Η έννοια του γονιδίου

Σταύρος Ιωαννίδης
ΙΦΕ/ΕΚΠΑ


GREGORIO J.
MENDEL
1884
1984
450
POSTE VATICANE
I.P.Z.S.-ROMA-1984
M. CODONI

Αναμειγνυόμενη κληρονομικότητα (blending inheritance)

Verhandlungen

des

naturforschenden Vereines

in Brünn.

IV. Band

1865.

Brünn, 1866.

Im Verlage des Vereines.

Versuche über Pflanzen-Hybriden.

Von

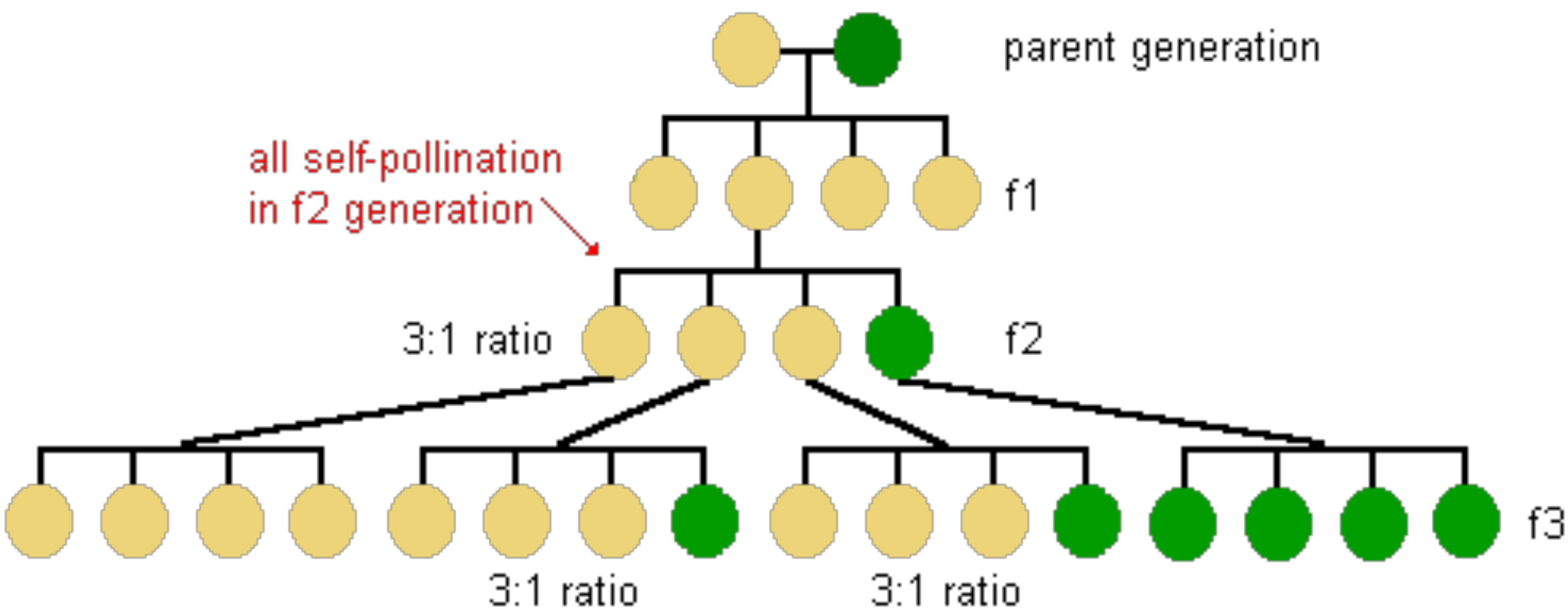
Gregor Mendel.

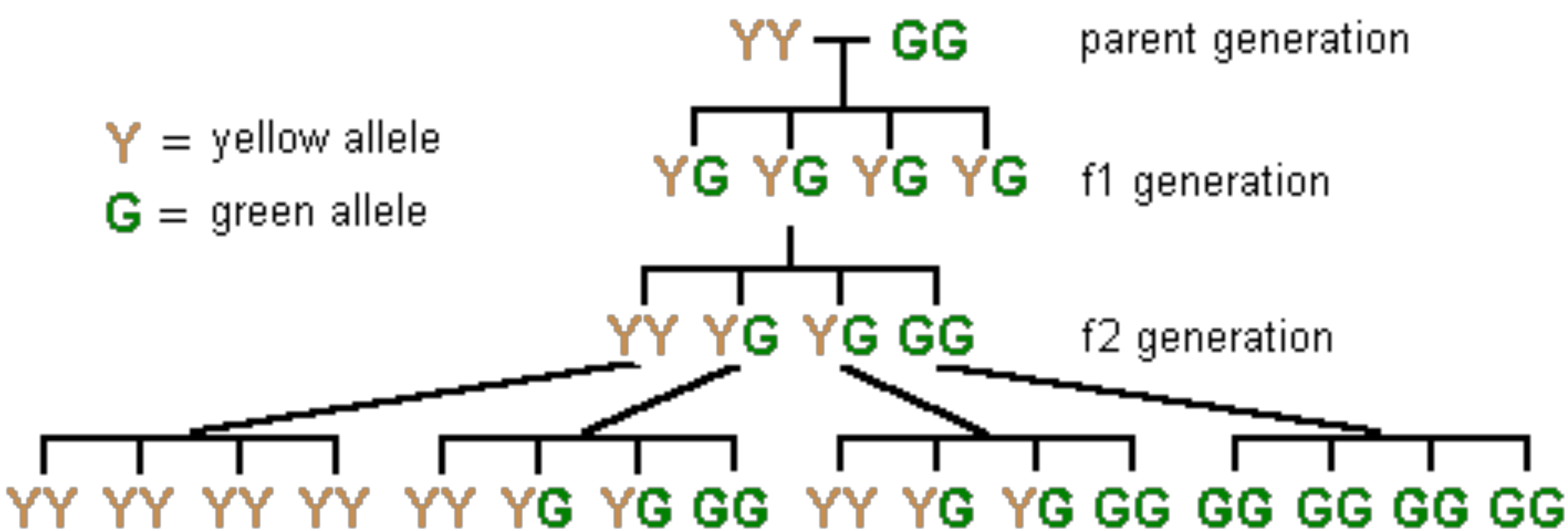
(Vorgelegt in den Sitzungen vom 8. Februar und 8. März 1865.)

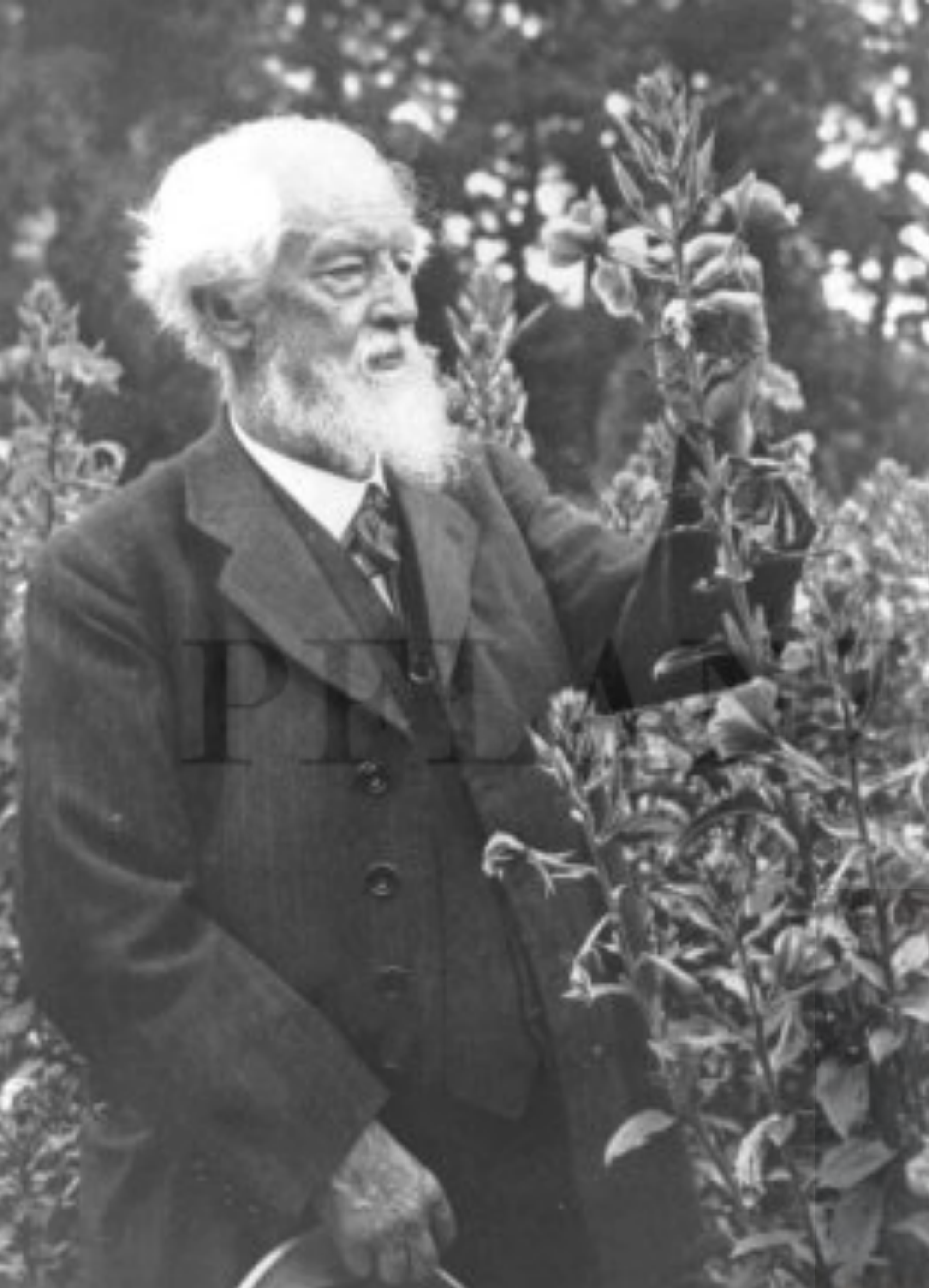
Einleitende Bemerkungen.

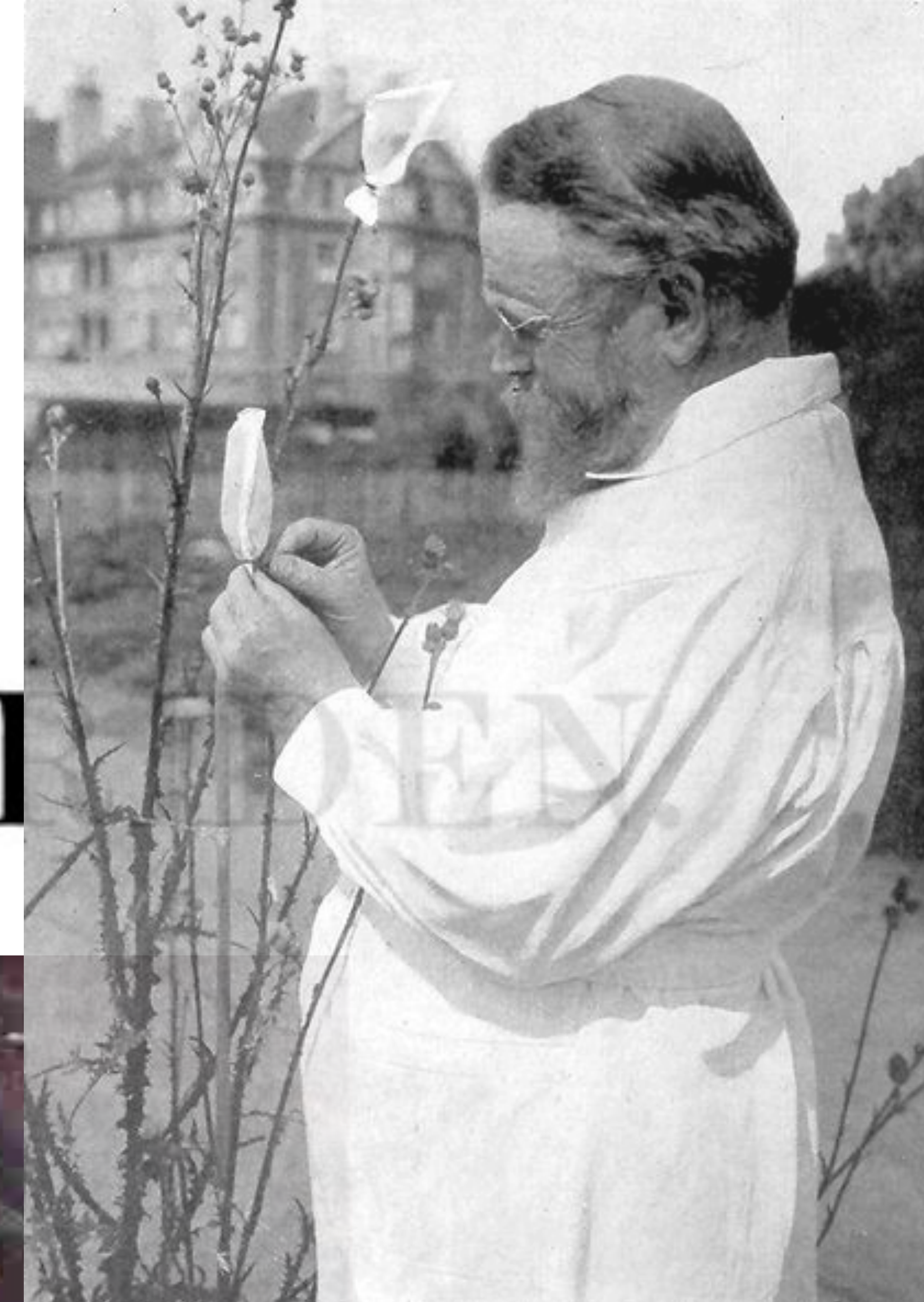
Künstliche Befruchtungen, welche an Zierpflanzen desshalb vorgenommen wurden, um neue Farben-Varianten zu erzielen, waren die Veranlassung zu den Versuchen, die her besprochen werden sollen. Die auffallende Regelmässigkeit, mit welcher dieselben Hybridformen immer wiederkehrten, so oft die Befruchtung zwischen gleichen Arten geschah, gab die Anregung zu weiteren Experimenten, deren Aufgabe es war, die Entwicklung der Hybriden in ihren Nachkommen zu verfolgen.

Dieser Aufgabe haben sorgfältige Beobachter, wie Kölreuter, Gärtner, Herbert, Lecocq, Wichura u. a. einen Theil ihres Lebens mit unermüdlicher Ausdauer geopfert. Namentlich hat Gärtner in seinem Werke „die Bastarderzeugung im Pflanzenreiche“ sehr schätzbare Beobachtungen niedergelegt, und in neuester Zeit wurden von Wichura gründliche Untersuchungen über die Bastarde der Weiden veröffentlicht. Wenn es noch nicht gelungen ist, ein allgemein giltiges Gesetz für die Bildung und Entwicklung der Hybriden aufzustellen, so kann das Niemanden Wunder nehmen, der den Umfang der Aufgabe kennt und die Schwierigkeiten zu würdigen weiss, mit denen Versuche dieser Art zu kämpfen haben. Eine endgiltige Entscheidung kann erst dann erfolgen, bis Detail-Versuche aus den verschiedensten Pflanzen-Familien vorliegen. Wer die Ar-


parent generation
all self-pollination
in f2 generation
f1
3:1 ratio
f2
f3
3:1 ratio
3:1 ratio


YY GG
parent generation
Y = yellow allele
G = green allele
YG YG YG YG
f1 generation
YY YG YG GG
f2 generation
YY YY YY YY YY YG YG GG YY YG YG GG GG GG GG GG





Πάνω: de Vries
Δεξιά πάνω: Correns
Μέση κάτω: Tschermak

GREGOR MENDEL, 1866

Enlarged from a group of the brethren of the Königskloster

MENDEL'S

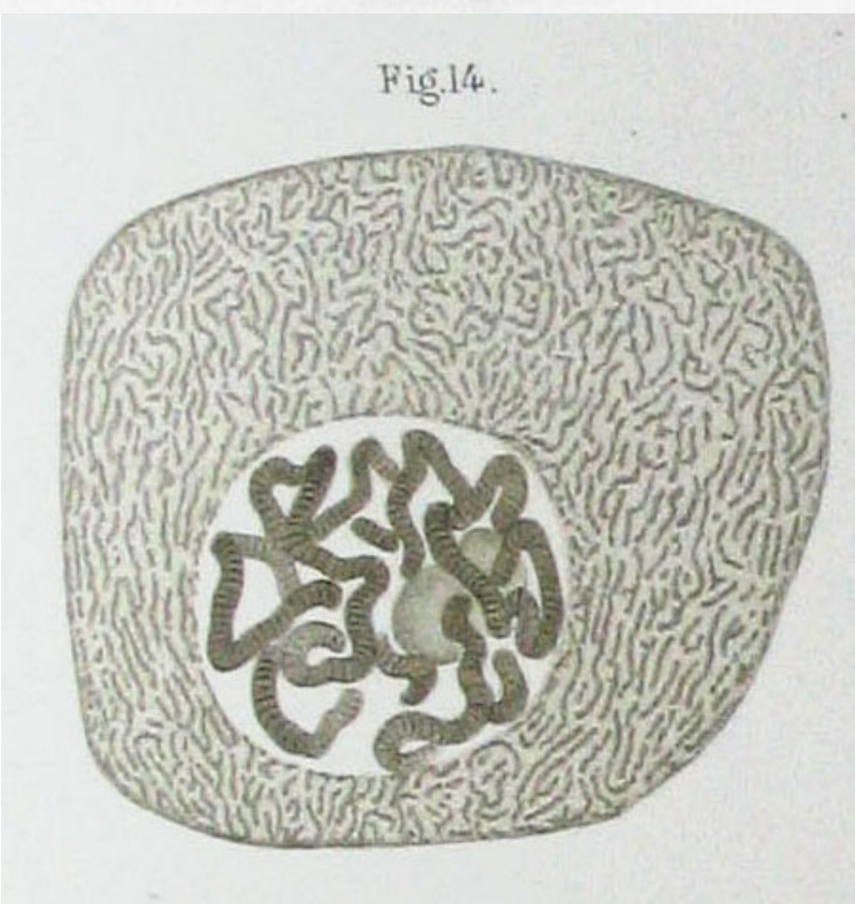
PRINCIPLES OF HEREDITY

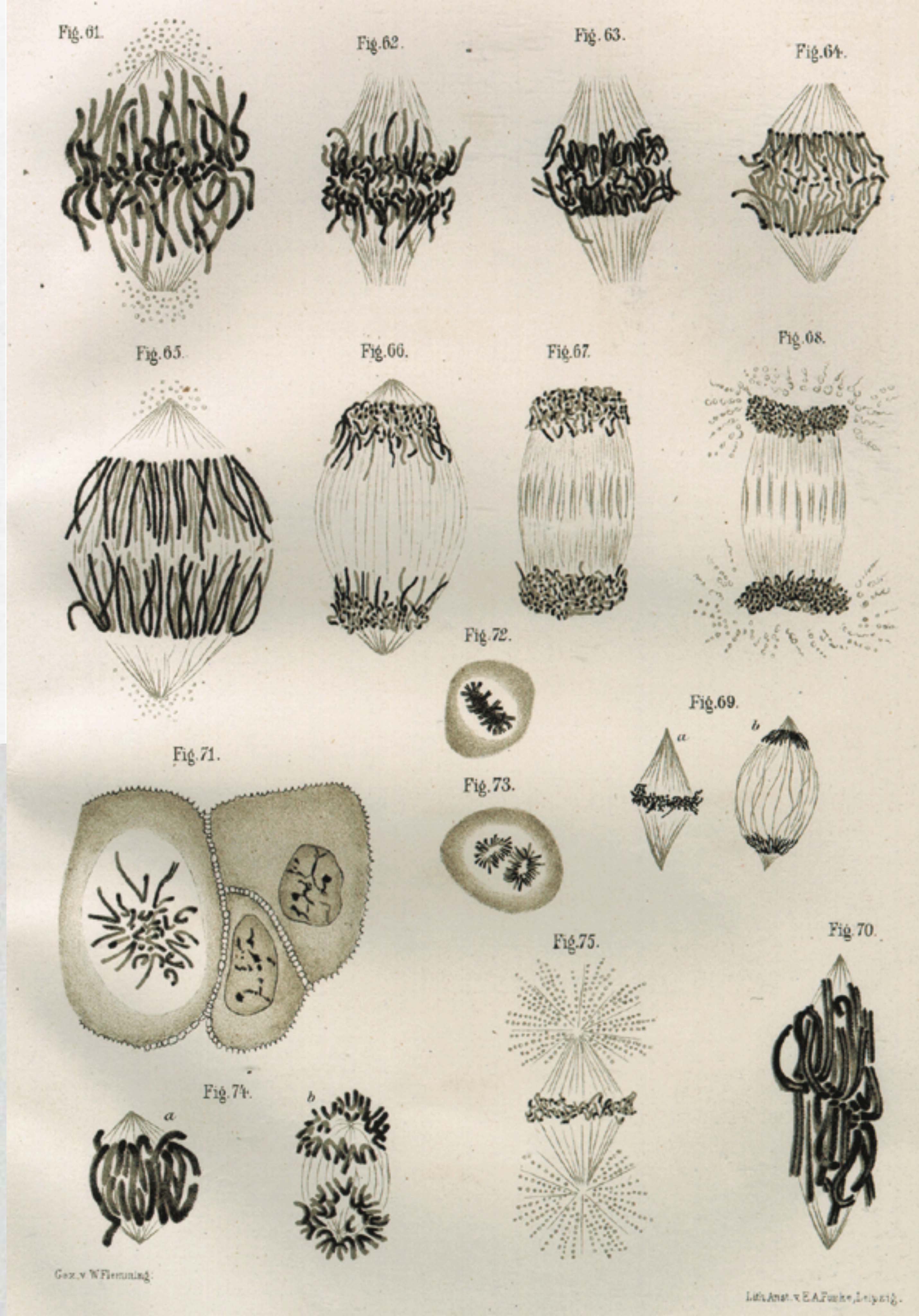
BY

W. BATESON, M.A., F.R.S., V.M.H.

HONORARY FELLOW OF ST JOHN'S COLLEGE,
DIRECTOR OF THE JOHN INNES HORTICULTURAL INSTITUTION

Cambridge:
at the University Press
1913





Αριστερά: Walther Flemming
Αριστερά κάτω: Πολυταινικά χρωμοσώματα από κύτταρο από τους σιελογόνους αδένες του Chironimus
Μεγάλη εικόνα: η διαδικασία της μίτωσης — Εικόνες από το βιβλίο του Flemming *Zellsubstanz, Kern und Zelltheilung* (1885)

T. H. Morgan

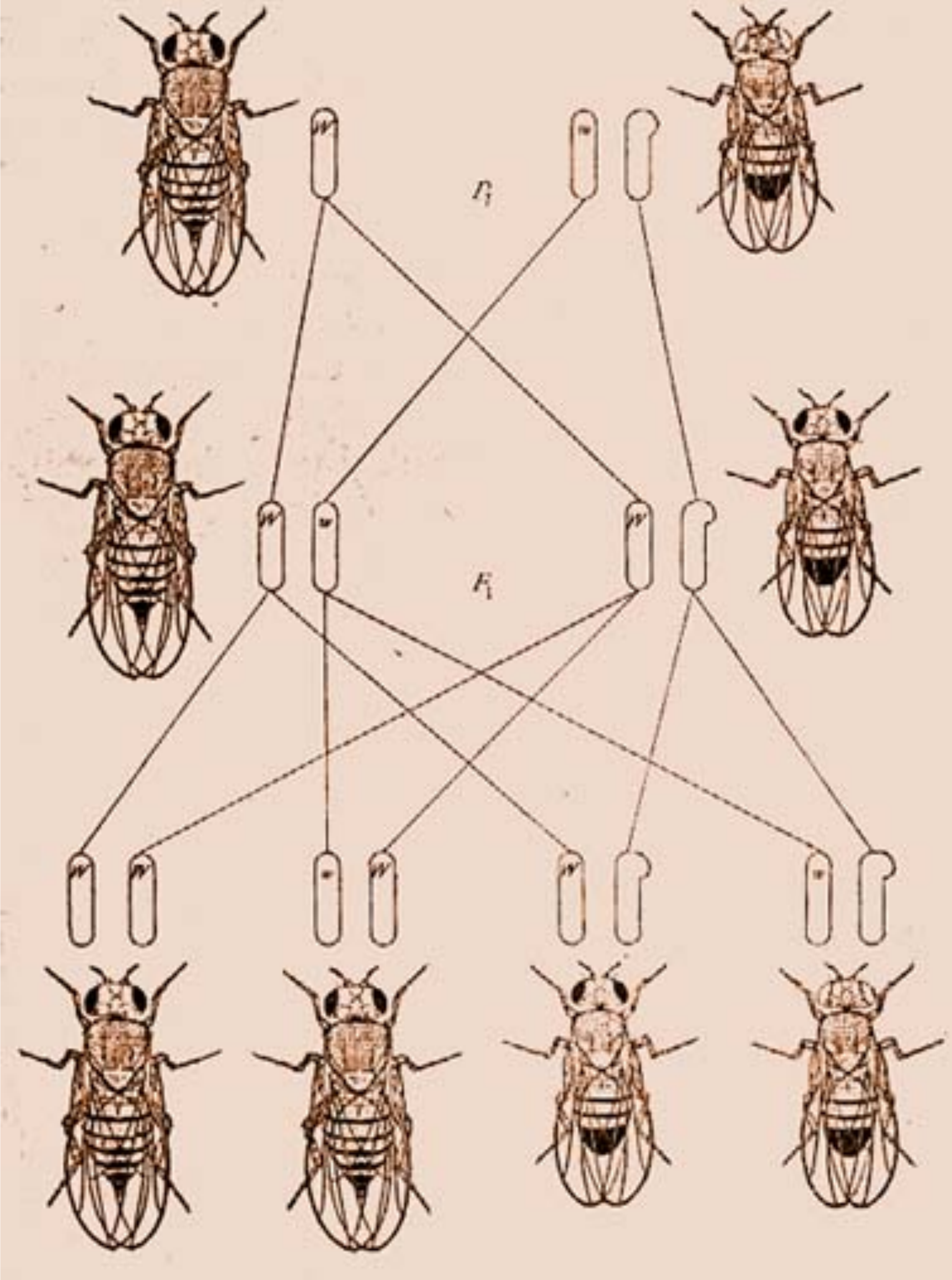
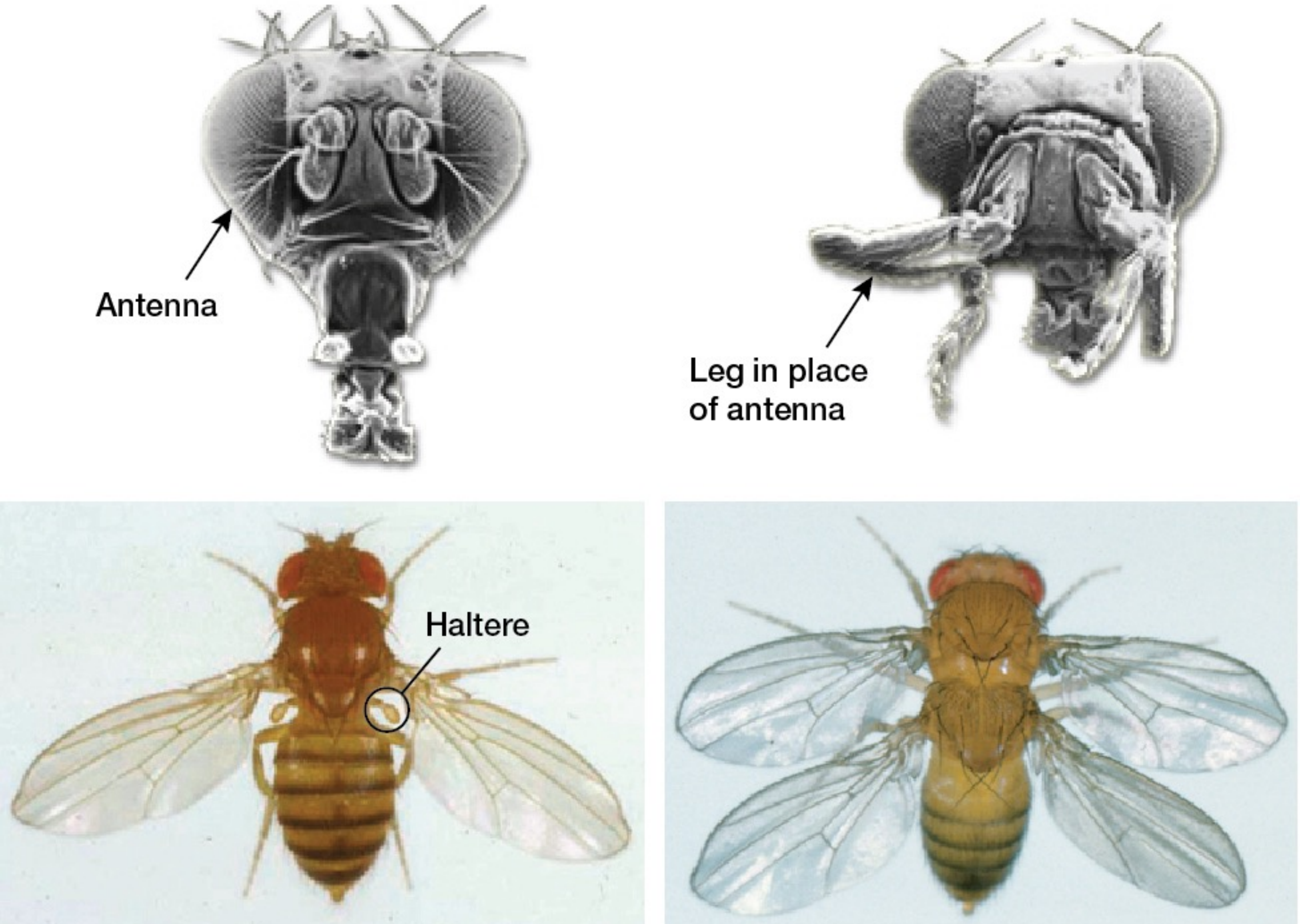


FIG. 9.—Red-eyed female by white-eyed male (D. melanogaster). This is the reciprocal of the cross shown in Fig. 10.

Αριστερά: Από Morgan, Sturtevant, Muller & Bridges (1915) *The Mechanism of Mendelian Heredity*
Πάνω: ο Morgan μπροστά από δροσόφιλες


White-eyed mutant fly
Red-eyed wild-type fly


Antenna
Leg in place of antenna
Haltere

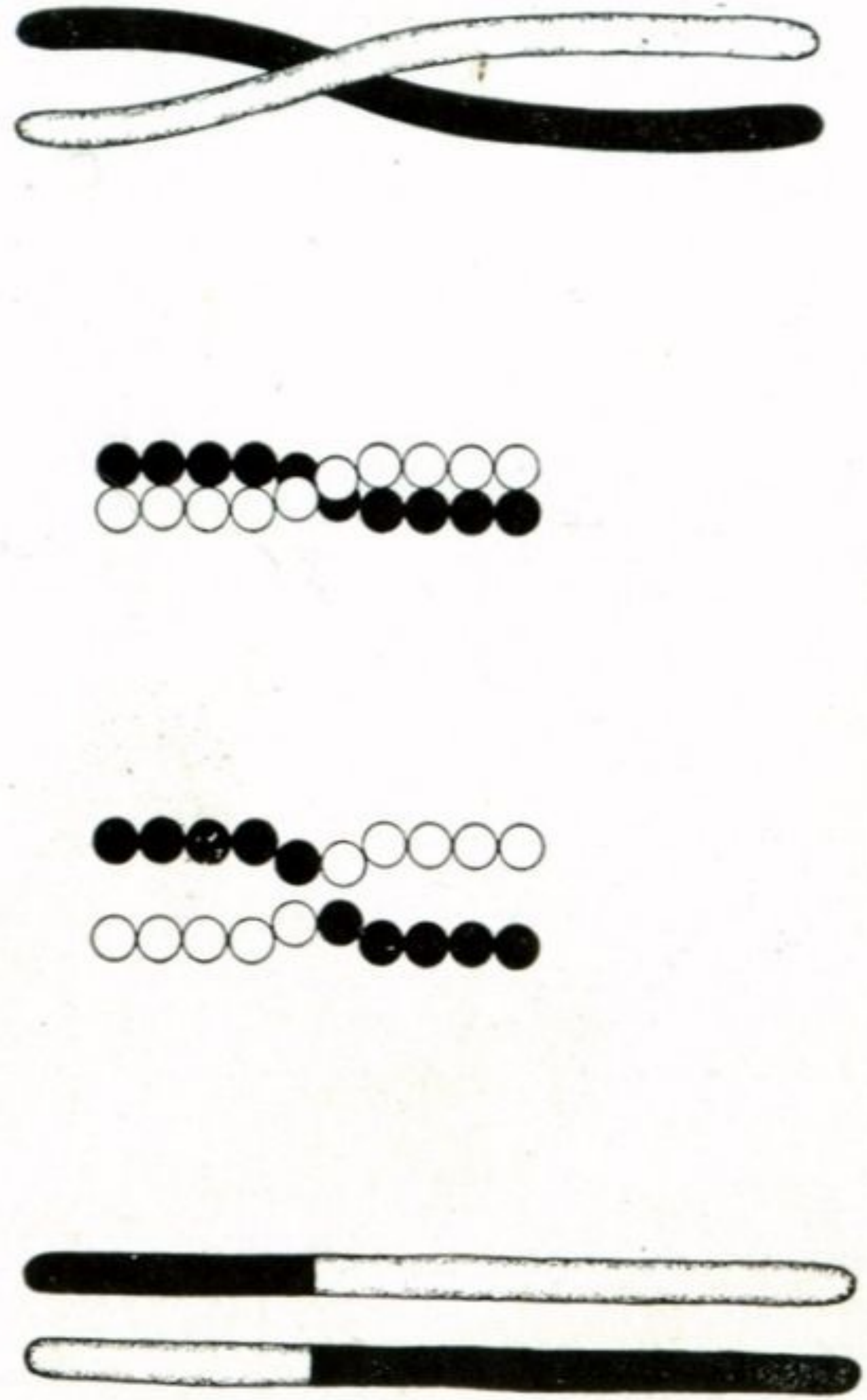
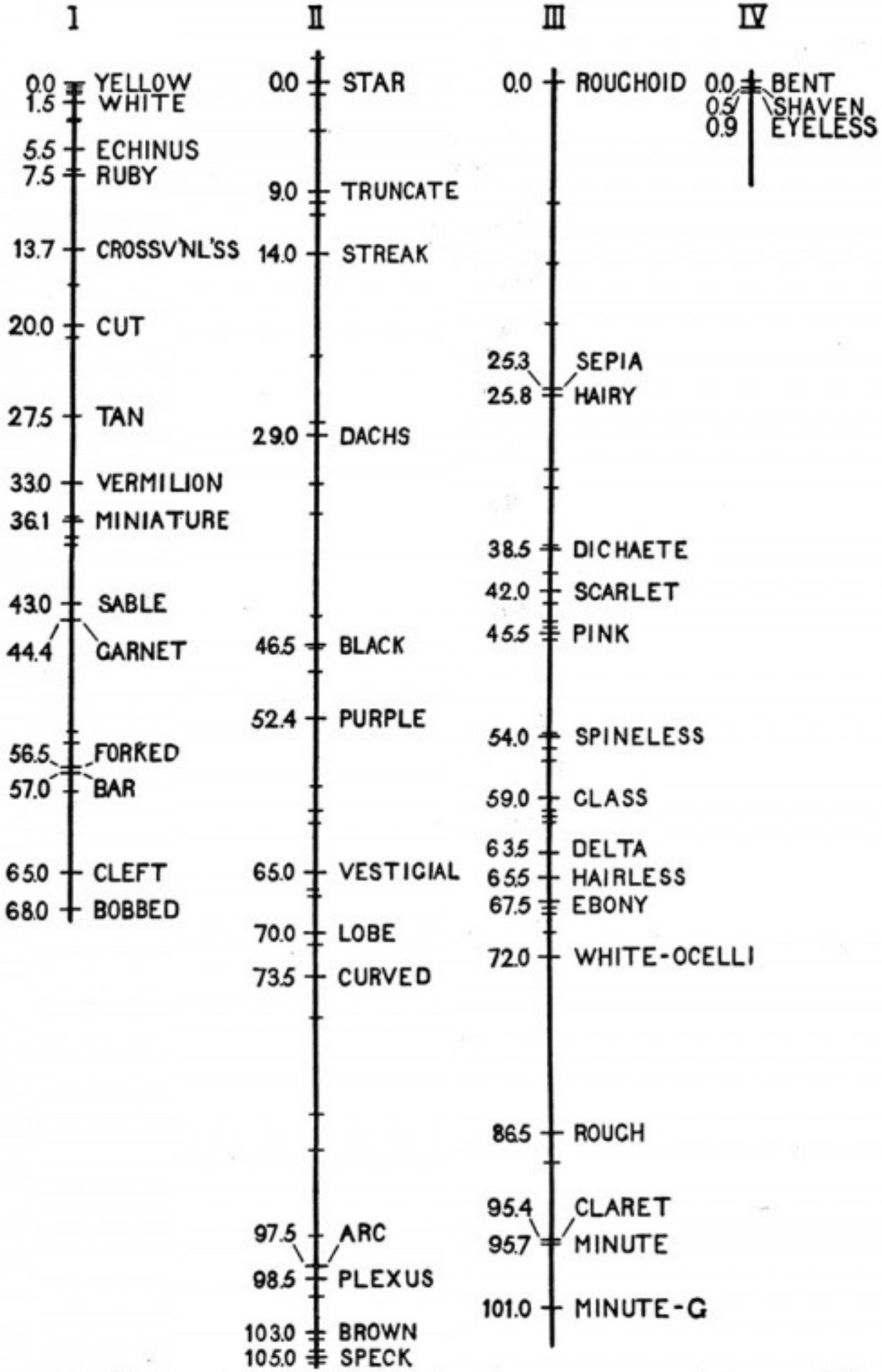
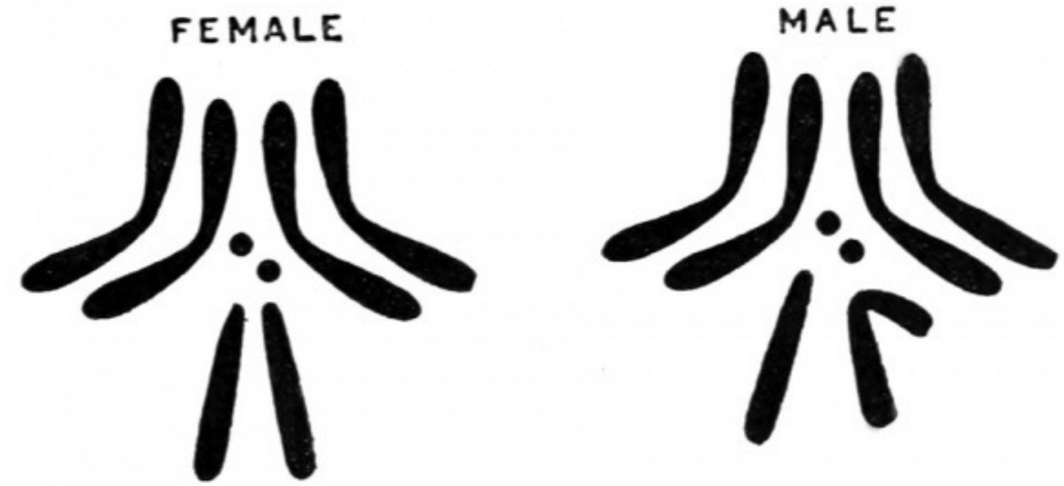
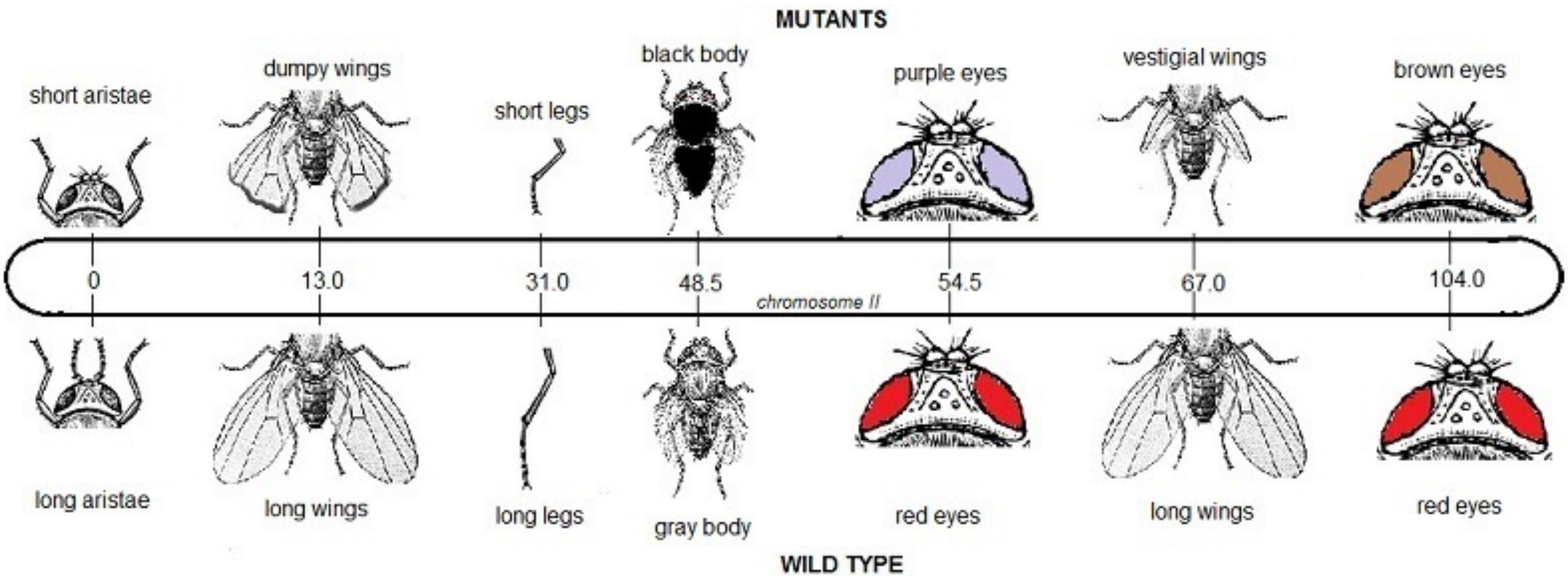


Fig. 64. Scheme to illustrate a method of crossing over of the chromosomes.

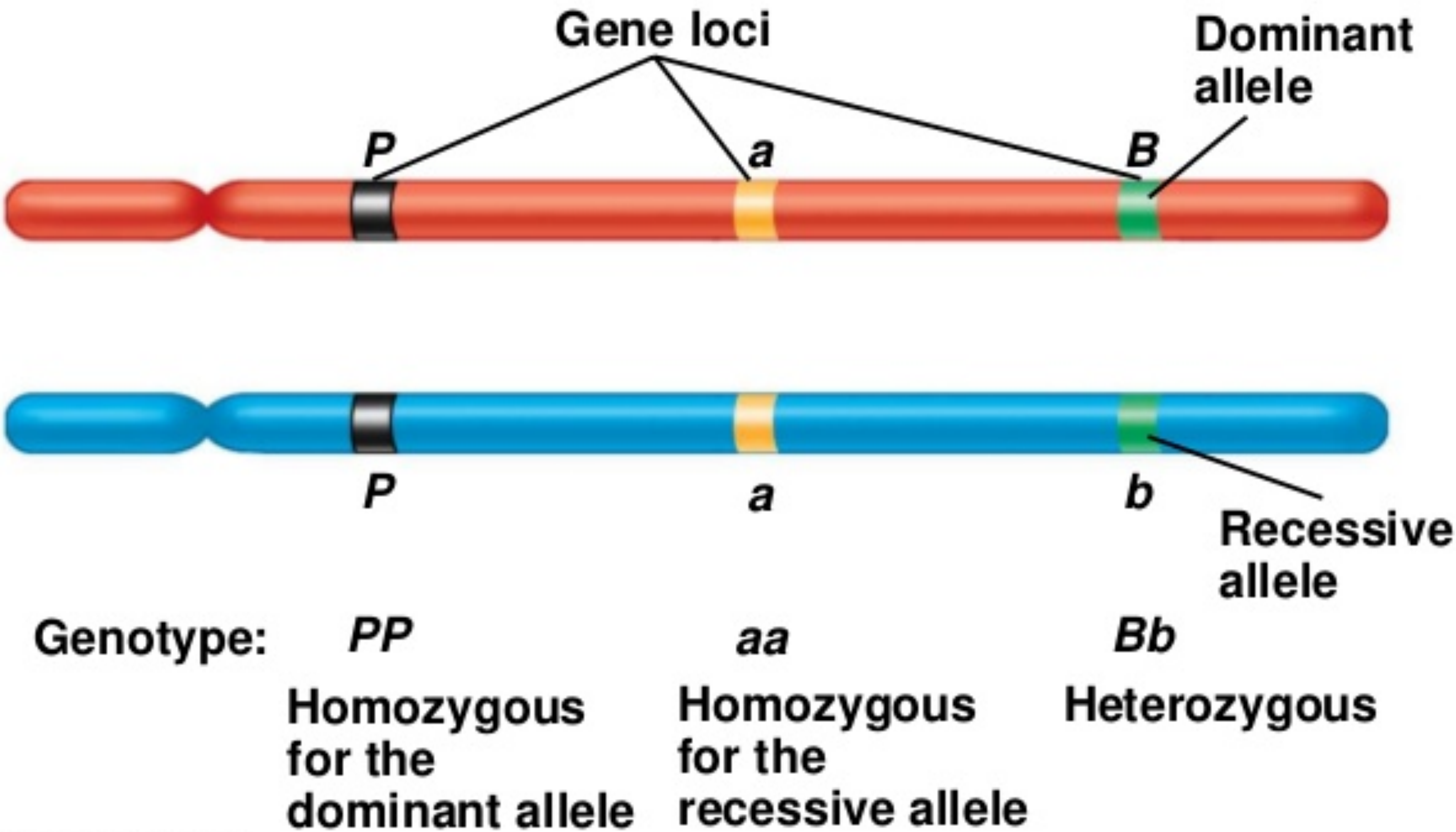




Αριστερά: Γονιδιακός χάρτης της Δροσόφιλας —τα νούμερα δείχνουν την απόσταση από το τέλος του χρωμοσώματος
Πάνω: τα 4 ζεύγη χρωμοσωμάτων



MUTANTS
short aristae
dumpy wings
short legs
black body
purple eyes
vestigial wings
brown eyes
0
13.0
31.0
48.5
54.5
67.0
104.0
chromosome II
long aristae
long wings
long legs
gray body
red eyes
long wings
red eyes
WILD TYPE


Gene loci
Dominant allele
P
a
B
P
a
b
Recessive allele
Genotype:
PP
aa
Bb
Homozygous for the dominant allele
Homozygous for the recessive allele
Heterozygous

-γονότυπος - φαινότυπος
-γονίδια πάνω σε χρωμοσώματα
-αλληλόμορφα -> εναλλακτικές μορφές ενός γονιδίου
-genetic locus

-> ένα γονίδιο μπορεί να επηρεάζει πολλούς φαινοτυπικούς χαρακτήρες (**πλειοτροπία / pleiotropy**)

[Morgan: 25 γονίδια επηρεάζουν το χρώμα ματιού στη Δροσόφιλα]

-> ένας φαινοτυπικός χαρακτήρας μπορεί να επηρεάζεται από πολλά γονίδια **polygeny**

Beadle & Tatum (1941) -> ‘one gene-one enzyme hypothesis’

-<u>τα γονίδια περί το 1950</u>:
φυσικά σωματίδια άγνωστης σύστασης, διατεταγμένα πάνω στα χρωμοσώματα, κληρονομούμενα σύμφωνα με τους νόμους του Mendel, και υπεύθυνα για την κατασκευή ενός ενζύμου

-> Το κλασικό γονίδιο ως ‘διαφοροποιητής’ (difference-maker)

Morgan:
Suppose, for instance, to take perhaps an extreme case, **all the genes** are instrumental in producing each organ of the body. This may only mean that they all produce chemical substances essential for the normal course of development

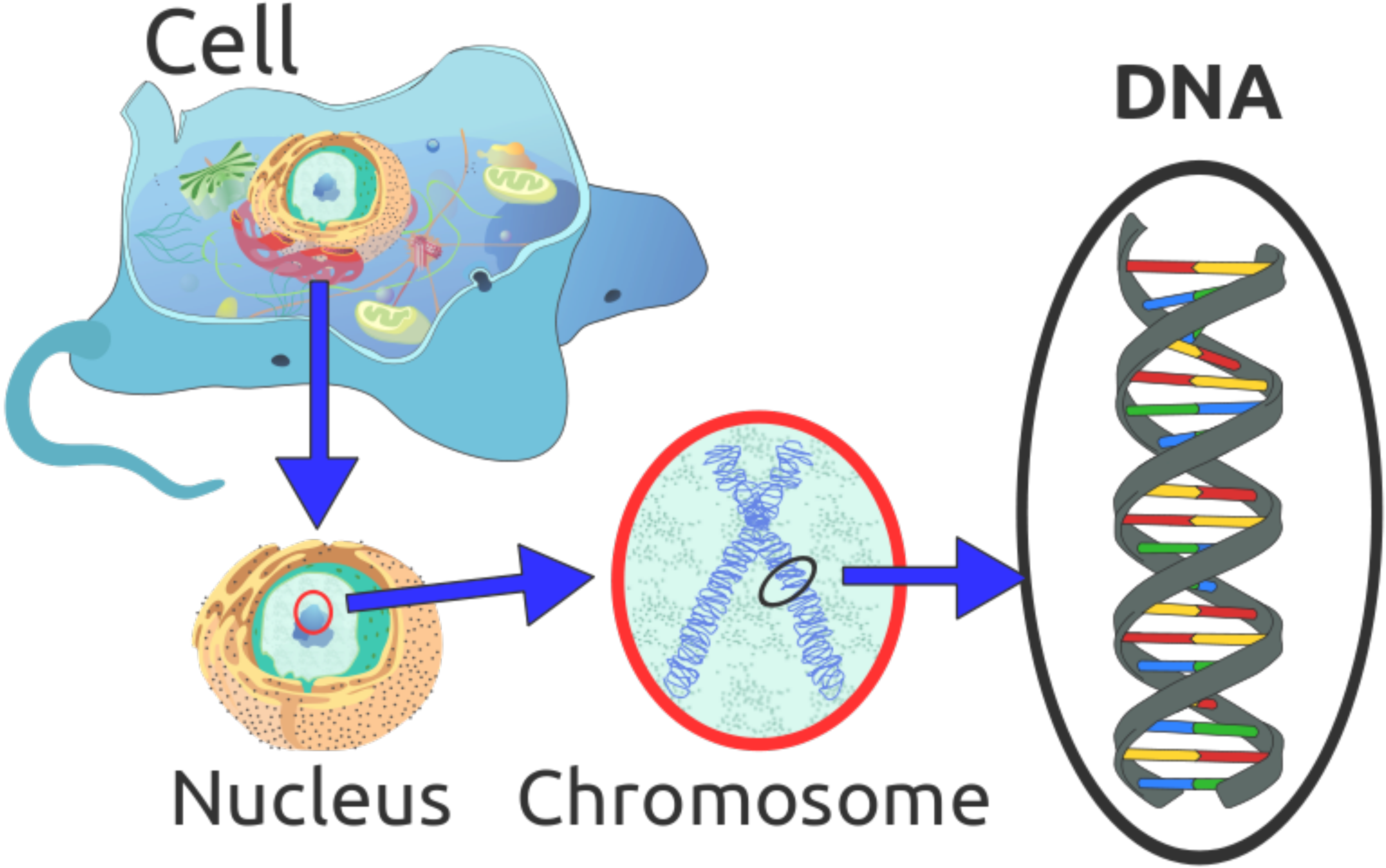
Morgan:
If now **one gene is changed** so that it produces some substance different from that which it produced before, the end-result may be **affected**, and if the change affects **one** organ predominatingly **it may appear the one gene alone has produced this effect**. In a strictly causal sense this is true, but the effect is produced only in conjunction with all the other genes. In other words, they are all still contributing, as before, to the end-result which is different in so far as one of them is different.

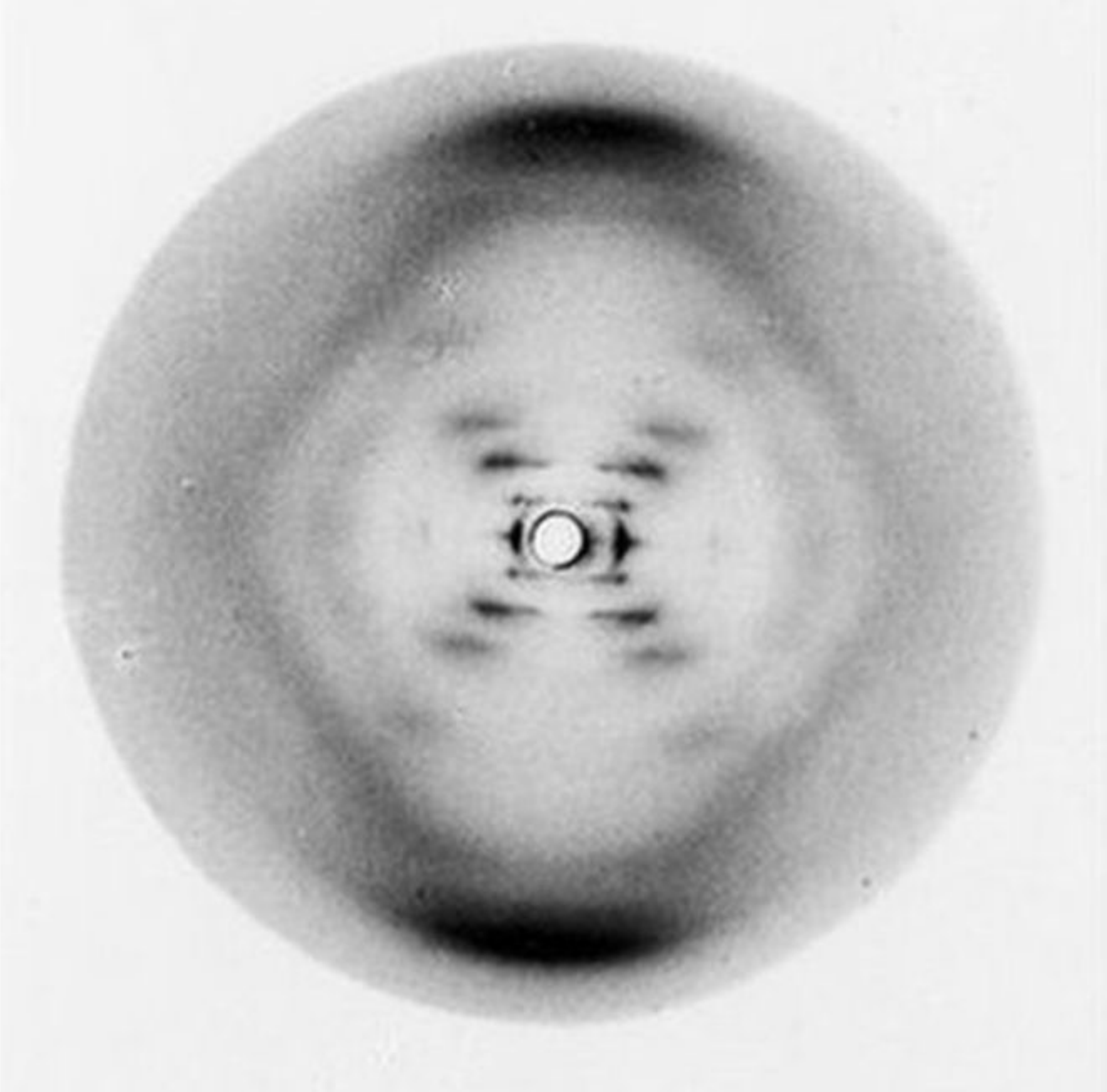
-Waters:
Difference principle: differences in a gene cause uniform phenotypic differences in particular genetic and environmental contexts.

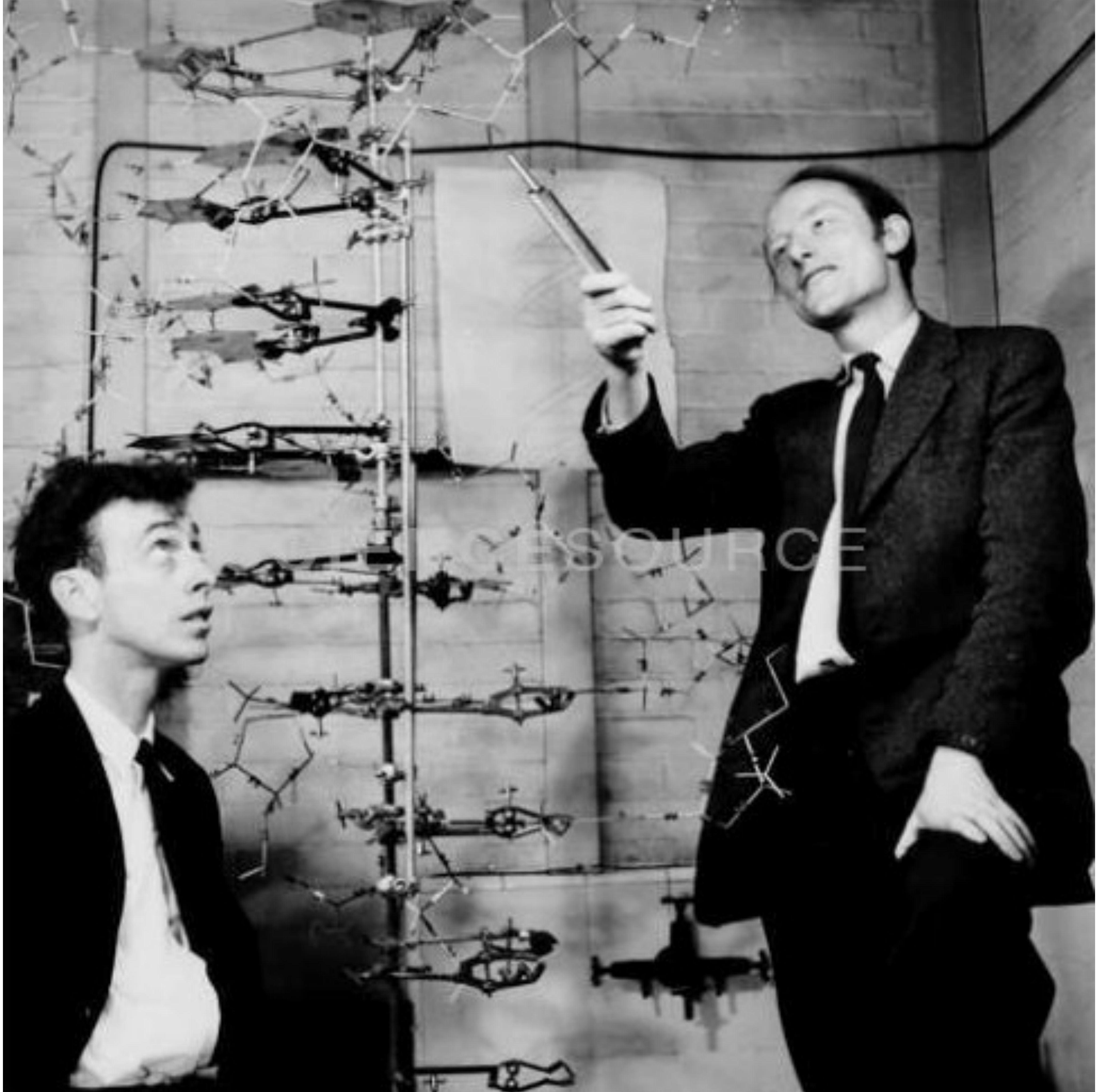
-> Το κλασικό γονίδιο ως θεωρητική οντότητα που εξηγεί δεδομένα διασταυρώσεων
-υπάρχουν στην πραγματικότητα ή όχι;

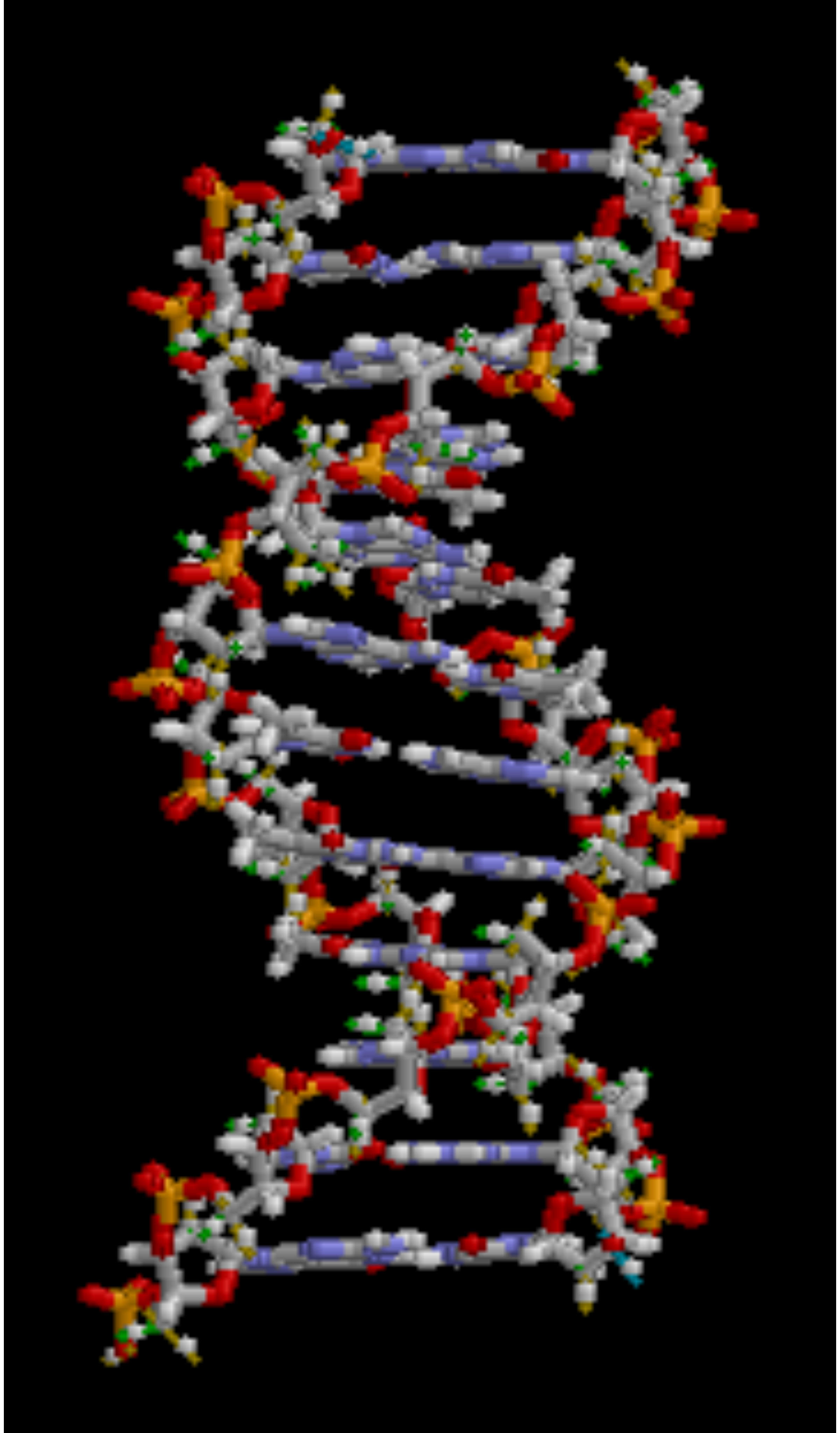
Δεν υπάρχει συμφωνία μεταξύ των γενετιστών για το αν τα γονίδια είναι πραγματικά ή υποθετικά, γιατί στο επίπεδο των πειραμάτων της γενετικής το γονίδιο μπορεί να κατανοηθεί είτε ως μια υποθετική μονάδα είτε ως ένα υλικό σωματίδιο χωρίς να υπάρχει καμία διαφορά.

Thomas Hunt Morgan, 1933


Cell
DNA
Nucleus
Chromosome







equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Discovery II* for their part in making the observations.

[1] Young, F. B., Gerrard, H., and Jevons, W., *Phil. Mag.*, **40**, 149 (1920).

[2] Longuet-Higgins, M. S., *Mon. Not. Roy. Astro. Soc., Geophys. Supp.*, **5**, 285 (1949).

[3] Von Arx, W. S., Woods Hole Papers in Phys. Oceanog. Meteor., **11** (3) (1950).

[4] Ekman, V. W., *Arkiv. Mat. Astron. Fysik. (Stockholm)*, **2** (11) (1905).

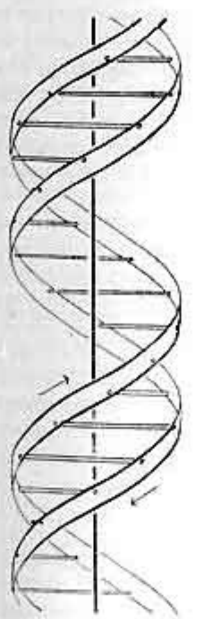
MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

We wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.



This figure is purely diagrammatic. The two ribbons symbolize the two phosphate—sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining β-D-deoxyribofuranose residues with 3′,5′ linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's[2] model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There is a residue on each chain every 3·4 A. in the z-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 A. The distance of a phosphorus atom from the fibre axis is 10 A. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally[3,4] that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data[5,6] on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

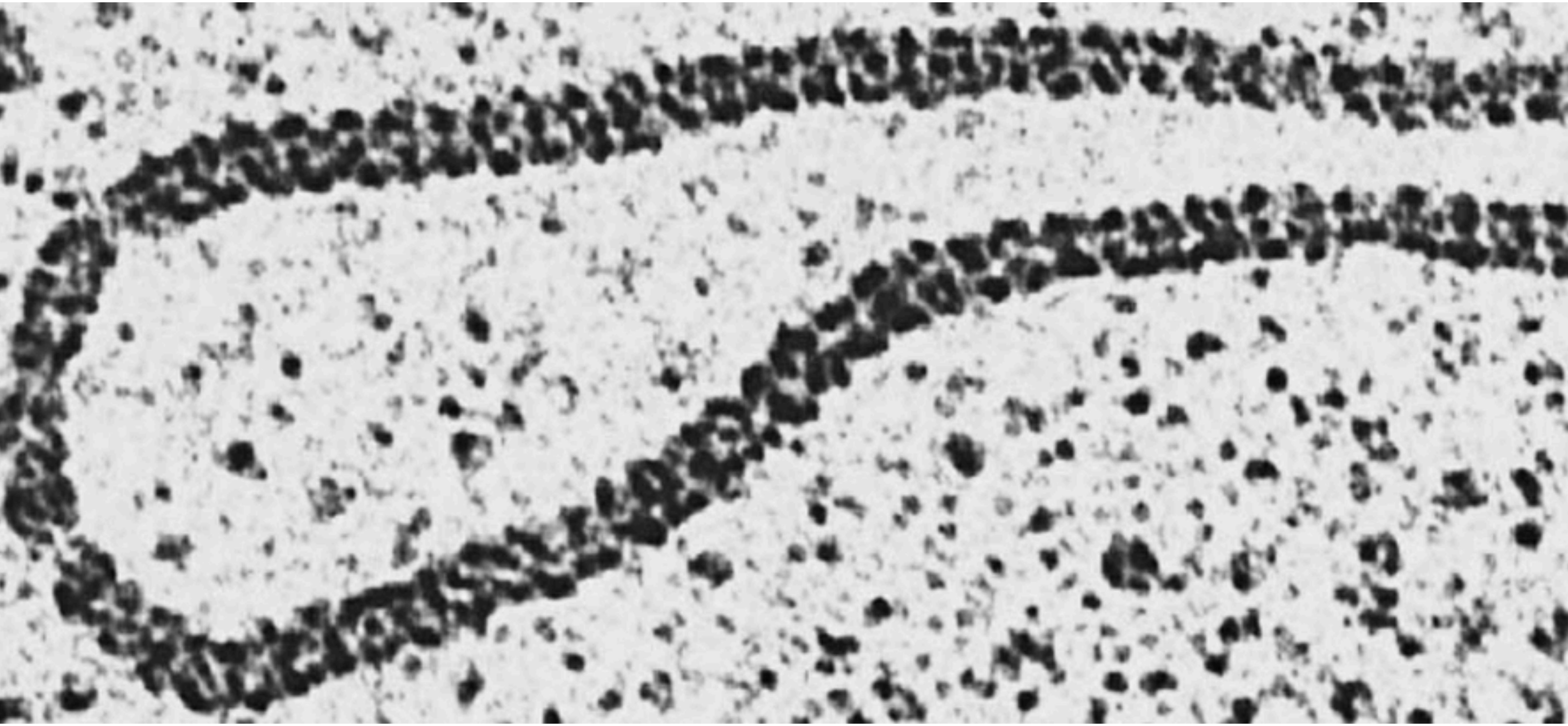
It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at

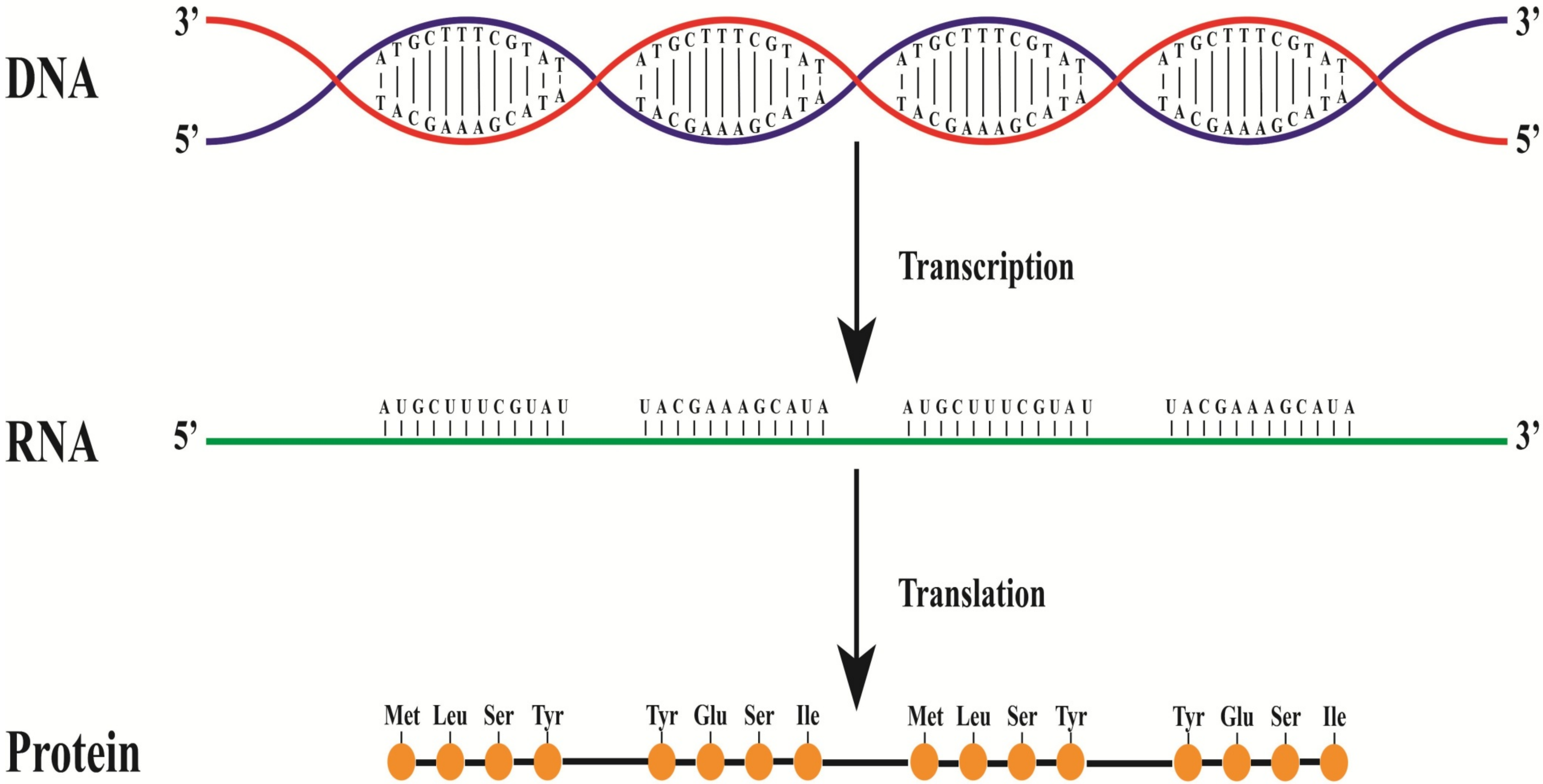
Nobel Prize in Physiology or Medicine (1962) -Crick, Watson & Wilkins

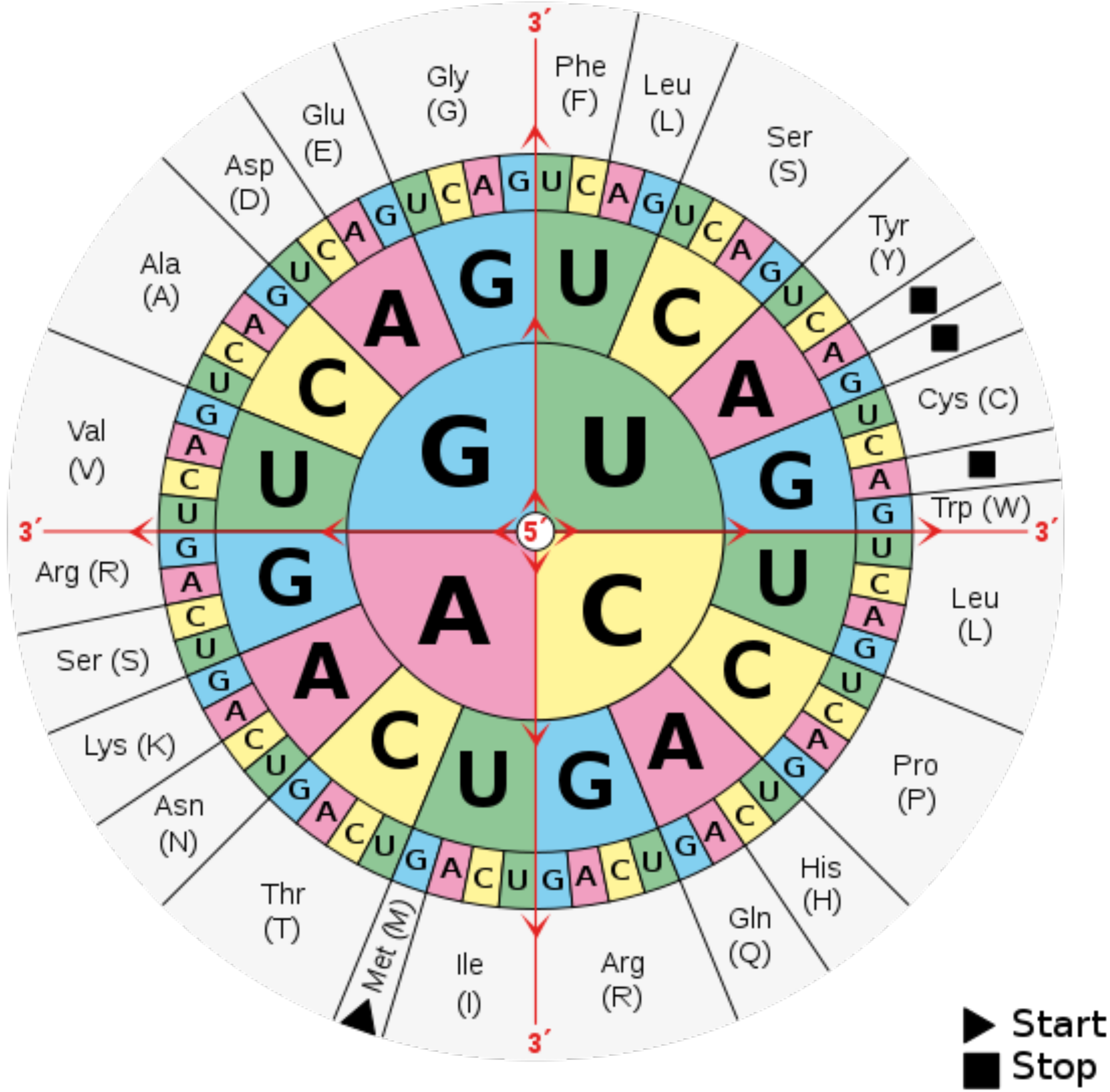
"for their discoveries concerning the **molecular structure of nucleic acids** and its significance for **information transfer in living material**"



-> το μοριακό γονίδιο (δεκαετία του ’60)

-> Crick: ‘sequence hypothesis’





5′
3′
3′
3′
3′
Phe (F)
Leu (L)
Ser (S)
Tyr (Y)
Cys (C)
Trp (W)
Leu (L)
Pro (P)
His (H)
Gln (Q)
Arg (R)
Ile (I)
Met (M)
Thr (T)
Asn (N)
Lys (K)
Ser (S)
Arg (R)
Val (V)
Ala (A)
Asp (D)
Glu (E)
Gly (G)
Start
Stop

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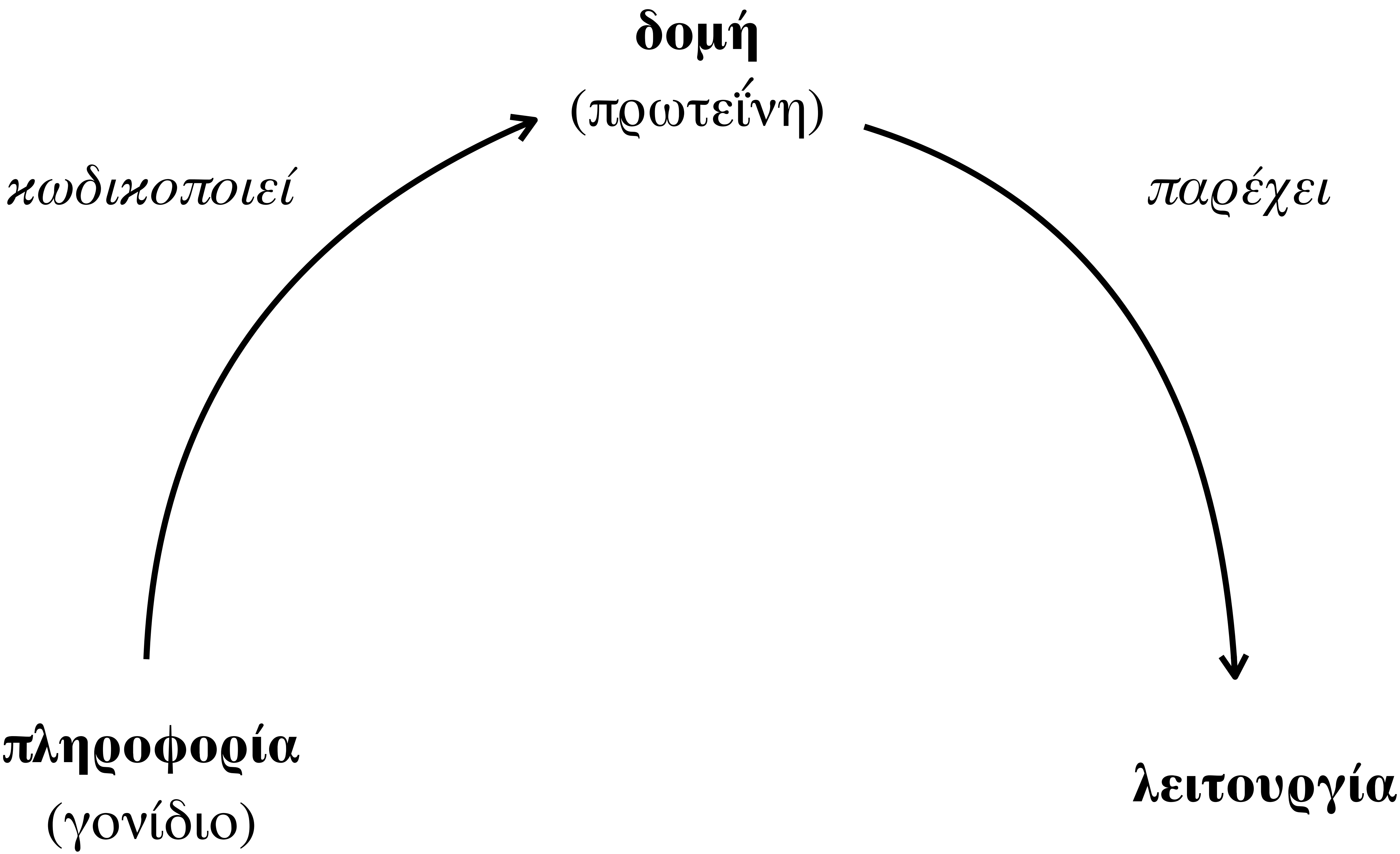
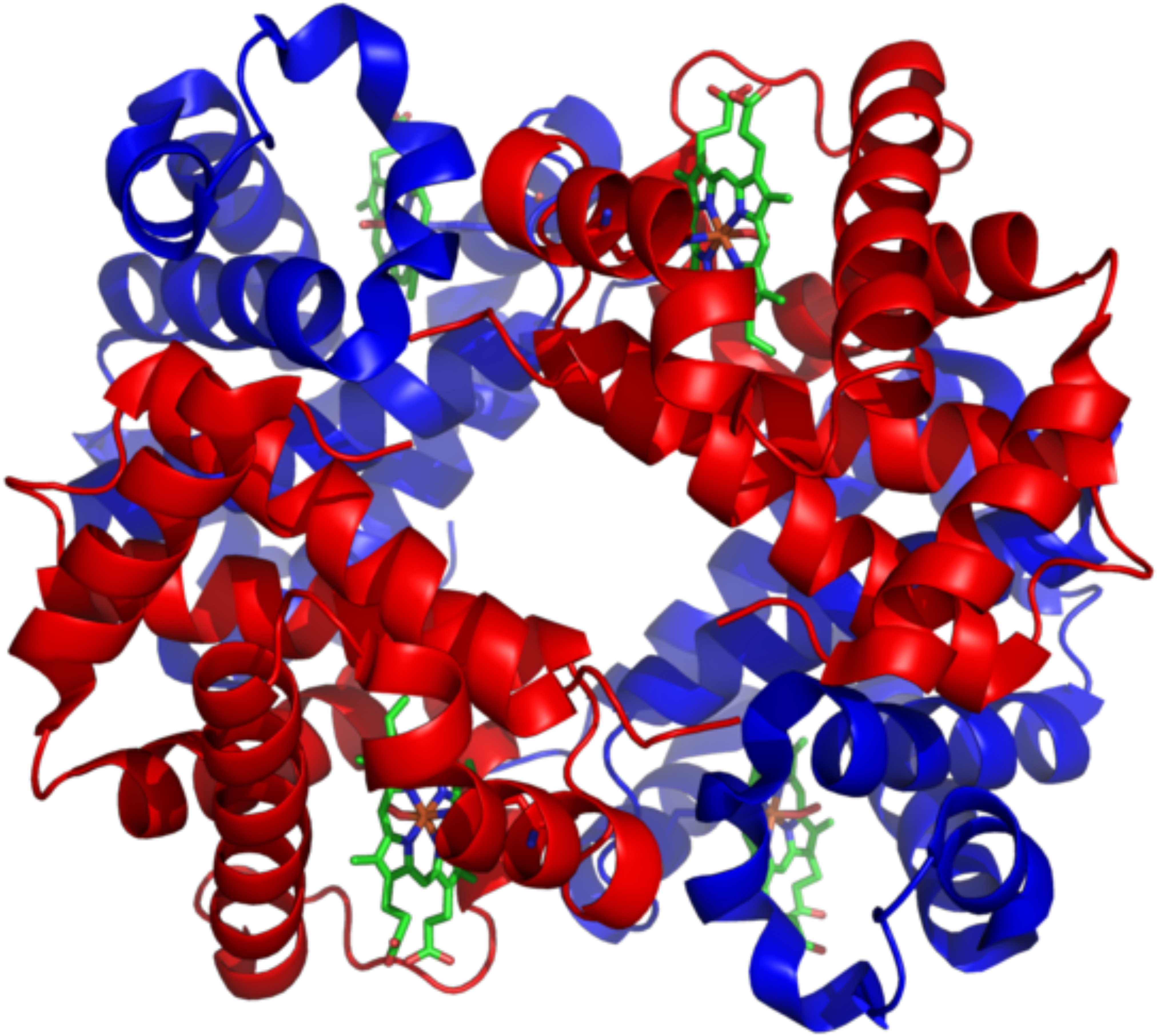

δομή
(πρωτεΐνη)
κωδικοποιεί
παρέχει
πληροφορία
(γονίδιο)
λειτουργία

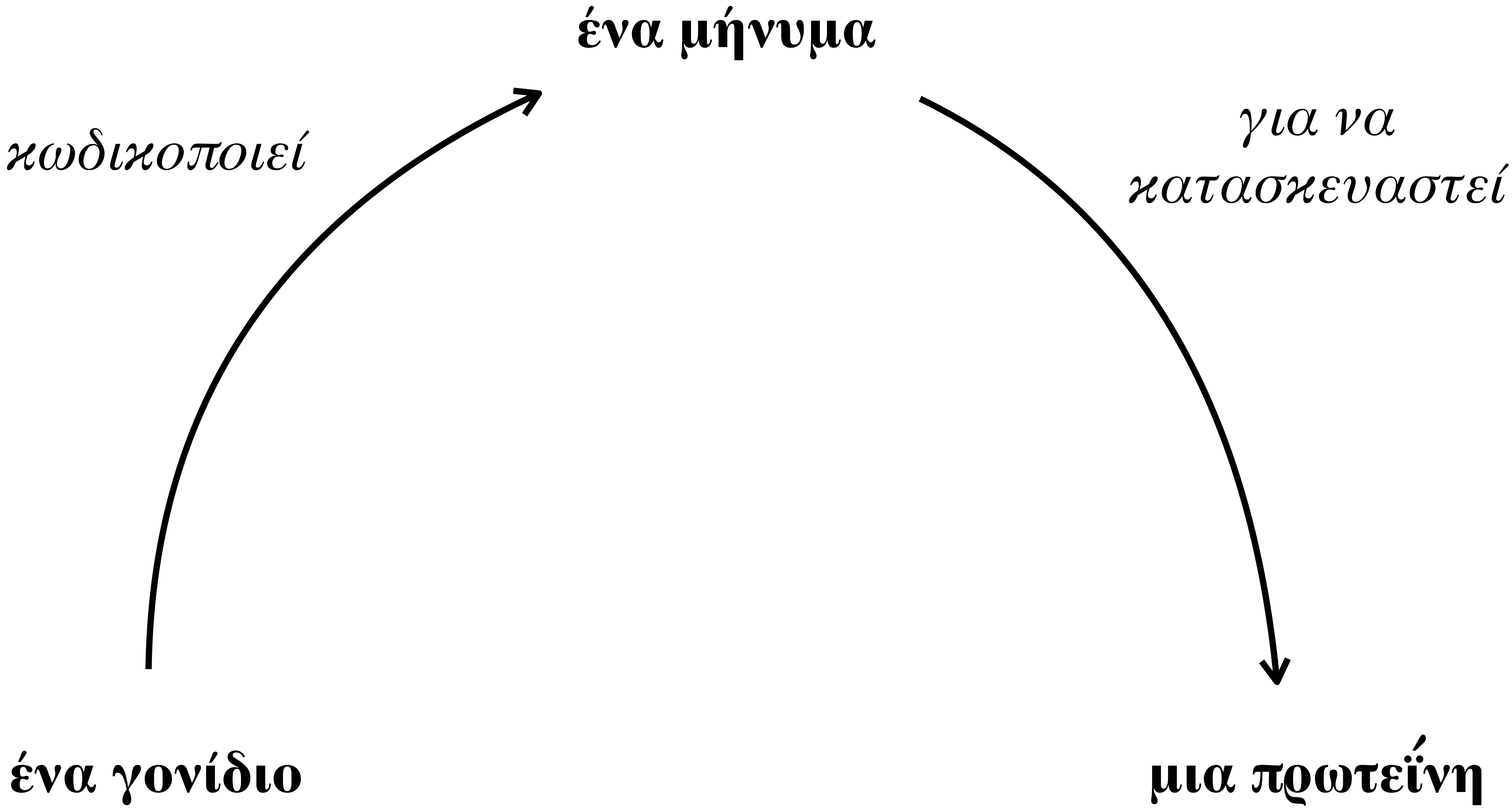


Το κεντρικό δόγμα της μοριακής βιολογίας

RNA

DNA

πρωτεΐνη


ένα μήνυμα
κωδικοποιεί
για να
κατασκευαστεί
ένα γονίδιο
μια πρωτεΐνη


16 February 2001
Science
Vol. 291 No. 5507
Pages 1145–1434 $9
THE HUMAN GENOME
American Association for the Advancement of Science

GATCCCTGCC TGGGCTTTGC CTCTGCAGCC CCCCGCCCCA CAGGTTCACA CCTCGGGTCT
TCTCCACCGC TGCCACACGC CAGAGCCTGT AGCGGGGCCT CAGAGTCTGG GAGGTGGGAC
TCCTGCACCT CAGCCATCAT CAGACCCATG GGGCCACCCA GGGAACCTTG GCAGGGACCA
TTACCAGTGA CCTGCCGAGG CCCCGGACTC TGCCAGCCAG CTGTGCCGGC CACCCTGCCC
CGGACAGTGC CGGTTCATGT GGGAACTAGG GGACGATGTG GTTCTTCGCA TCTGATGATG
AAGGCCCTGG GCCACTTGGC ACGGGCGGGC GCTCCCGAGA TGGATATGAG GAGCCCCCTC
TGCCCAACTC CCAGAAAGGC CGAGGCTCTG CAGCGGGAGG AAGTCCTGCG ATGTCCTGGG
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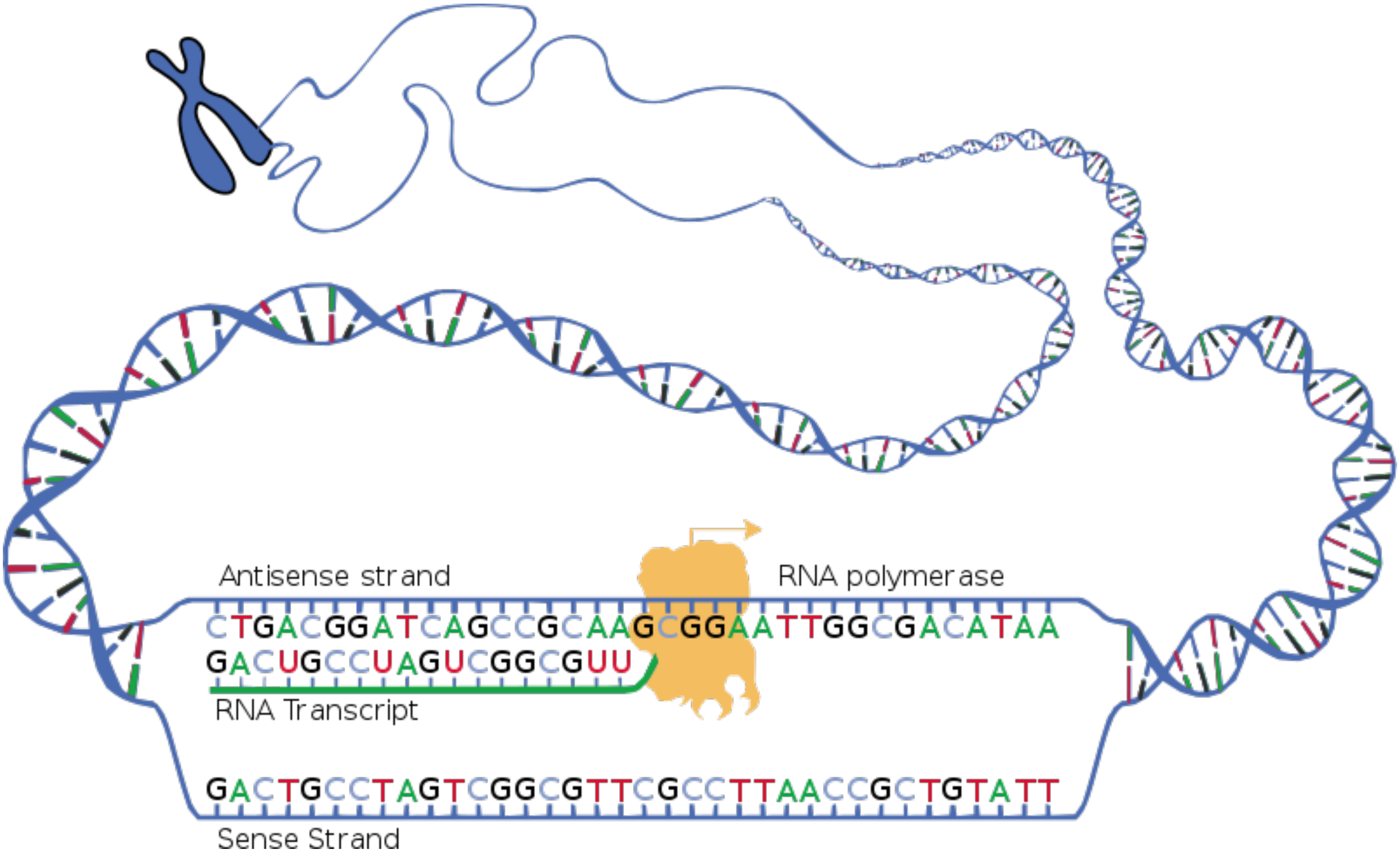
Antisense strand
RNA polymerase
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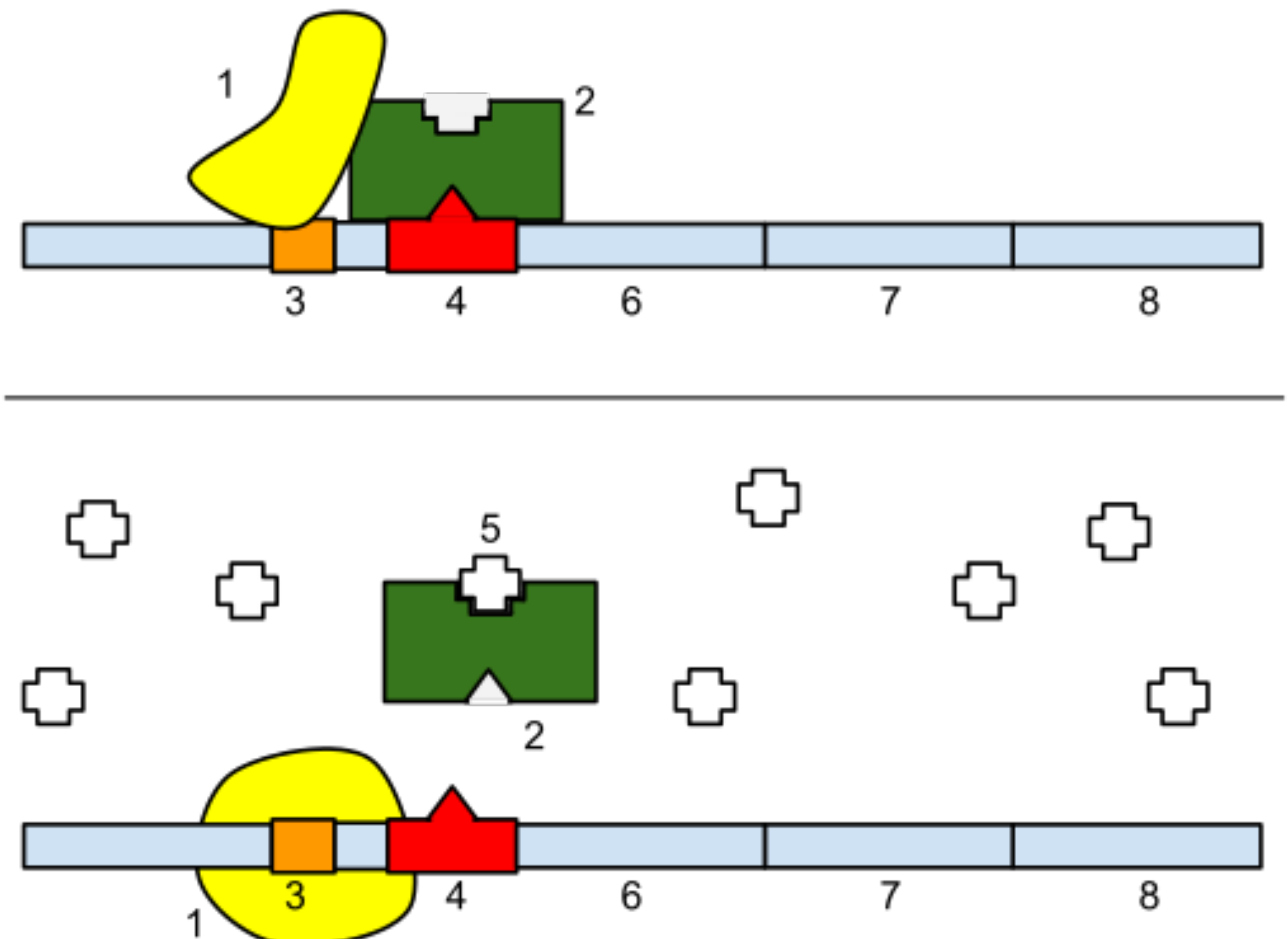
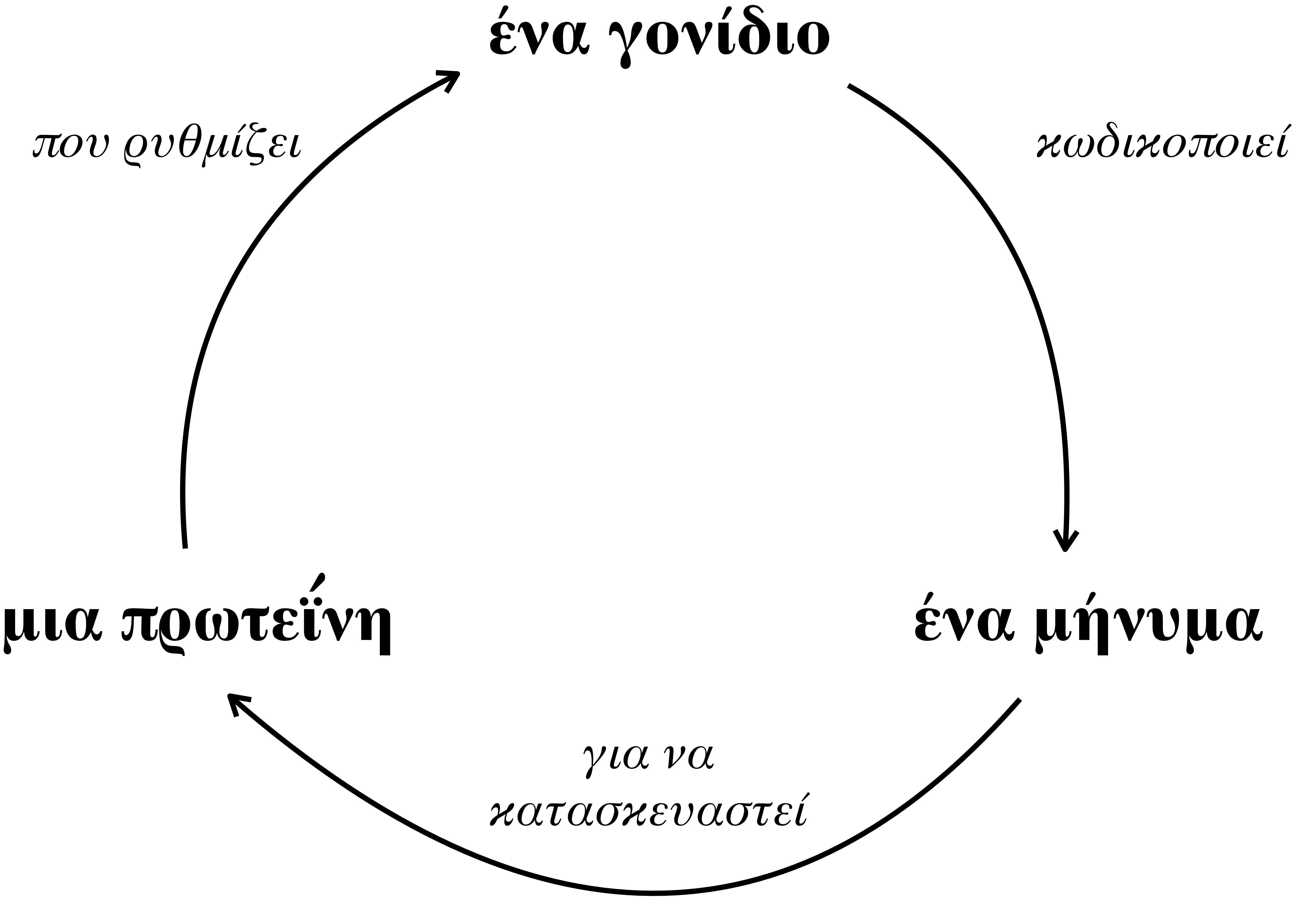
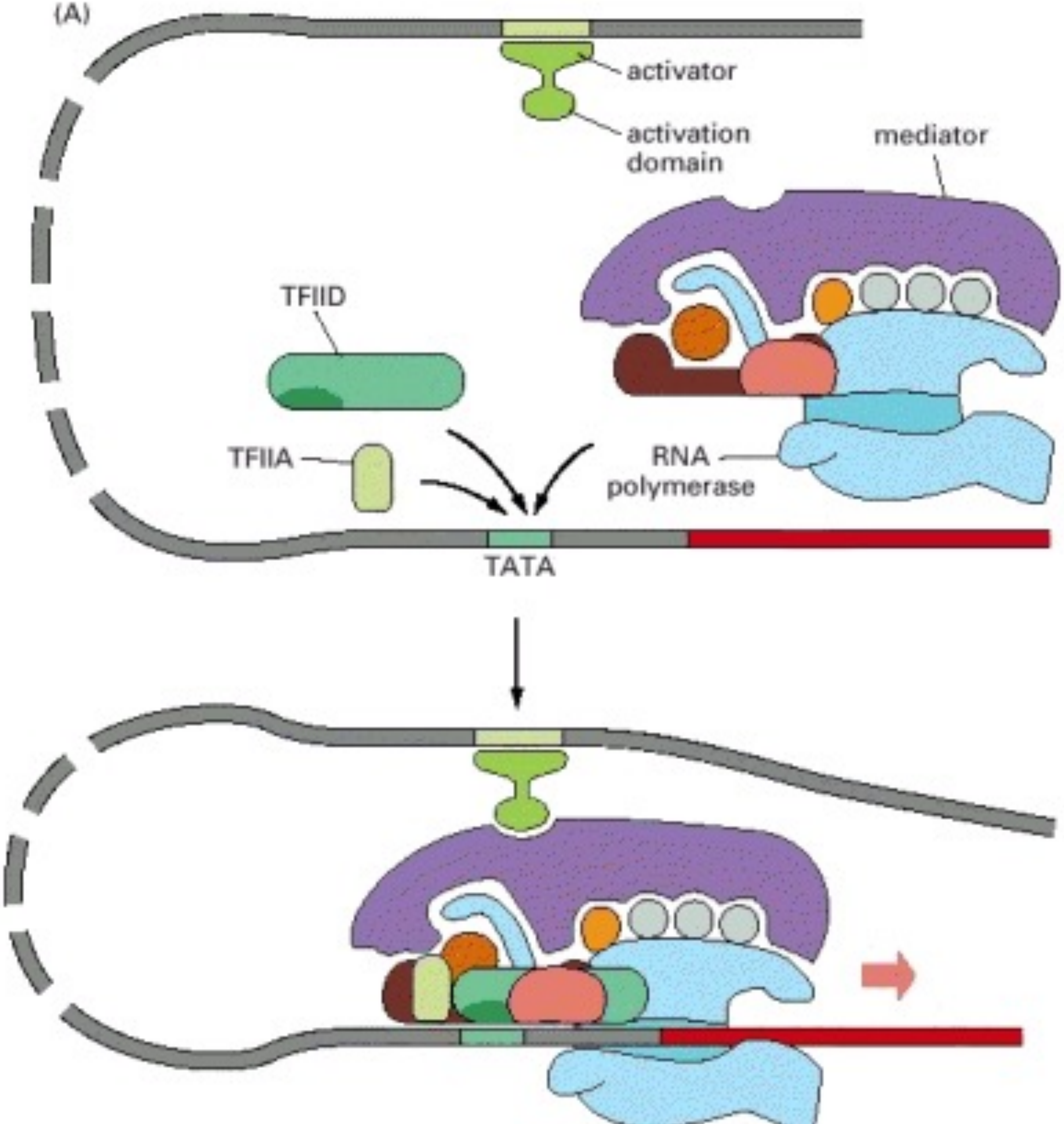
GACUGCCUAGUCGGCGUU
RNA Transcript
GACTGCCTAGTCGGCGTTCGCCTTAACCGCTGTATT
Sense Strand

-> οπερόνιο



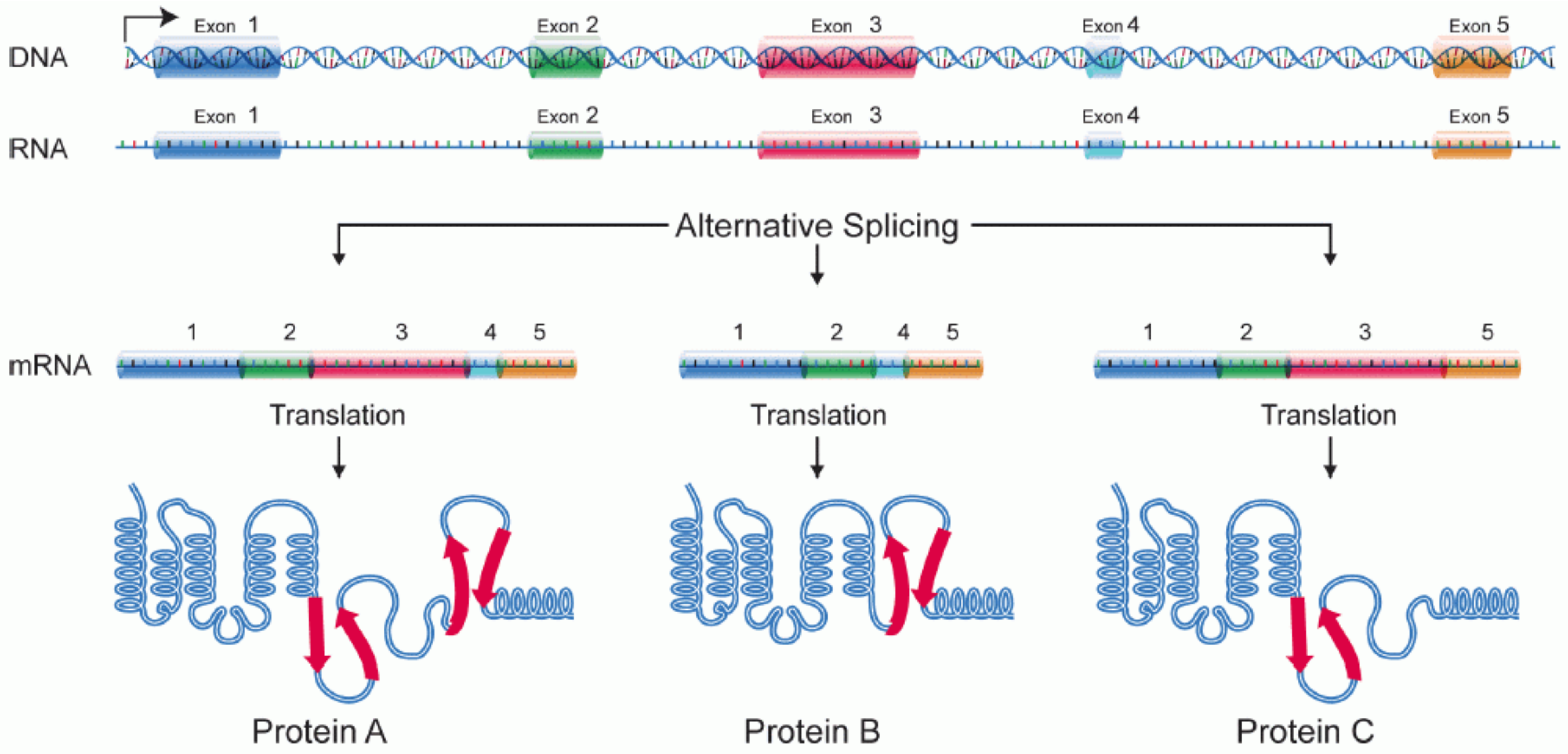


ένα γονίδιο
κωδικοποιεί
ένα μήνυμα
για να κατασκευαστεί
μια πρωτεΐνη
που ρυθμίζει

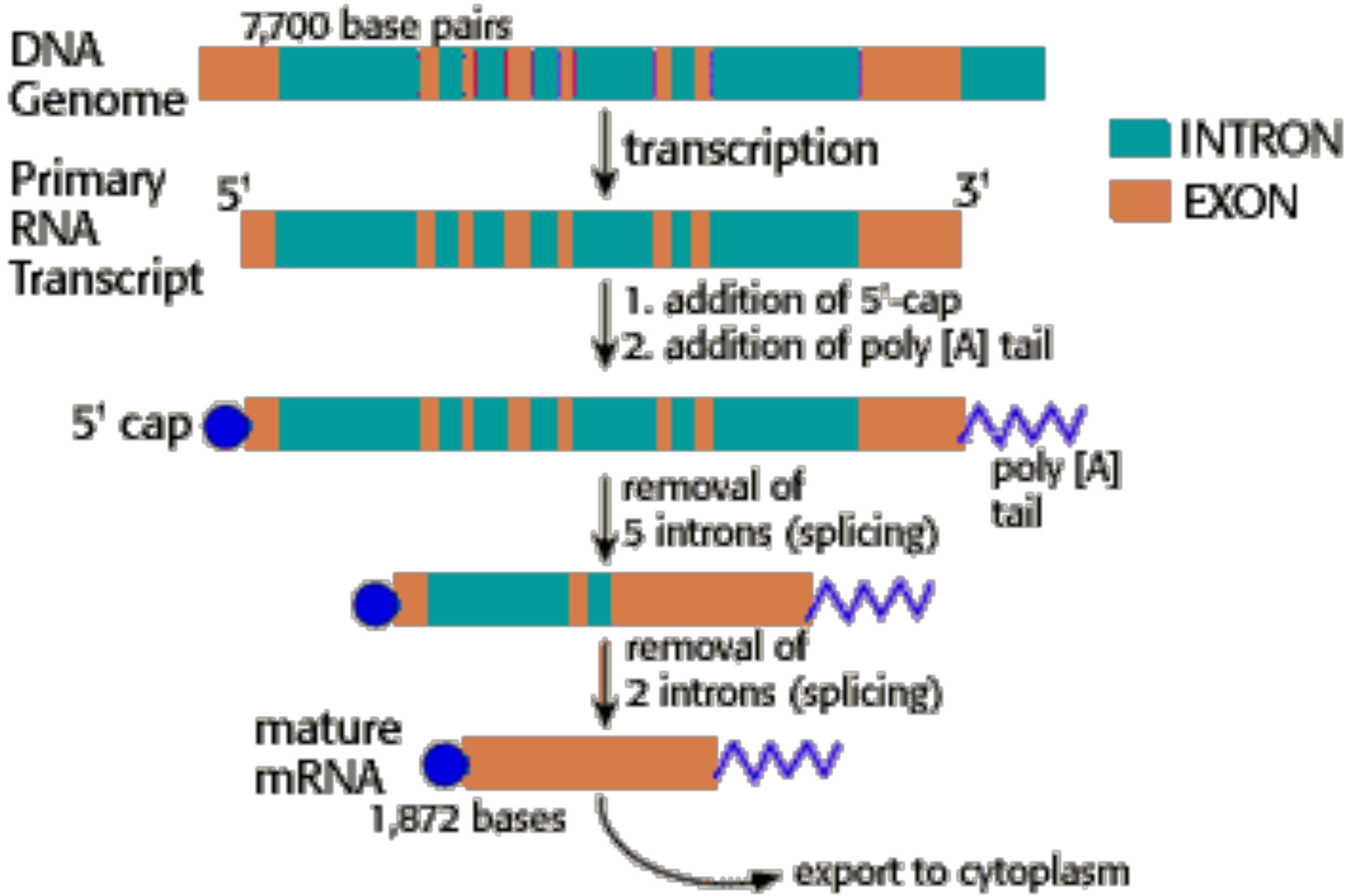

(A)
activator
activation domain
mediator
TFIID
TFIIA
RNA polymerase
TATA

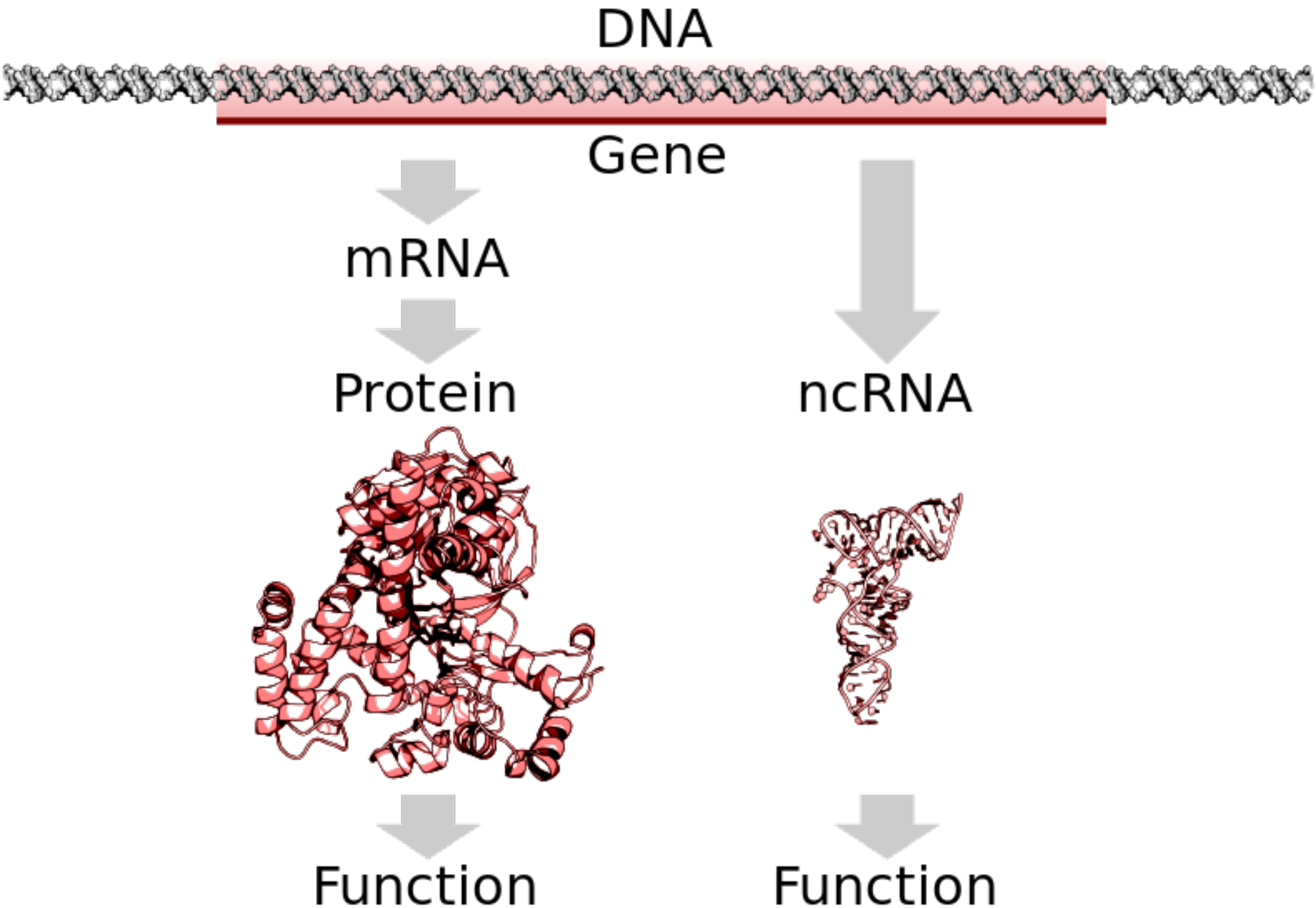
www.dnalc.org

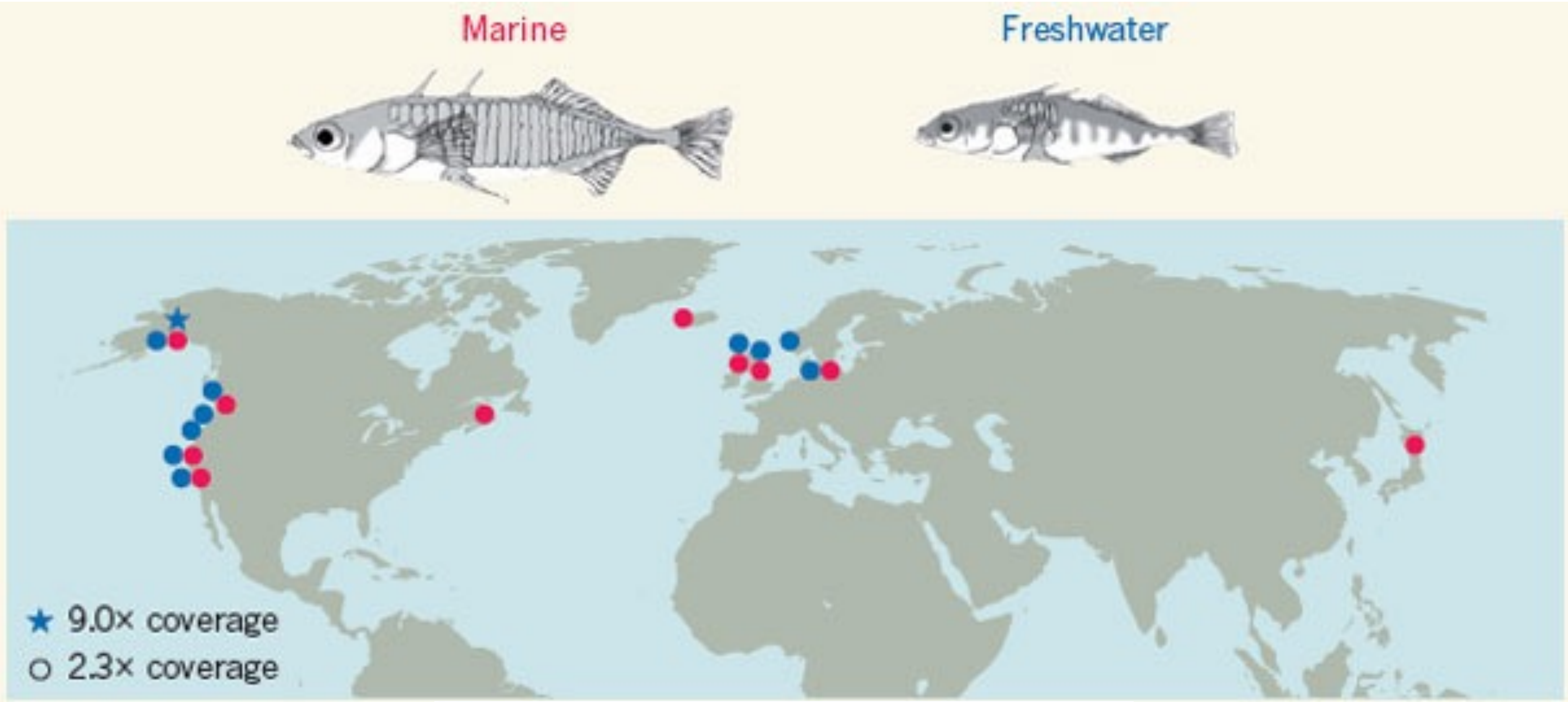
-> εναλλακτικό μάτισμα

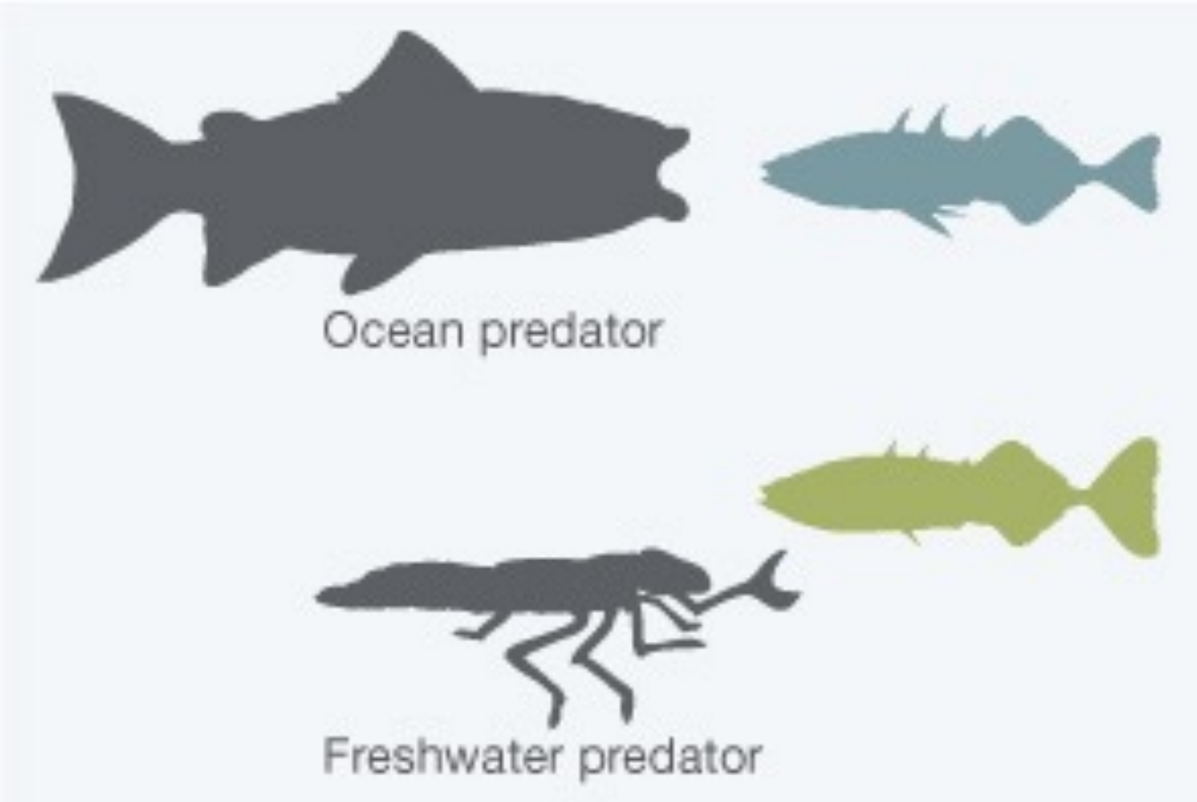


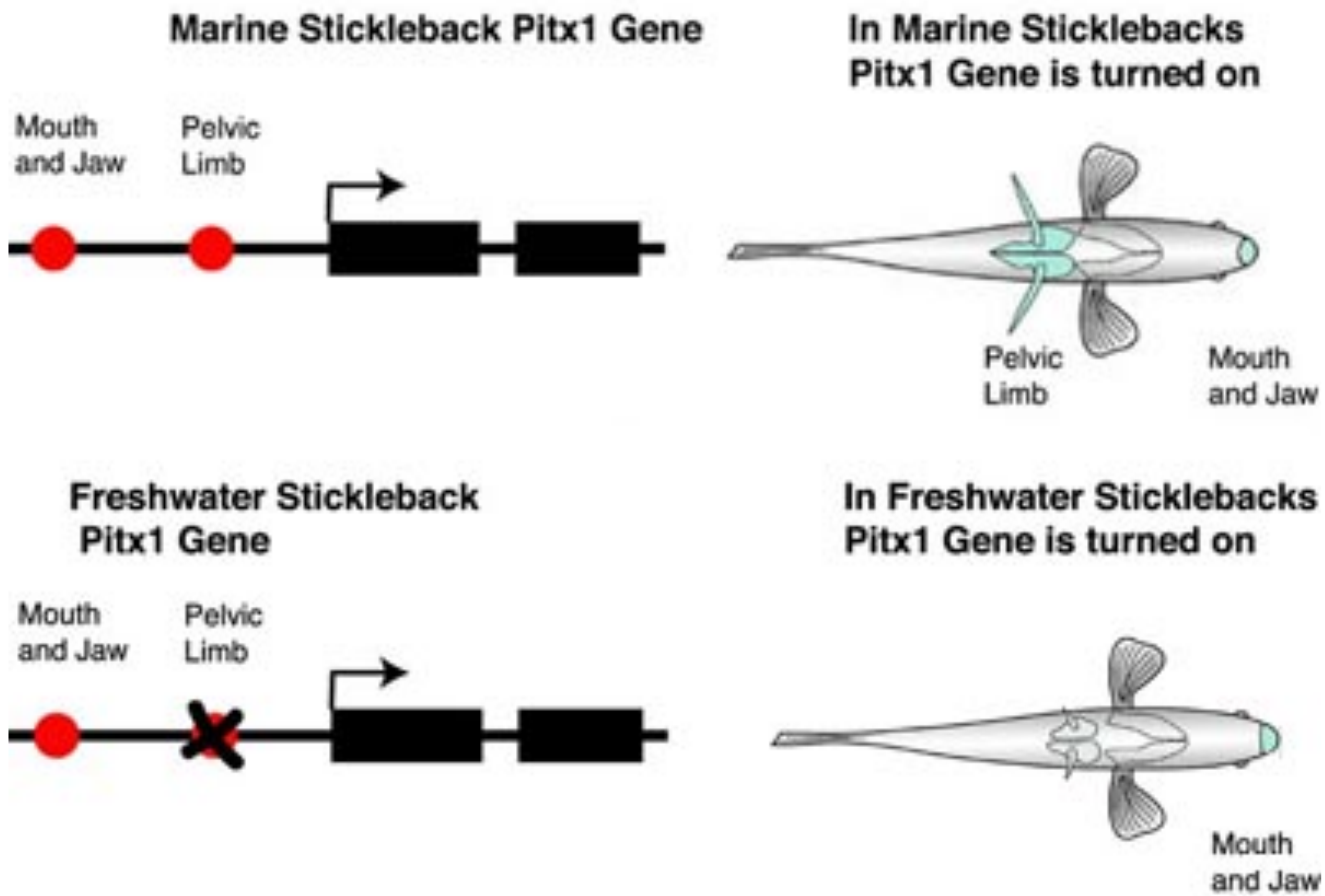
Ovalbumin processing

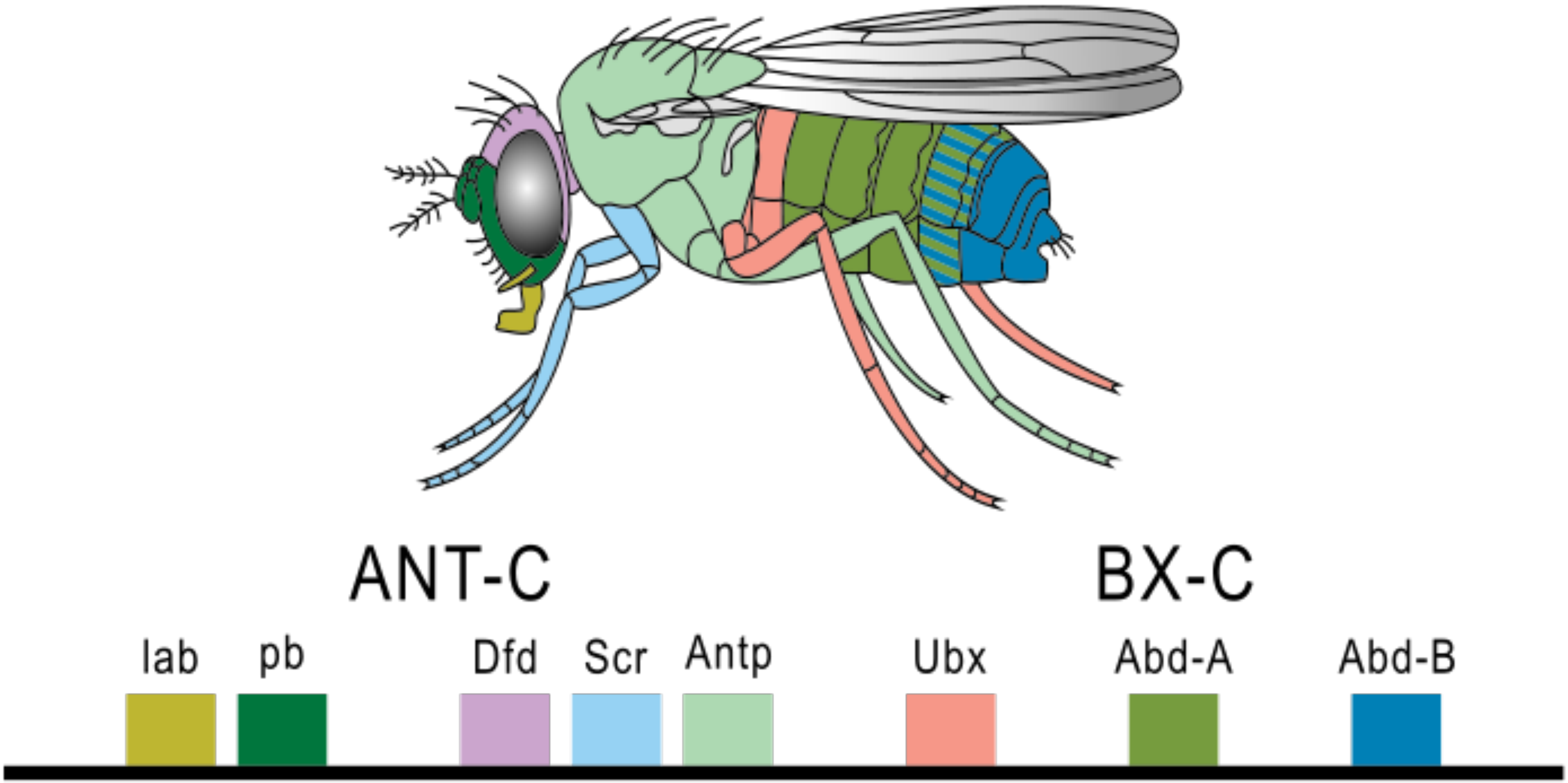


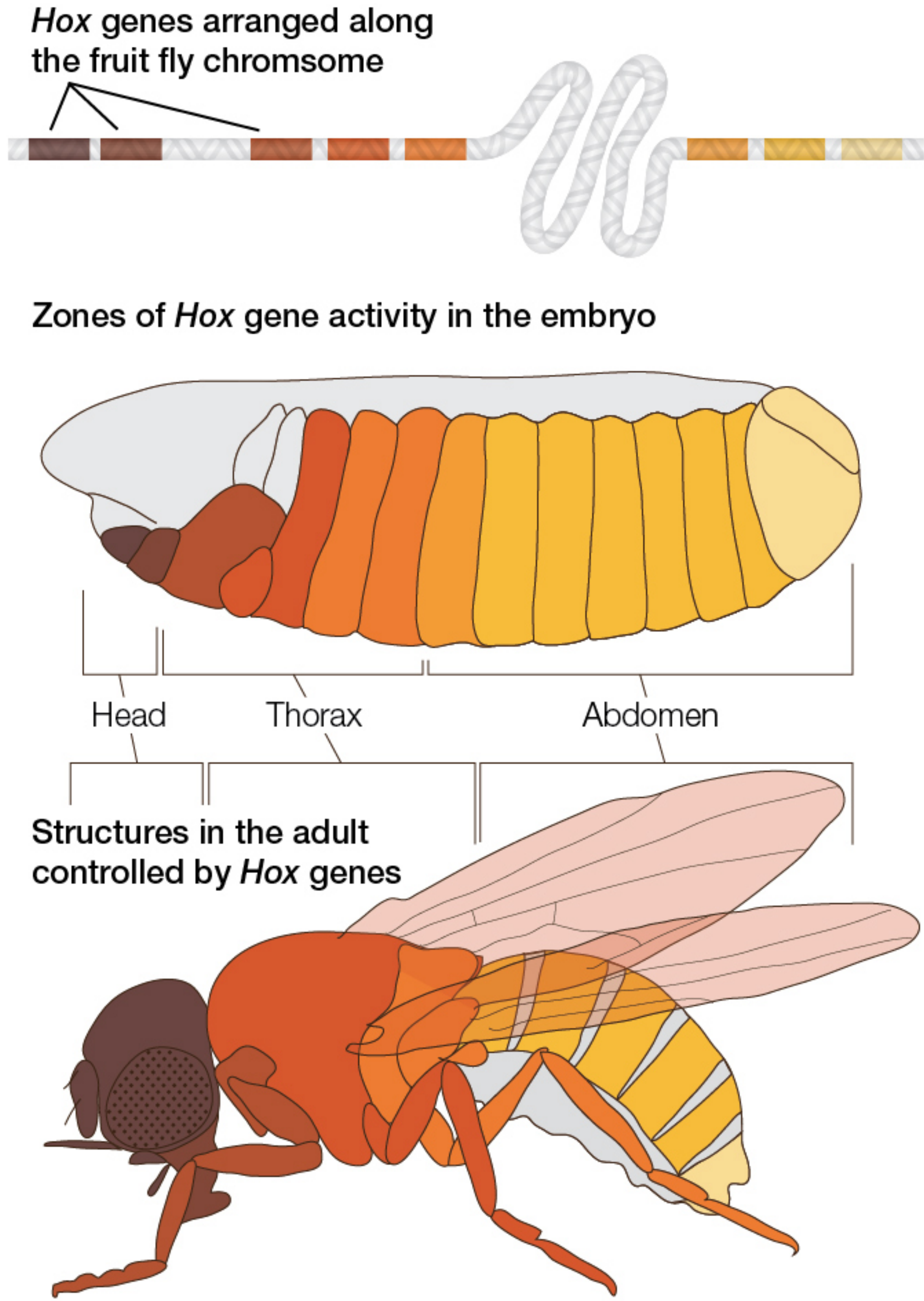

DNA
Gene
mRNA
Protein
ncRNA
Function
Function



Marine
Freshwater
★ 9.0× coverage
○ 2.3× coverage

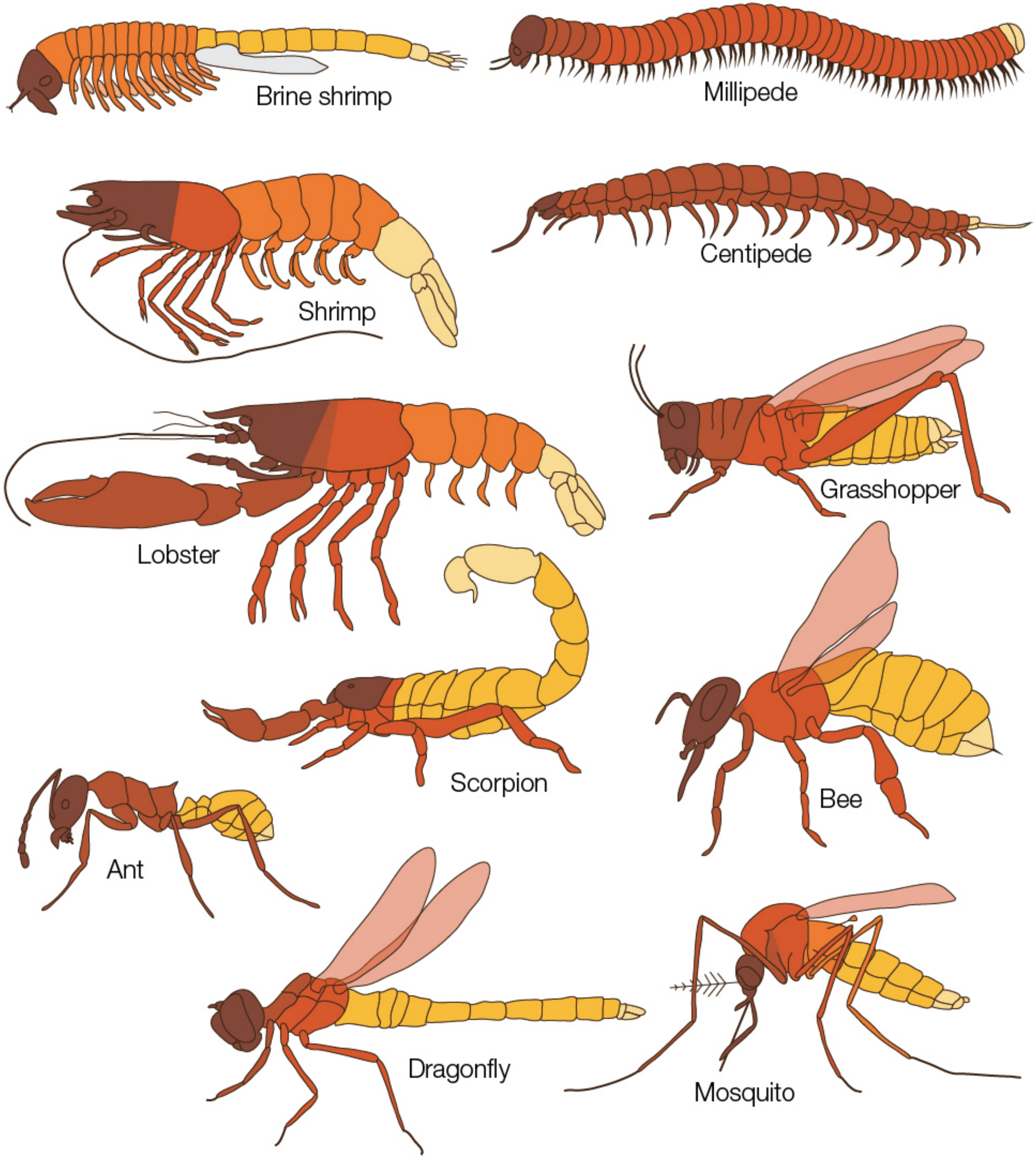

Ocean predator
Freshwater predator

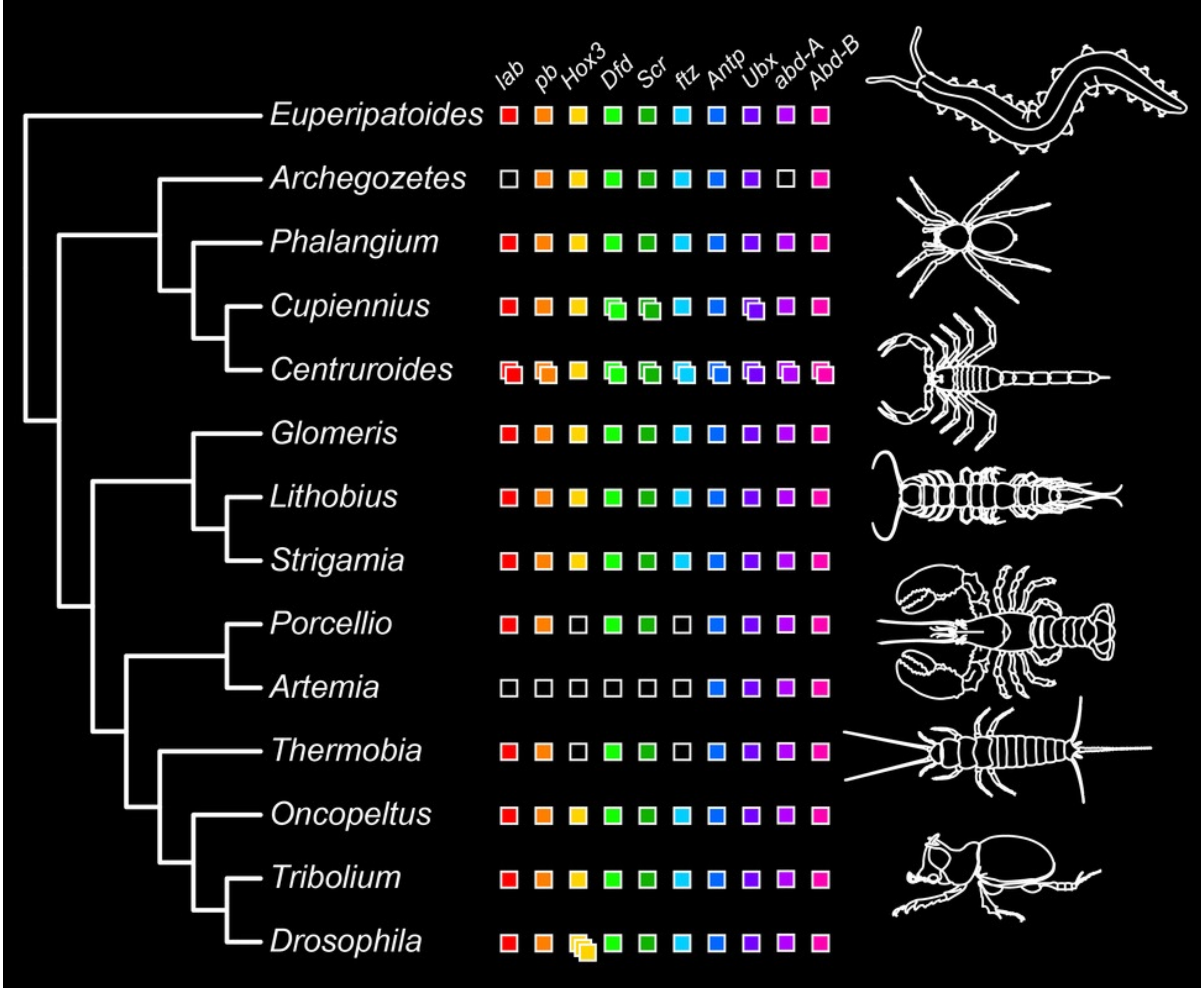

Marine Stickleback Pitx1 Gene
Mouth and Jaw
Pelvic Limb
In Marine Sticklebacks Pitx1 Gene is turned on
Pelvic Limb
Mouth and Jaw
Freshwater Stickleback Pitx1 Gene
Mouth and Jaw
Pelvic Limb
In Freshwater Sticklebacks Pitx1 Gene is turned on
Mouth and Jaw

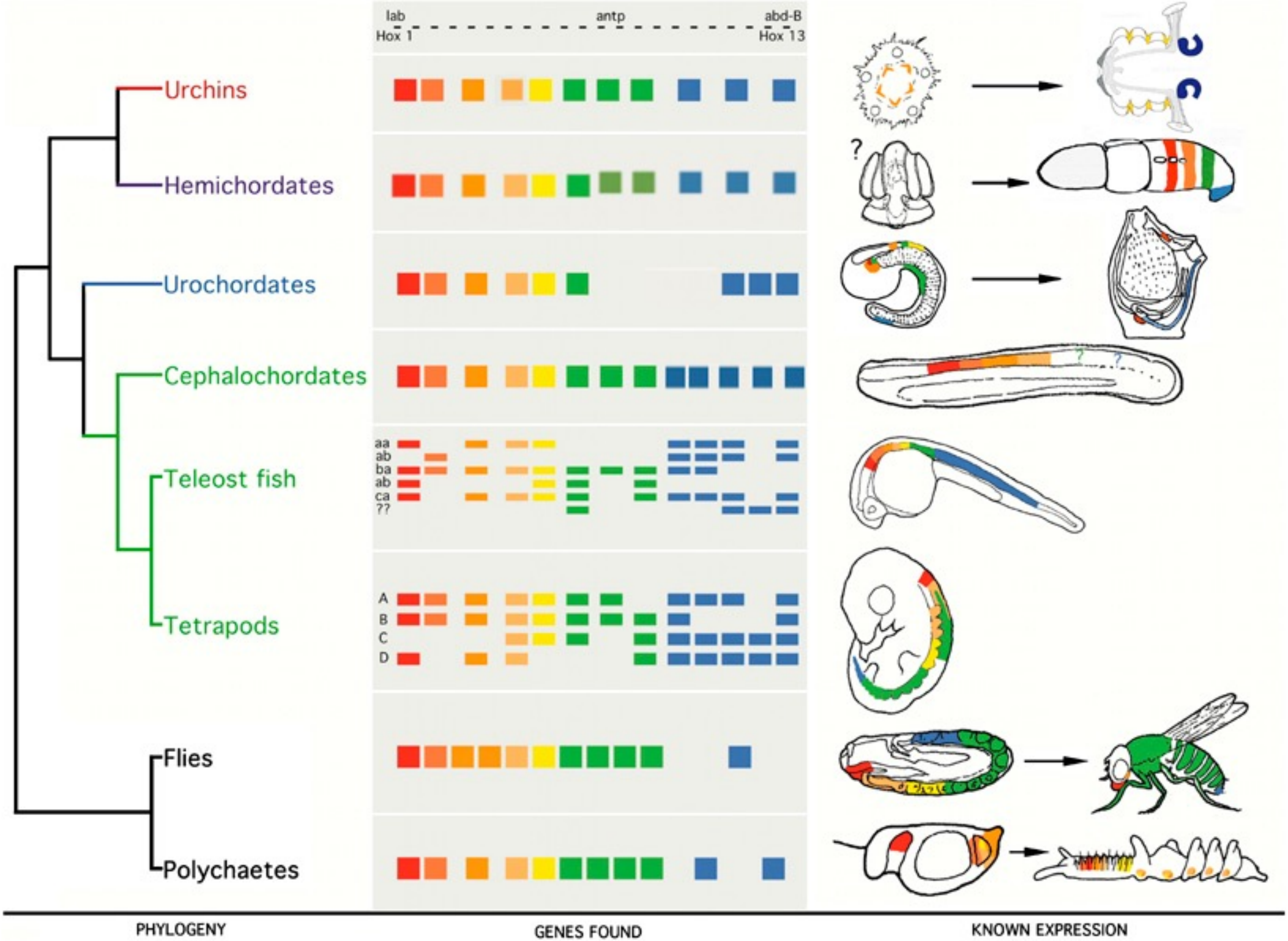


ANT-C
BX-C
lab
pb
Dfd
Scr
Antp
Ubx
Abd-A
Abd-B



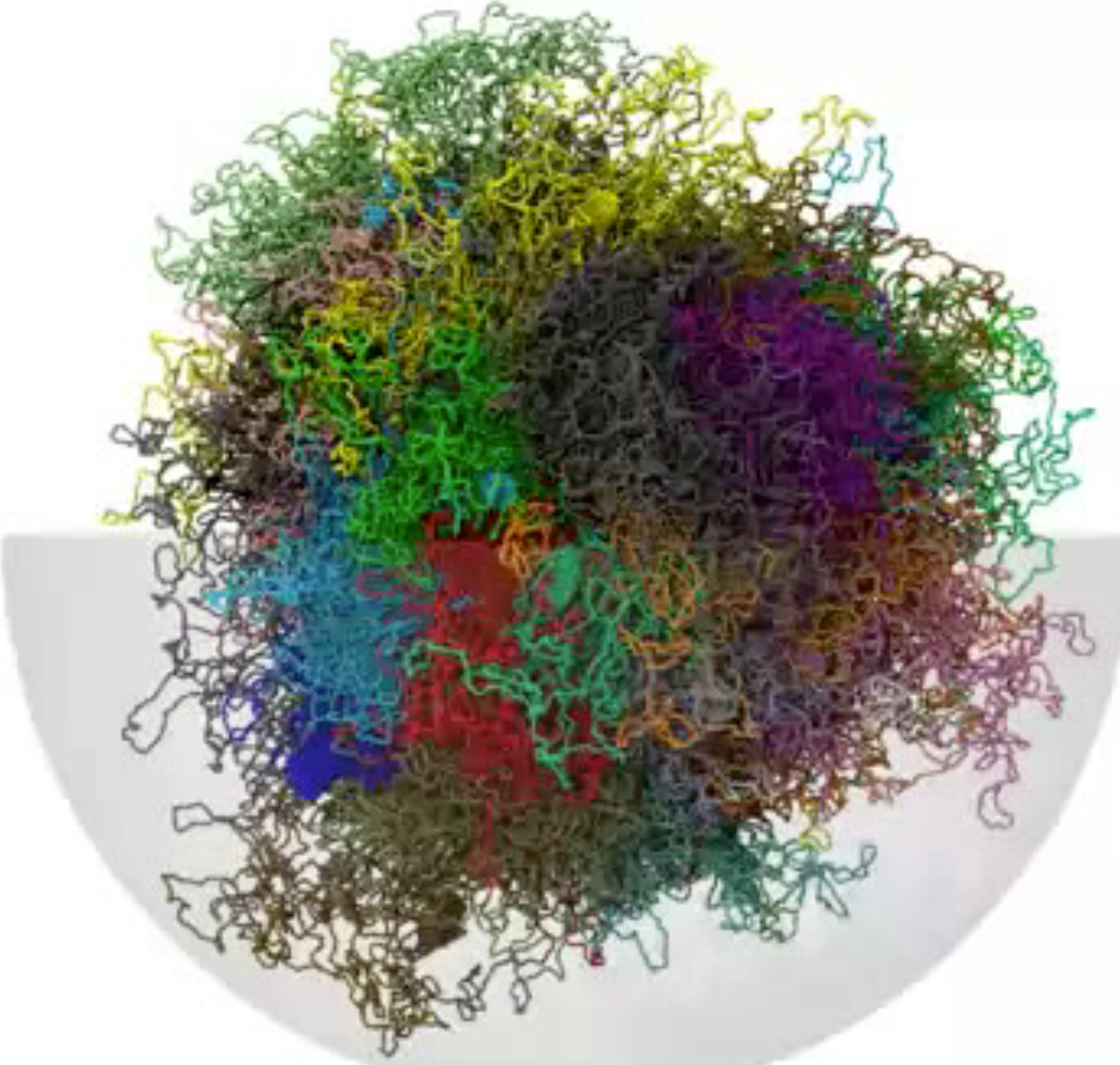
Hox genes arranged along the fruit fly chromsome
Zones of *Hox* gene activity in the embryo
Head
Thorax
Abdomen
Structures in the adult controlled by *Hox* genes


Brine shrimp
Millipede
Shrimp
Centipede
Grasshopper
Lobster
Scorpion
Bee
Ant
Dragonfly
Mosquito


lab
pb
Hox3
Dfd
Scr
ftz
Antp
Ubx
abd-A
Abd-B
Euperipatoides
Archegozetes
Phalangium
Cupiennius
Centruroides
Glomeris
Lithobius
Strigamia
Porcellio
Artemia
Thermobia
Oncopeltus
Tribolium
Drosophila



lab
antp
abd-B
Hox 1
Hox 13
Urchins
Hemichordates
Urochordates
Cephalochordates
Teleost fish
Tetrapods
Flies
Polychaetes
aa
ab
ba
ab
ca
??
A
B
C
D
?
PHYLOGENY
GENES FOUND
KNOWN EXPRESSION



Ποια είναι η σχέση κλασικού & μοριακού γονιδίου;

-> οι δυο έννοιες γονιδίου έχουν την **ίδια αναφορά**

-> **αναγωγή** <u>κλασικής γενετικής</u> σε <u>μοριακή γενετική</u>

-> η μοριακή βιολογία έδειξε ότι οι κλασικοί γενετιστές **είχαν εν μέρει δίκιο**:

-> τα γονίδια είχαν εισαχθεί ως <u>αντικείμενα με συγκεκριμένο αιτιακό ρόλο</u>, και οι μοριακοί βιολόγοι ανακάλυψαν ότι αποτελούνταν από κομμάτια DNA που κωδικοποιούν πρωτεΐνες

-<u>**νόμος γέφυρα**</u>: ‘το γονίδιο είναι μέρος DNA που κωδικοποιεί μια πρωτεΐνη’

-> η θέση περί αναγωγής της κλασικής γενετικής στη μοριακή γενετική έχει **απορριφθεί** από τους περισσότερους φιλοσόφους της βιολογίας

Ποια είναι η σχέση κλασικού & μοριακού γονιδίου;

Waters: anti-reductionist consensus

Κριτικές:

επιχείρημα #1: το επιχείρημα του Kitcher για το νόμο διαχωρισμού του Mendel, ο οποίος εξηγείται στο κυτταρικό επίπεδο (1953 and all that)

επιχείρημα #2: ο <u>νόμος γέφυρα</u> είναι **λανθασμένος**
-> μεντελιανά γονίδια που <u>δεν είναι</u> μοριακά γονίδια

Ποια είναι η σχέση κλασικού & μοριακού γονιδίου;

επιχείρημα #3: έννοιες κλασικής γενετικής που δε μπορούν να οριστούν με μοριακούς όρους
-> επικρατές γονίδιο
-> η επικράτηση (dominance) **πραγματώνεται πολλαπλά** (multiple realisation)

επιχείρημα #4: το μεντελιανό γονίδιο δεν έχει αντικατασταθεί από το μοριακό
-> γονίδια στην πληθυσμιακή γενετική
-> εγωιστικό γονίδιο Dawkins

Ποια είναι η σχέση κλασικού & μοριακού γονιδίου;

-> ο Benzer εισάγει τον όρο **cistron (σιστρόνιο)**
-**ανασυνδυασμός** (recombination) και **επιχιασμός** (crossing over) γονιδίων

-> λειτουργική μονάδα ≠ κληρονομική μονάδα Griffiths Stotz process theory of the gene

-> <u>**γενική τάση**</u>: **διάφορες έννοιες γονιδίου**
-**μεγάλη αλλαγή** σε έννοια μεντελιανού κλασικού γονίδιου

Moss: **gene-P** (predictive, preformation) vs **gene-D** (development)

-> ‘διάλυση’ της έννοιας;
-promoter (υποκινητής) -> ρυθμιστικές περιοχές
-introns - RNA alternative splicing, trans-splicing κλπ

-> γενικά: γενετικά συστήματα πολύ **πιο περίπλοκα** από γονίδια διατεταγμένα σαν ‘χάντρες σε κορδόνι’

Για περαιτέρω μελέτη:

-Godfrey-Smith, *Φιλοσοφία της Βιολογίας*, κεφ. 6

-Griffiths & Neumann-Held (1999) 'The many faces of the gene'

-Sterelny & Griffiths

-Griffits & Stotz (2013) Genetics and philosophy

-https://plato.stanford.edu/entries/gene/

-https://plato.stanford.edu/entries/molecular-genetics/

-https://plato.stanford.edu/entries/molecular-biology/

- particulate theory
- mendelian chomosomal theory of inheritance
- Johannsen - genotypic theory of inheritance
- Hox genes
- Denis Noble, the music of life