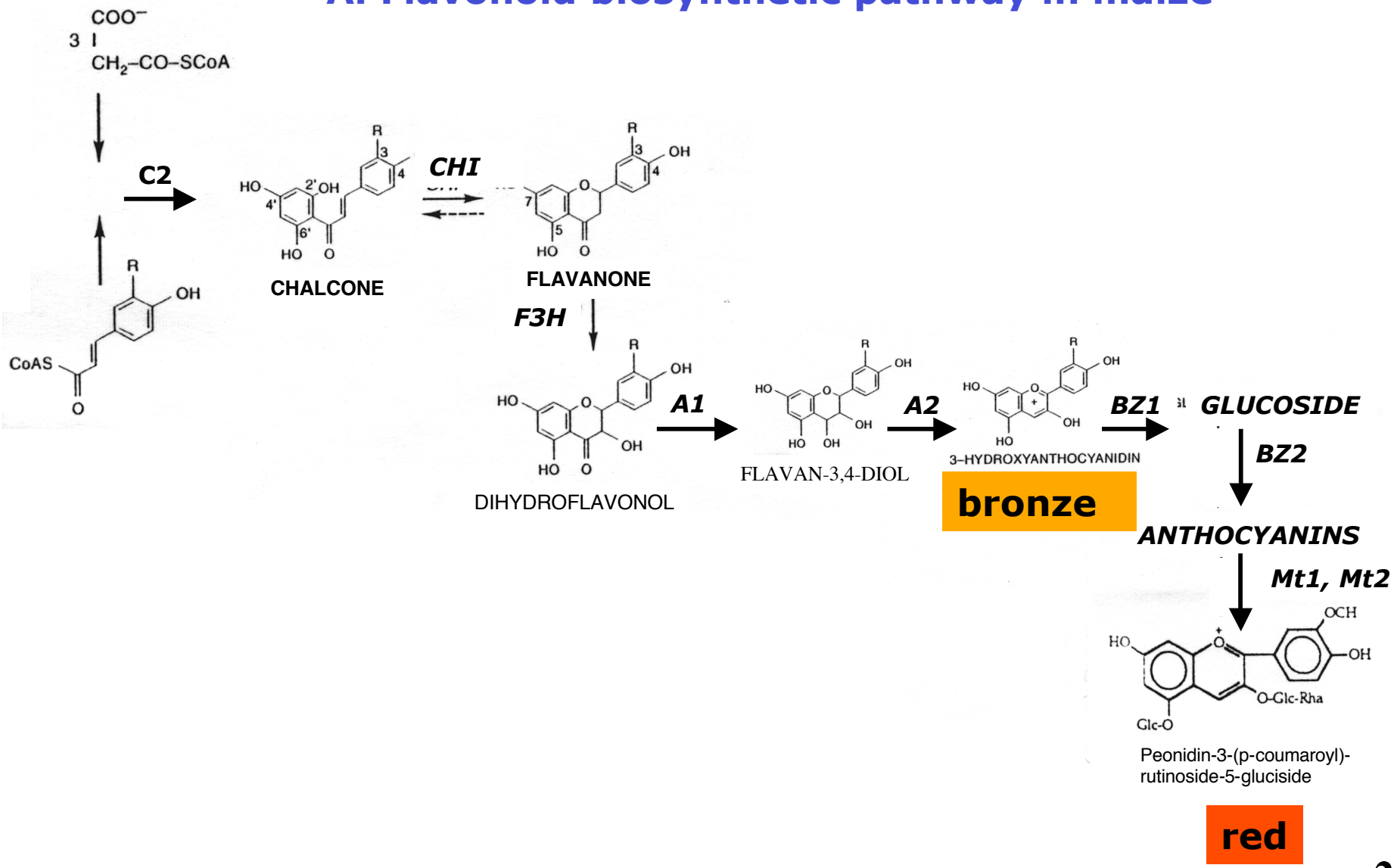
Lecture 5: Genetic interactions and epistasis

A. Epistasis in a biochemical pathway
B. Epistasis in a regulatory pathway
C. Additive interactions
D. Synergistic interactions
E. Suppressions

Read 14.7 (p632-634); p434-435; 428-429
Fig. 14.36; 10.32; 10. 27; 10.28

epistasis analyses (genetic interactions among different mutations)

A. Flavonoid biosynthetic pathway in maize



WT:	**Red**
Mutations in c2, a1, a2:	**Colorless**
Mutations in bz1, bz2:	**bronze**

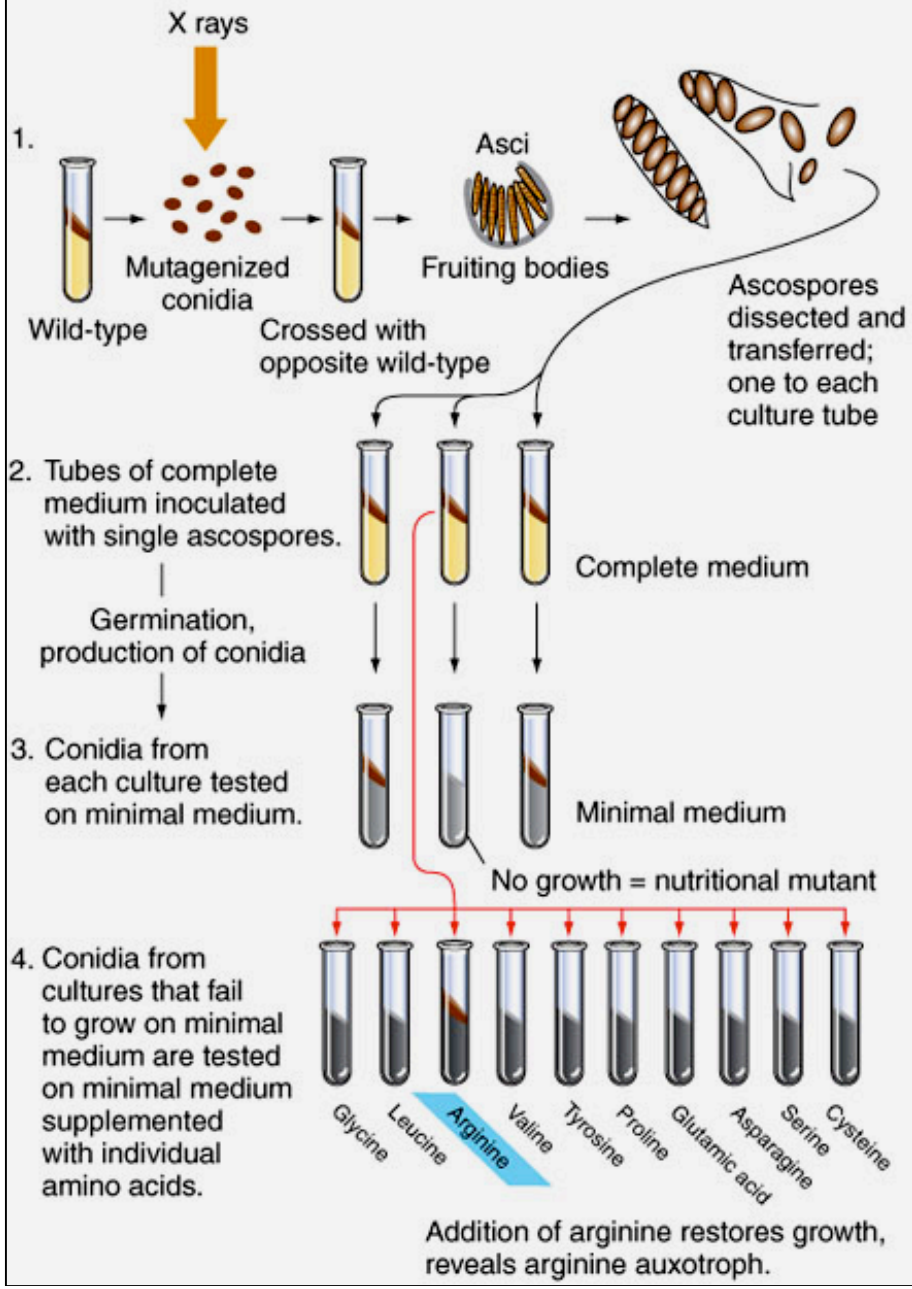
Double mutants

C2/a1: colourless-but uninformative
bz1/a1: colorless-a1 comes before bz1
bz2/a1: colorless-a1 comes before bz2

For biosynthetic pathways, the phenotype of the earlier gene in the pathway shows in the double mutant.
ie. the earlier-step mutant is epistatic to the late-step mutant

Determine relationship between a1 and c2 by feeding experiment:
add flavanone (naringenin): c2+naringenin = red
a1+naringenin = colorless

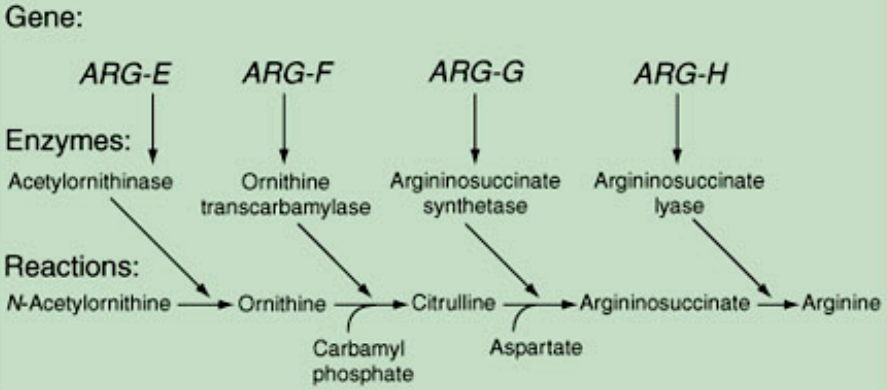
Fig. 7.20 Biochemical Pathways



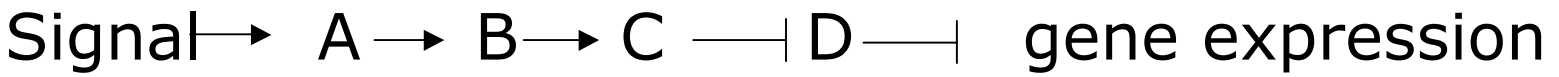
(b) Growth response if nutrient is added to minimal medium

Mutant strain	Supplements: Nothing	Ornithine	Citrulline	Arginino-succinate	Arginine
Wildtype: *Arg*$^+$	+	+	+	+	+
Arg-E$^-$	–	+	+	+	+
Arg-F$^-$	–	–	+	+	+
Arg-G$^-$	–	–	–	+	+
Arg-H$^-$	–	–	–	–	+

(c) Inferred biochemical pathway



B. Regulatory pathways



→ Positive action-stimulate next step.
Null mutation makes insensitive to signal

⊣ Negative action-represses next step.
Null mutation makes the gene turned on at all time (constitutively)

b^-: gene expression never turned on
even in the presence of the signal

d^-: gene expression constitutively on
even in the absence of signal

$b^-d^- = d^-$: constitutively on

For regulatory pathways, the phenotype of the later-acting genes shows in the double mutant.
ie. the later-acting mutant is epistatic to the earlier-acting mutant

wt wt *ctr1 ein2*

ethylene air air ethylene

ctr ein2 :?

Ethylene ⊣ CTR1 (Kinase) ⊣ EIN2 → triple response

For regulatory pathways, the phenotype of the later-acting genes shows in the double mutant.

ie. the later-acting mutant is epistatic to the earlier-acting mutant

C. Additive pathways

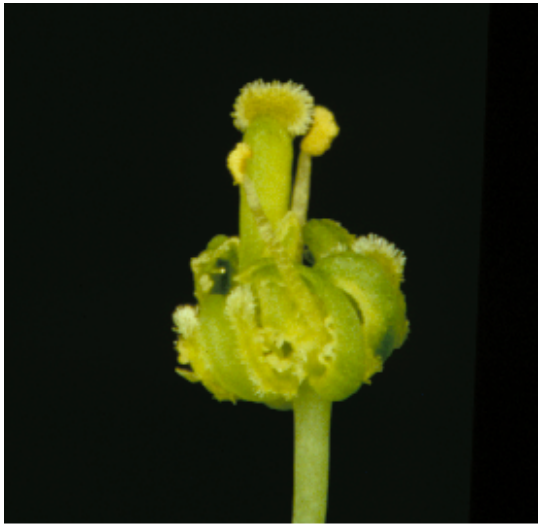
Double mutants of dissimilar phenotypes produce a combination of both phenotypes

Indicate that the two mutations are in genes acting in separate pathways

ap2-2 (flower abnormal) X *gl* (no trichome)

ap2-2 gl double mutant
abnormal flower and no trichome

ap2-2



gl1

D. Synergistic interactions (enhancement)

Two genes may act at the same step of a pathway

Or in parallel or (redundant) pathways


ap1-1


WT


ap1-1 cal-1


ap1-1 cal-1

E. Suppression

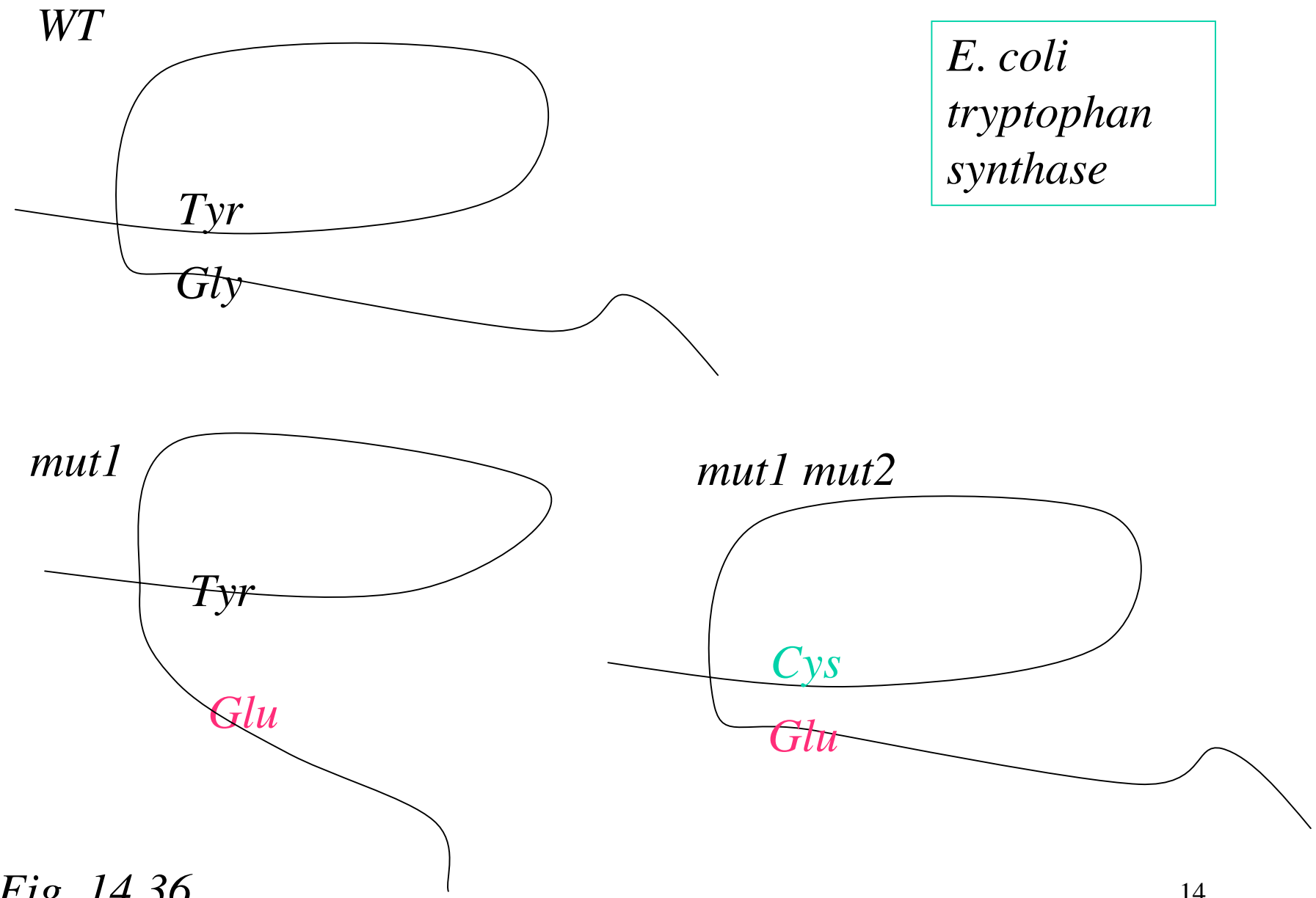
Intrgenic suppressors

Extragenic suppressors

Allele-specific suppression

Suppressors are defined classically as mutations that correct the phenotypic defects of another mutation without restoring its wild-type sequence. Suppressors may be intragenic (affecting the same gene) or they may be extragenic (affecting a different gene).

Intragenic suppressors



E. coli tryptophan synthase

Fig. 14.36

Intragenic suppressor

Frameshift mutation caused by a single base insertion can be suppressed by a second mutation that cause a single base deletion downstream from the first mutation.
See Fig. 10.27-10.28 and p 428-429

Extragenic suppressors

Mutation in one gene could correct the effect of a mutation in another gene

Nonsense (information) suppressor

Mutations in genes whose protein products interact

Nonsense (information) suppressors

In c. elegans, eight suppressors encode identical tRNAs in which a single C→T substitution changes the anticodon of a tRNATrp gene from 5′ -CCA-3′ to 5′ -CUA-3′ . The anticodon change thus allows mutant tRNAs to read the amber codon UAG.

Extragenic suppressors

Particularly useful during genetic analyses, because they often identify additional components of a biological system or process.