Gene, Brain, and Behavior

–Elucidating nondeterministic functions using deterministic techniques–

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2004–current: Research Organization of Information and Systems
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1972–1998: School of Science, The University of Tokyo
1967–1972: California Institute of Technology
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Global Focus of Knowledge, July 8, 2009

The University of Tokyo

Dialectical development of Life Science

Natural historical descriptive discipline

↓ **Genetics, DNA-nomy**

Universal and unified understanding of life

↓ **Genetic Engineering**

Natural history of molecules: Genomics

↓ **Life Informatics?**

↓ **Systems Biology?**

?????????

Revolutions in Life Science

The First Revolution

Early 20th century:

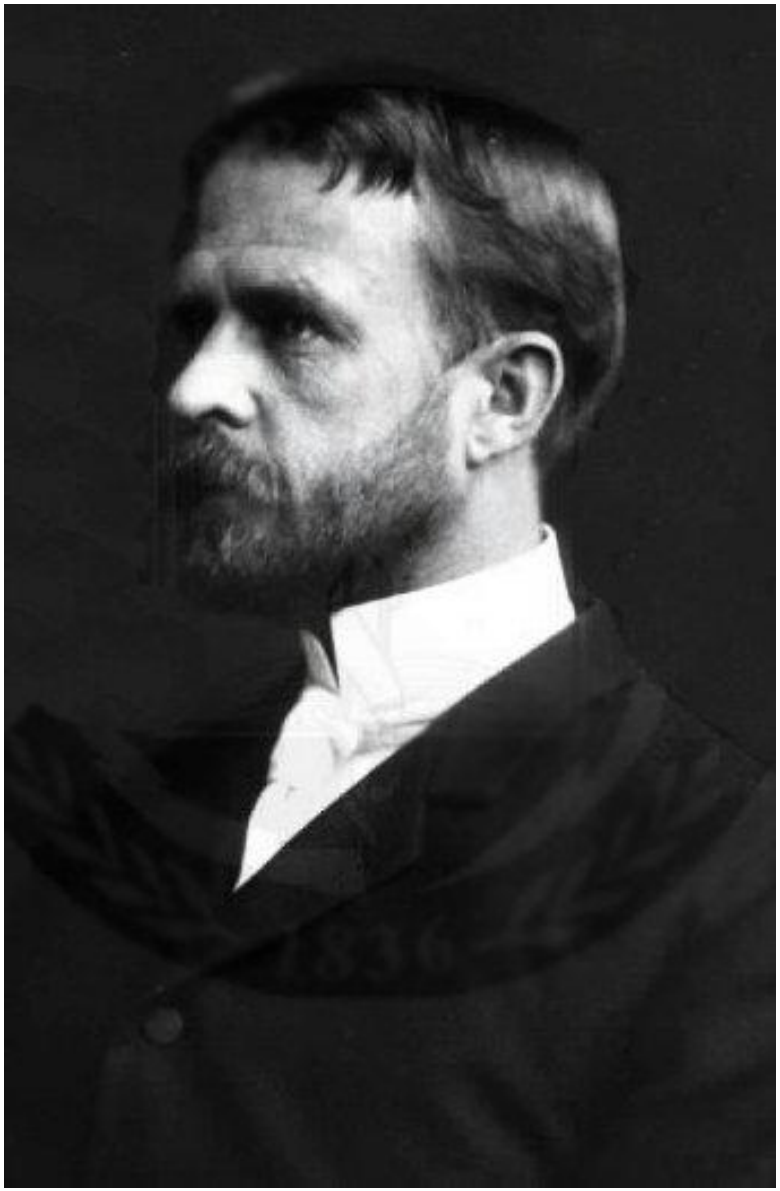
Rediscovery of Mendelian inheritance

Universal law applicable to all species

→ Drosophila genetics
→ Chromosome map
→ Biochemical genetics **(**one gene-one enzyme hypothesis**)**
→ Molecular genetics of phage and E. coli

Establishment of the concept of an

“experimental model of organism”



http://en.wikipedia.org/wiki/File:Thomas_Hunt_Morgan.jpg

Founder of drosophila genetics
Thomas Hunt Morgan (1917)

The Physical Basis of Heredity

“Complexity of life phenomena simply looks complex because of our ignorance”

“Genesis phenomena are the development of genes”

The Second Revolution

1953 DNA double helix

→ Molecular mechanisms of replication, transcription, and translation

Universality of the genetic code

→ The end of molecular genetics??

1975–present

Cloning & gene transfer

(Genetics beyond the species barrier)

→ Elucidation of brain, development, and genetic diseases

Two approaches to research on life

Determinism-focused research

Genetics, Ethology

Strict and precise research

Mechanistic, Gene, Instinct

Indeterminism-focused research

Embryology, Psychology

Enjoyable research that emphasizes the flexibility and variety of living organisms

Intercellular interactions, Leaning

Unified in the 1980s

Methods of analysis of complex phenomena that comprise Life

- **Analyzing and understanding by breaking down into constituent elements**

  Molecular biology, Biochemistry

  Understanding the whole as a sum of each element

- **Understanding the system as a whole**

  Mendelian genetics, Darwin's theory of evolution

  Understanding the whole even if each elementary process is not well known

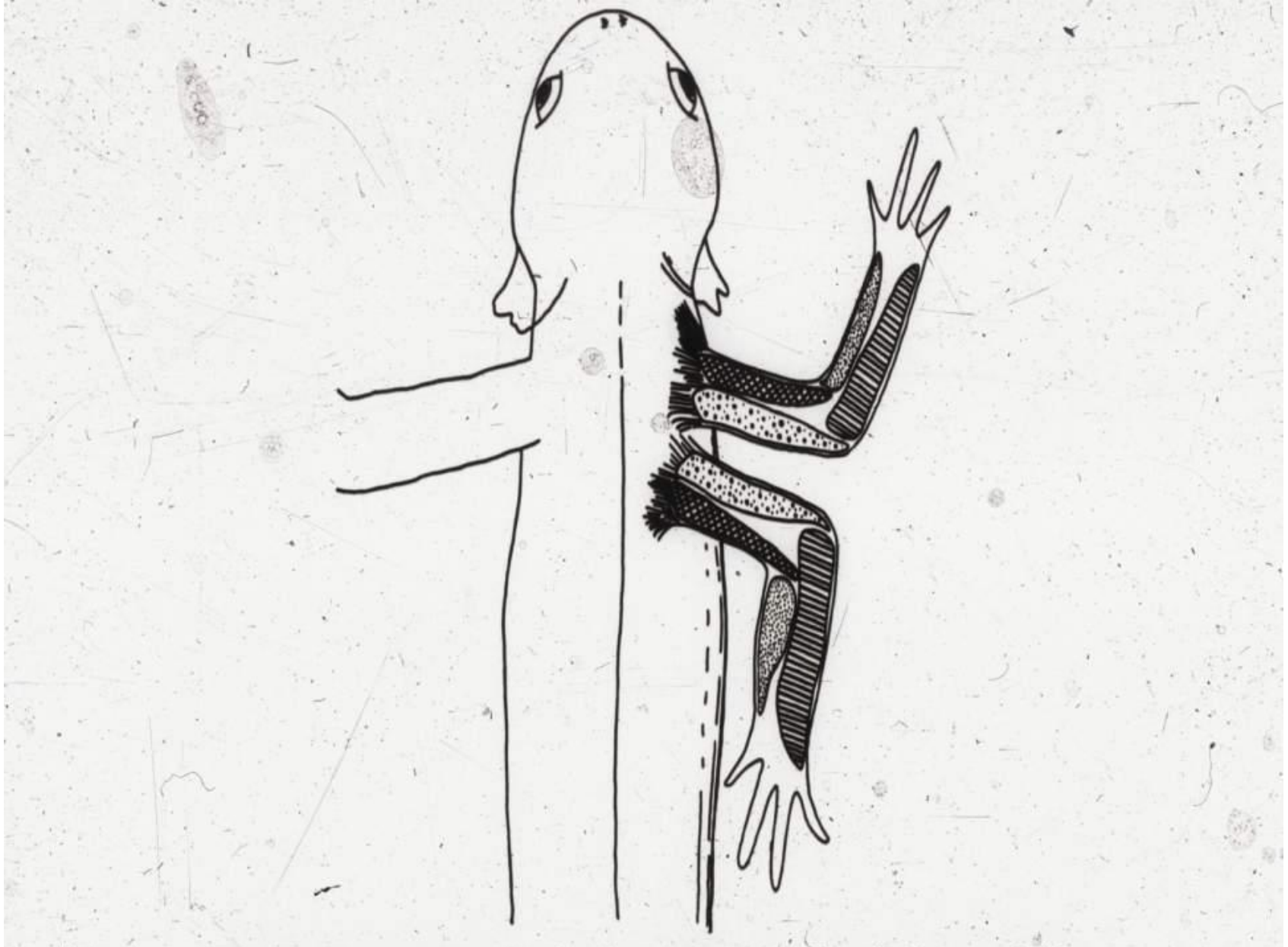


FIG. 2.2. Diagram to show the mirror-image arrangement of muscles in a normal right limb and a supernumary left limb transplanted near by with reversed rostrocaudal orientation. Muscles of identical names are indicated by identical shading. From Weiss, 1950.

‡ "Molecular Genetics", Haruo Ozeki and Mitsuru Takanami (Iwanami Koza Gendai Seibutsu Kagaku, Vol 2), Iwanami Shoten,1974–1975

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‡ http://ja.wikipedia.org/wiki/ファイル:Niobe050905-Siamese_Cat.jpeg

Gene → Brain

(Determinism?) (Indeterminism?)

Biologist's (my) interests

- Are the central nervous circuits determined by genes?
- What is the relationship between instinctive behavior and genes?
- Evolution of organisms and genes
- Development of organisms and genes
- What is the relationship between susceptibility to disease and genetic information?
- Are the individual differences of side effects of drugs related to the genome?

Advantages of drosophila

From molecule to individual, to group

From differentiation to evolution

Disadvantages of drosophila

Invertebrate

Not accepted as a research model at medical schools

No similarity with humans!

(Is it true?)

Human

Fly

Vertebrate

Invertebrate

Origins of Life

Human

Fly

Origins of Life

Gene → ? →▪▪▪→ ? → Behavior

Intermediate stages are a black box

Genetics way of thinking

Mutation →▪▪▪→ Behavioral abnormality

"Brain" should be able to be studied through "behavioral mutation"

What elements are required to identify behavioral mutants?

1. **An experimental model system in which experiments are easy to conduct**
2. **Easy and highly reliable techniques to observe behavior**
3. **Highly dedicated, enthusiastic researchers**

Diffusion ⟷ **Attractive force of phototaxis**

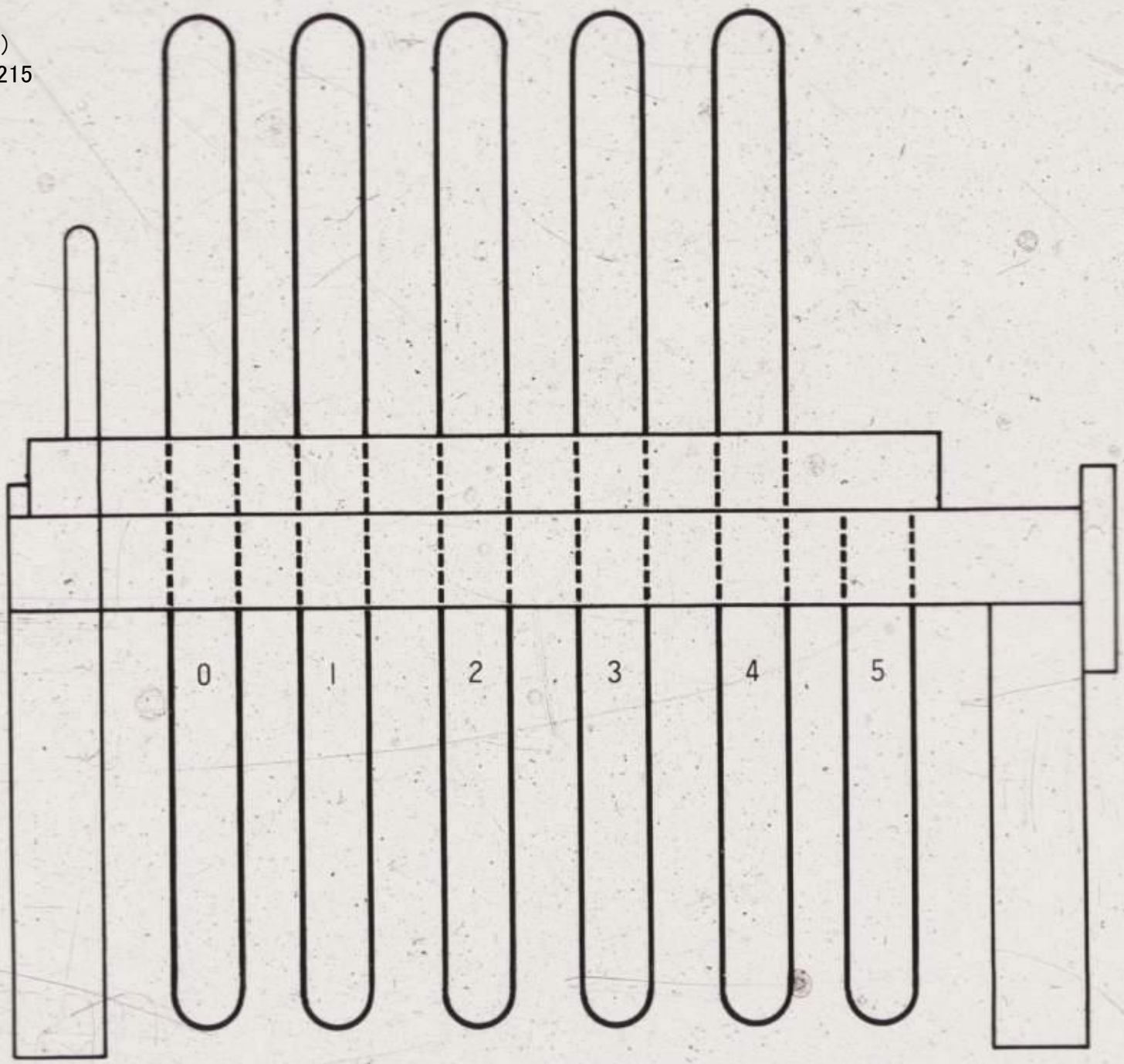
Scale to indicate phototaxis

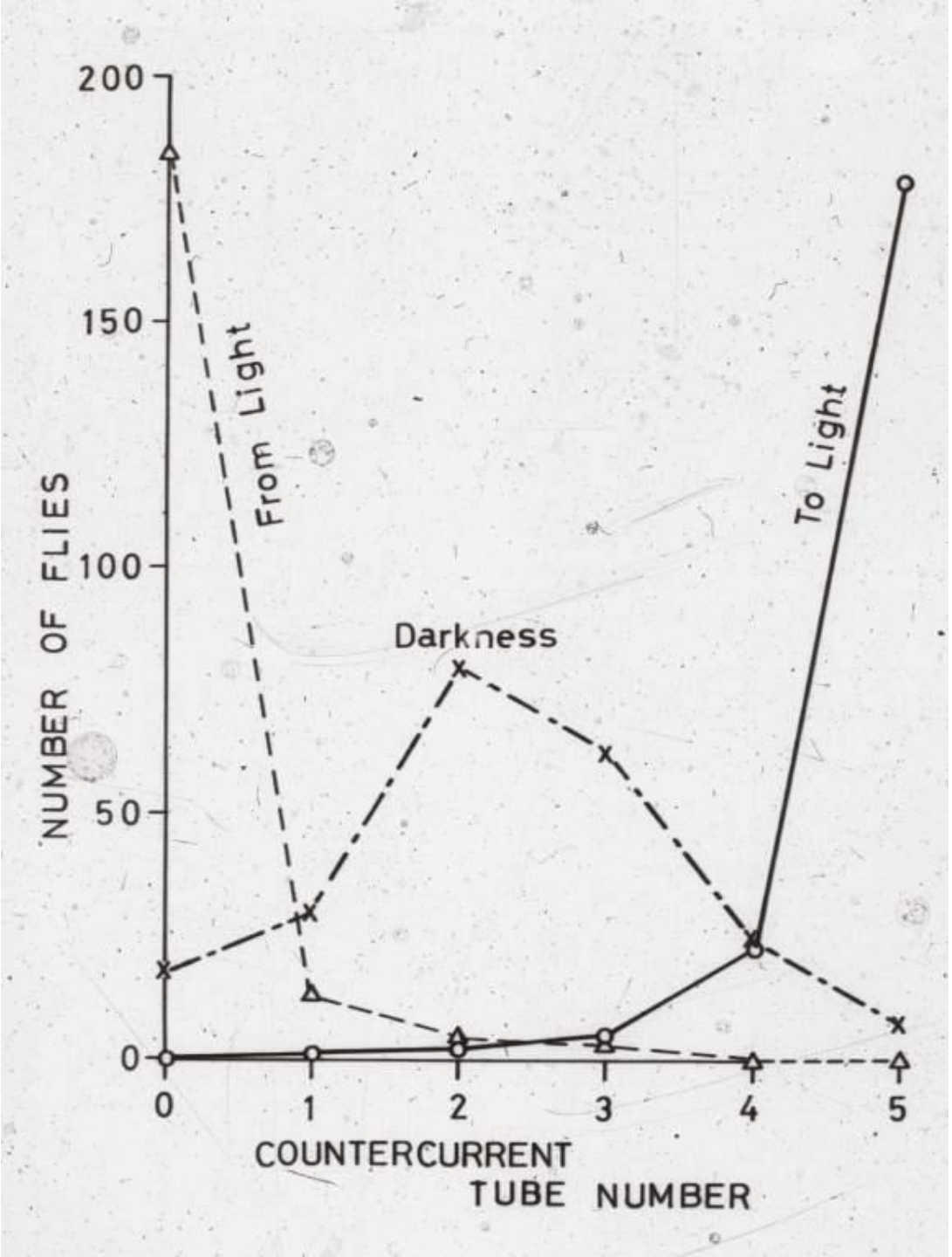
$$p = \frac{(A)}{(A)+(B)}$$

$$P.I. = 50 \times \log \frac{(A)}{(B)}$$

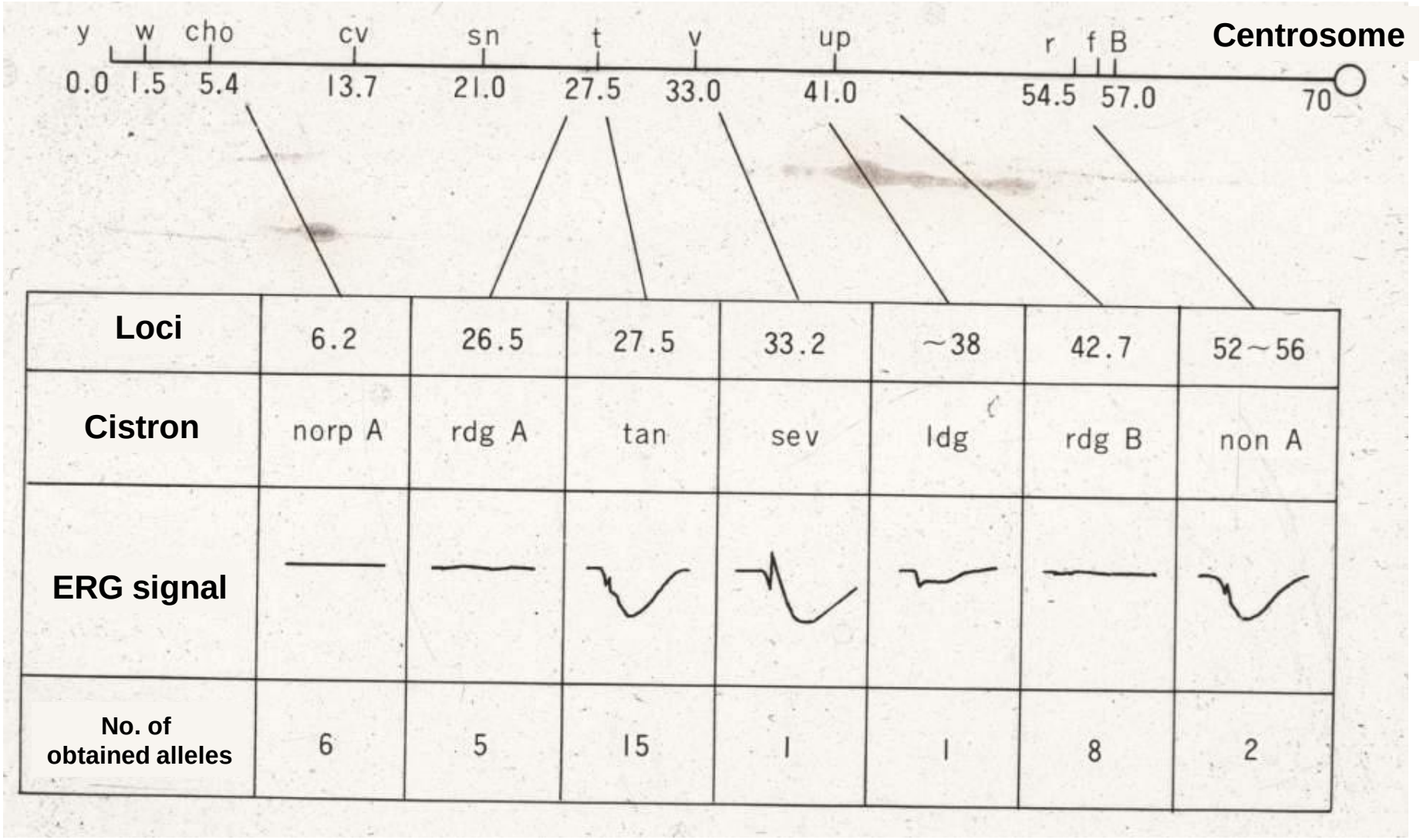
Phototaxis Index

Kagaku (1975)
vol.45 No.4 p215




200
150
100
50
0
NUMBER OF FLIES
From Light
Darkness
To Light
0
1
2
3
4
5
COUNTERCURRENT
TUBE NUMBER

‡ Kagaku (1975)
vol.45 No.4 p215



Loci	6.2	26.5	27.5	33.2	~38	42.7	52~56
Cistron	norp A	rdg A	tan	sev	ldg	rdg B	non A
ERG signal							
No. of obtained alleles	6	5	15	1	1	8	2

Research on non-phototactic mutation
The second stage

Where are the abnormalities? (location)

Eye? Brain? Motor nerve? Muscle?

What abnormalities are present? (characteristics)

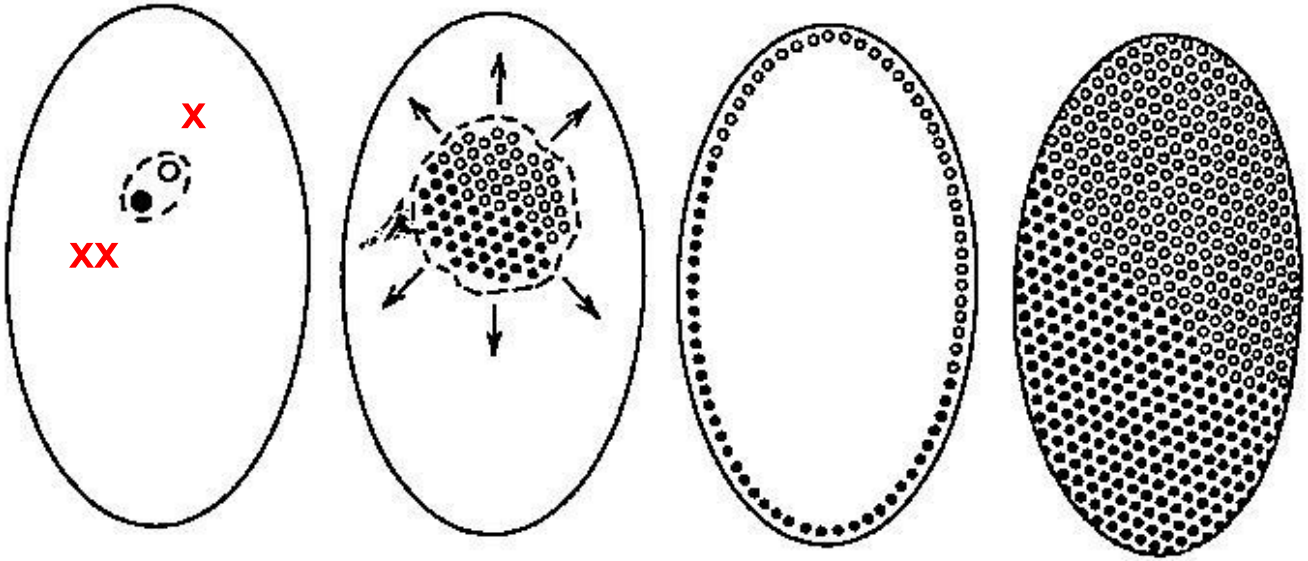
Absence of specific cells?

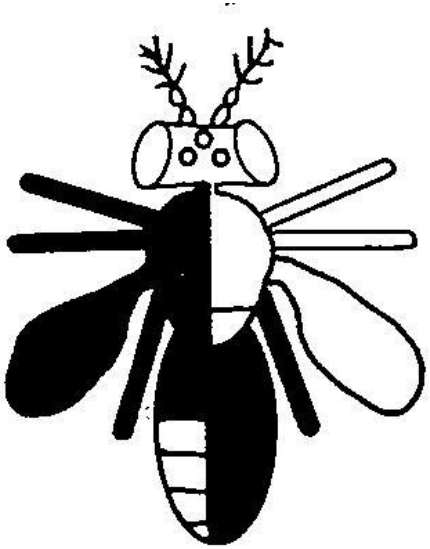
No differentiation?

Death after differentiation?

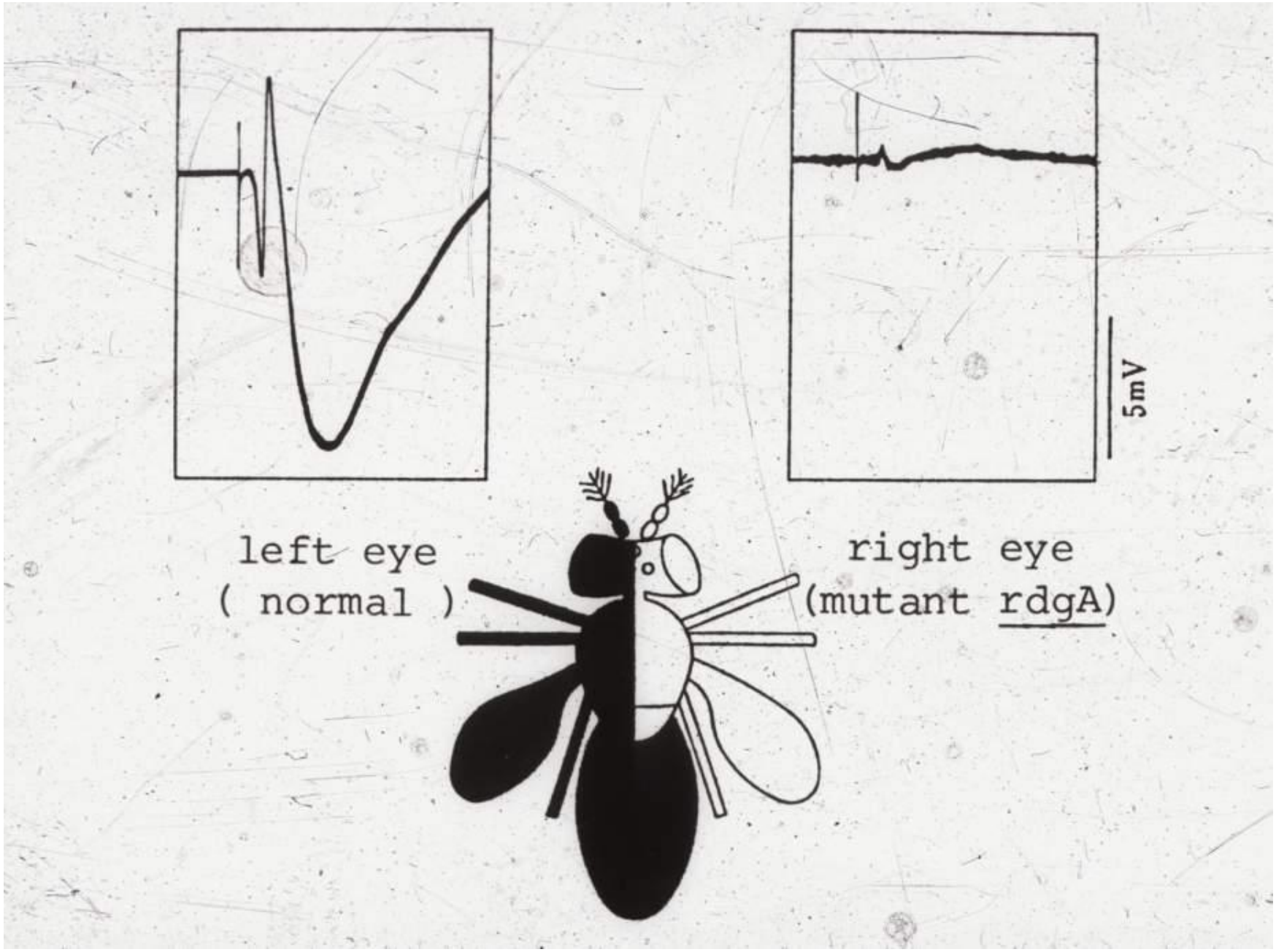
Differentiated into different cells?

Vitamin A deficiency ….. ?

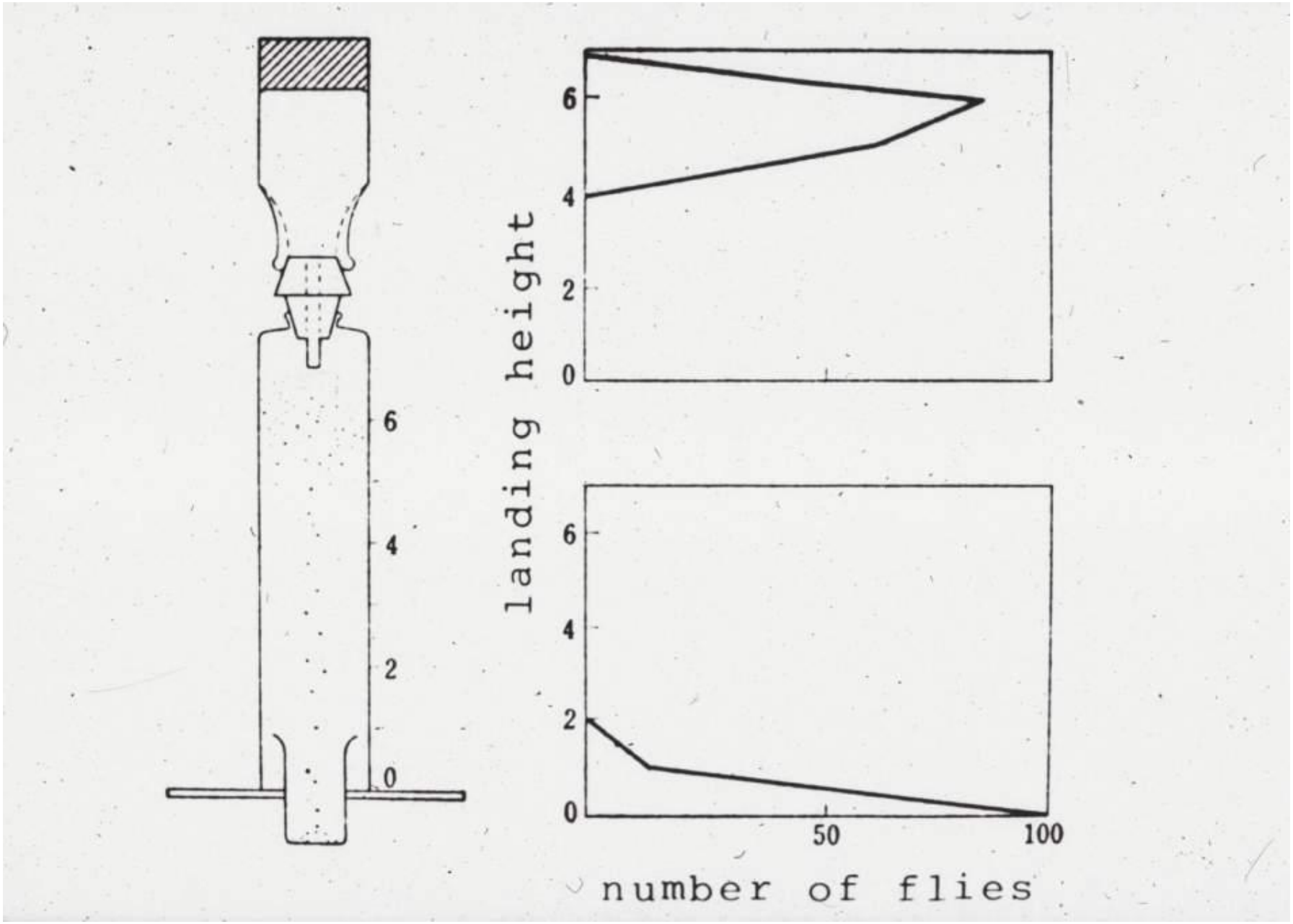




‡ Hotta & Benzer, Nature, vol 240, 527–535, copyright (1972)



‡ “Development and Differentiation of Nervous System” (Modern Biology Series; 28) Yuzo Tsukada, Kyoritsu Shuppan, 1976



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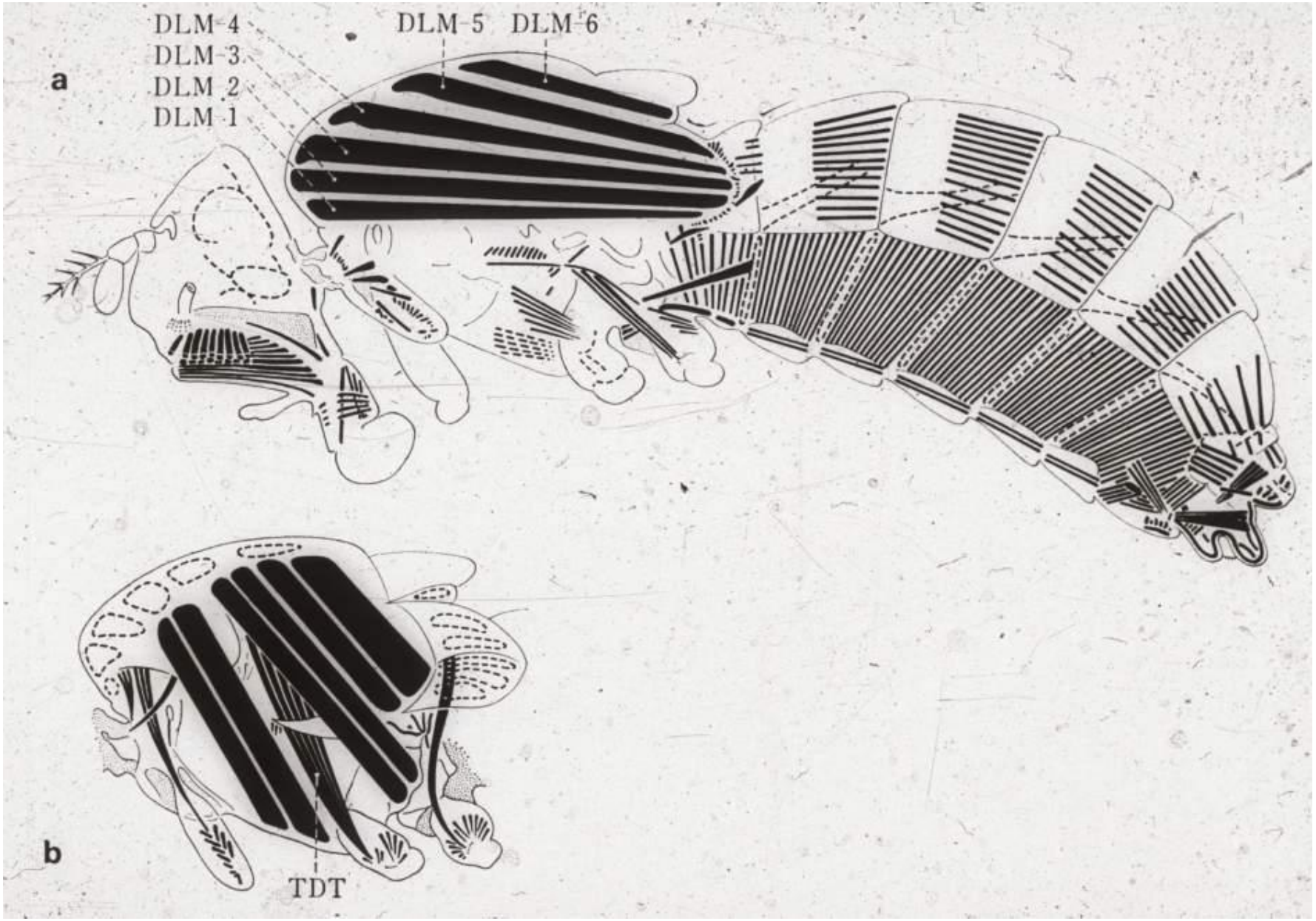

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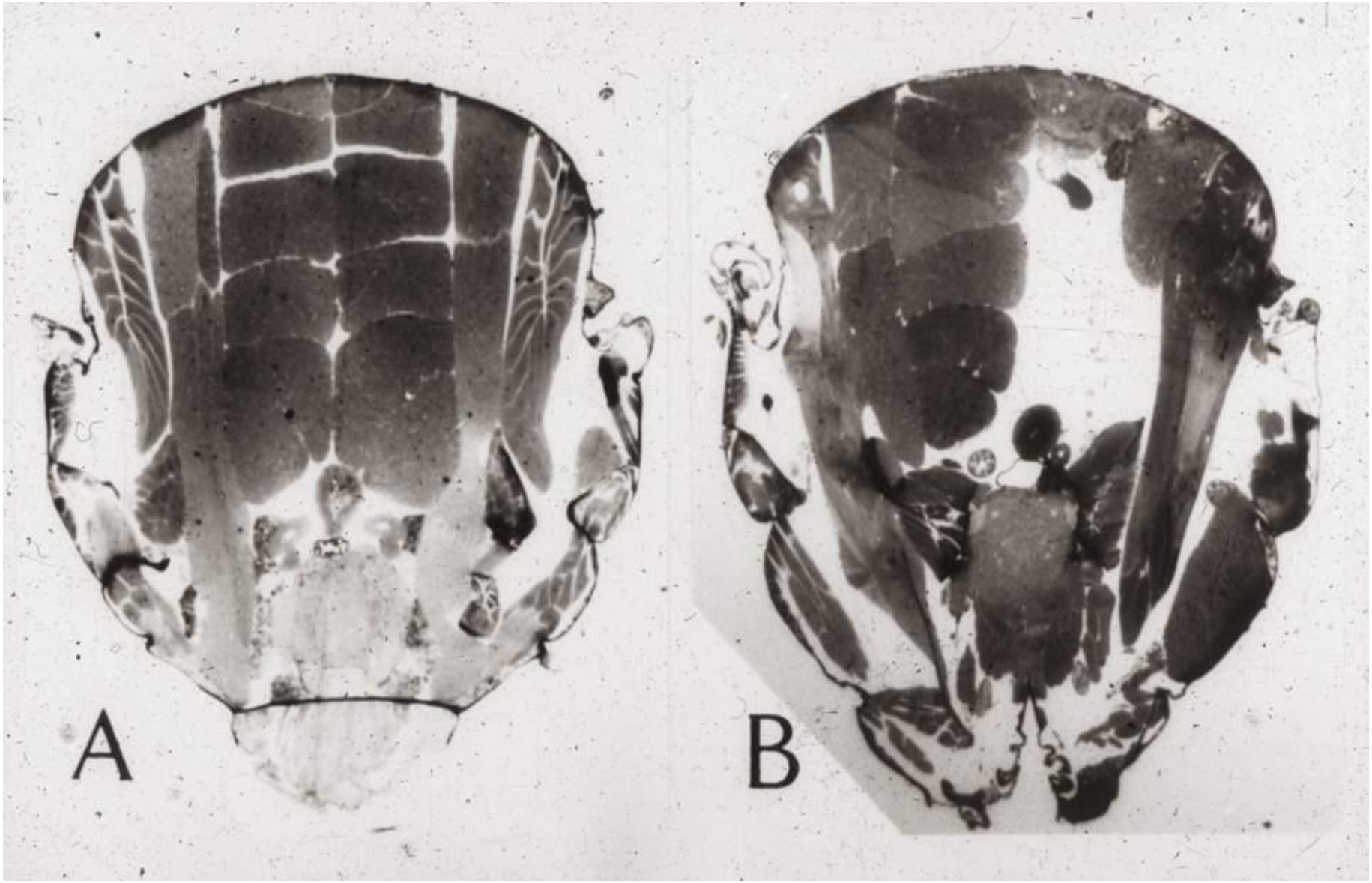

‡ “Seitai no Kagaku”, October 1972, Vol.23, No.5, p232

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“Behavior and Adaptation of Insects: Intersection of Genetics and Ecology”, Chozo Oshima
Publisher: Baifukan
Published in 1974
P119 Fig. 6-2C

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“Behavior and Adaptation of Insects: Intersection of Genetics and Ecology”, Chozo Oshima
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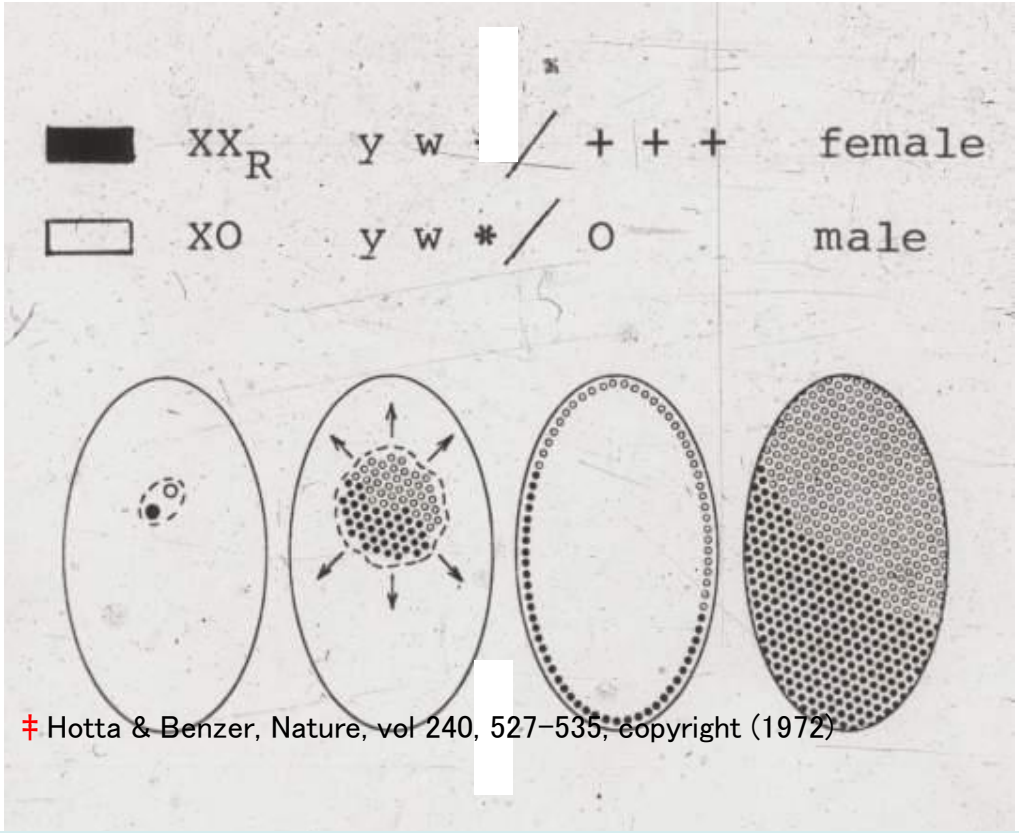
P122-123 Fig. 6-4(1)&(2)



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"Behavior and Adaptation of Insects: Intersection of Genetics and Ecology", Chozo Oshima
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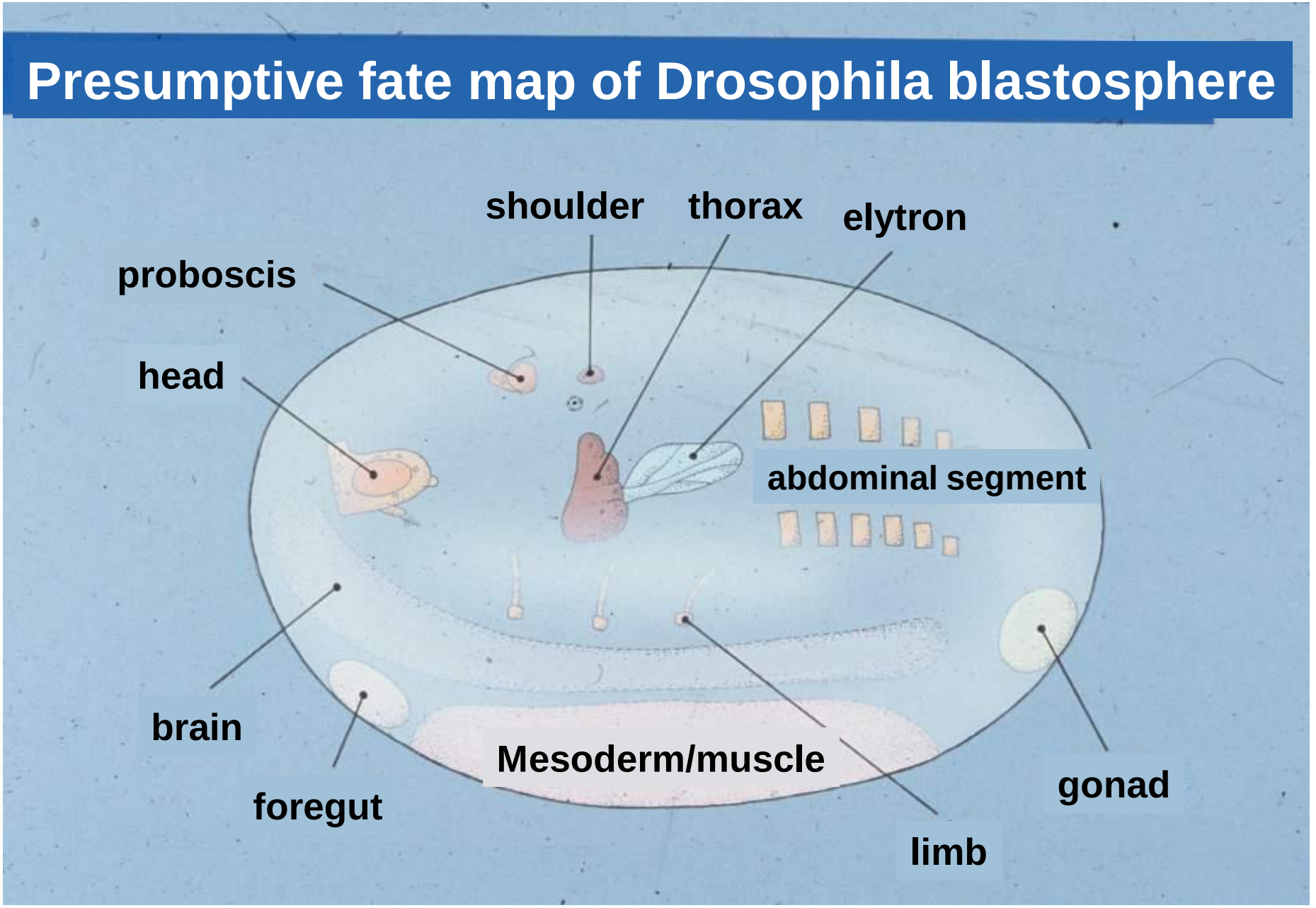
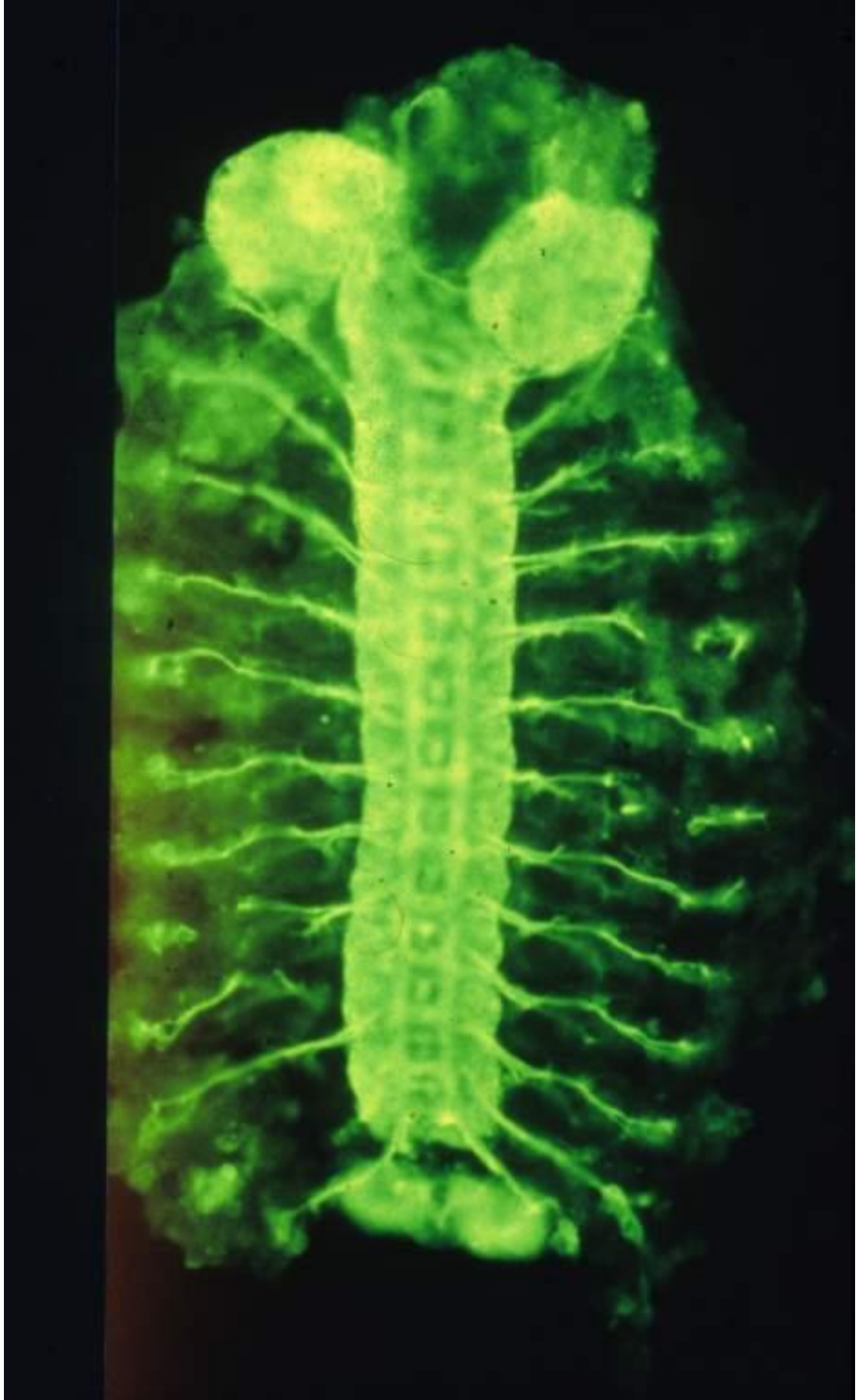
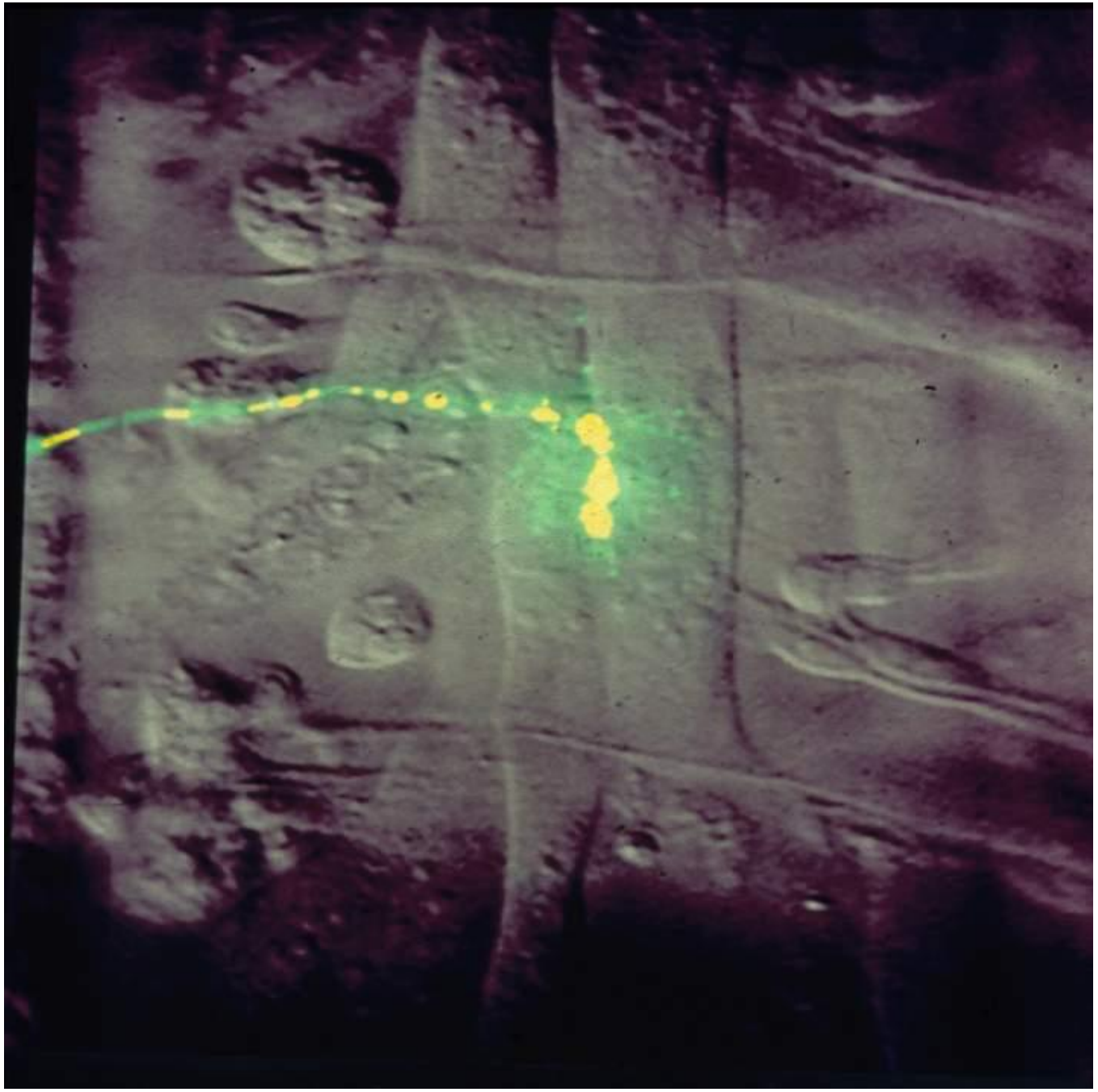
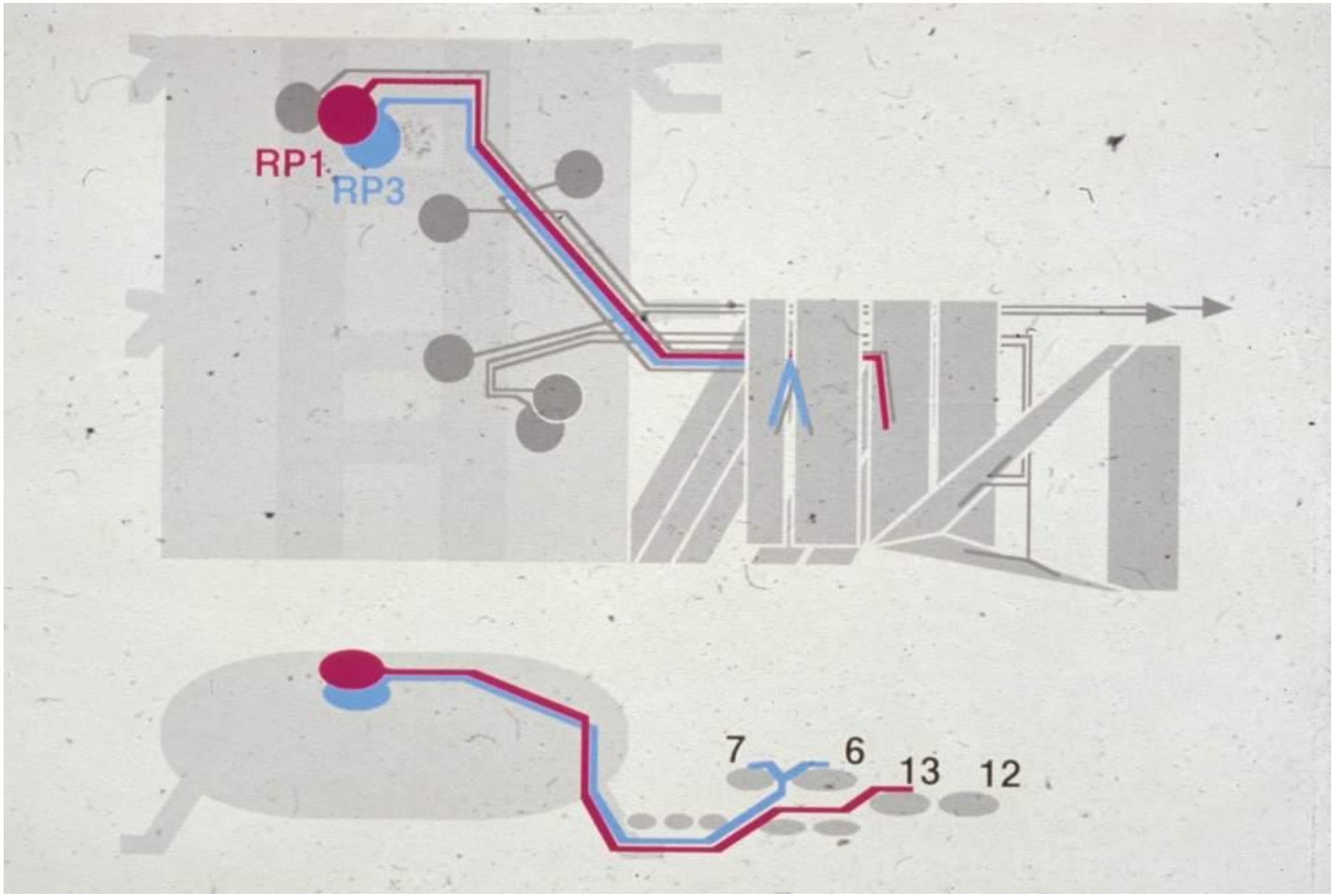
P117 Fig. 6-1

Presumptive fate map of Drosophila blastosphere

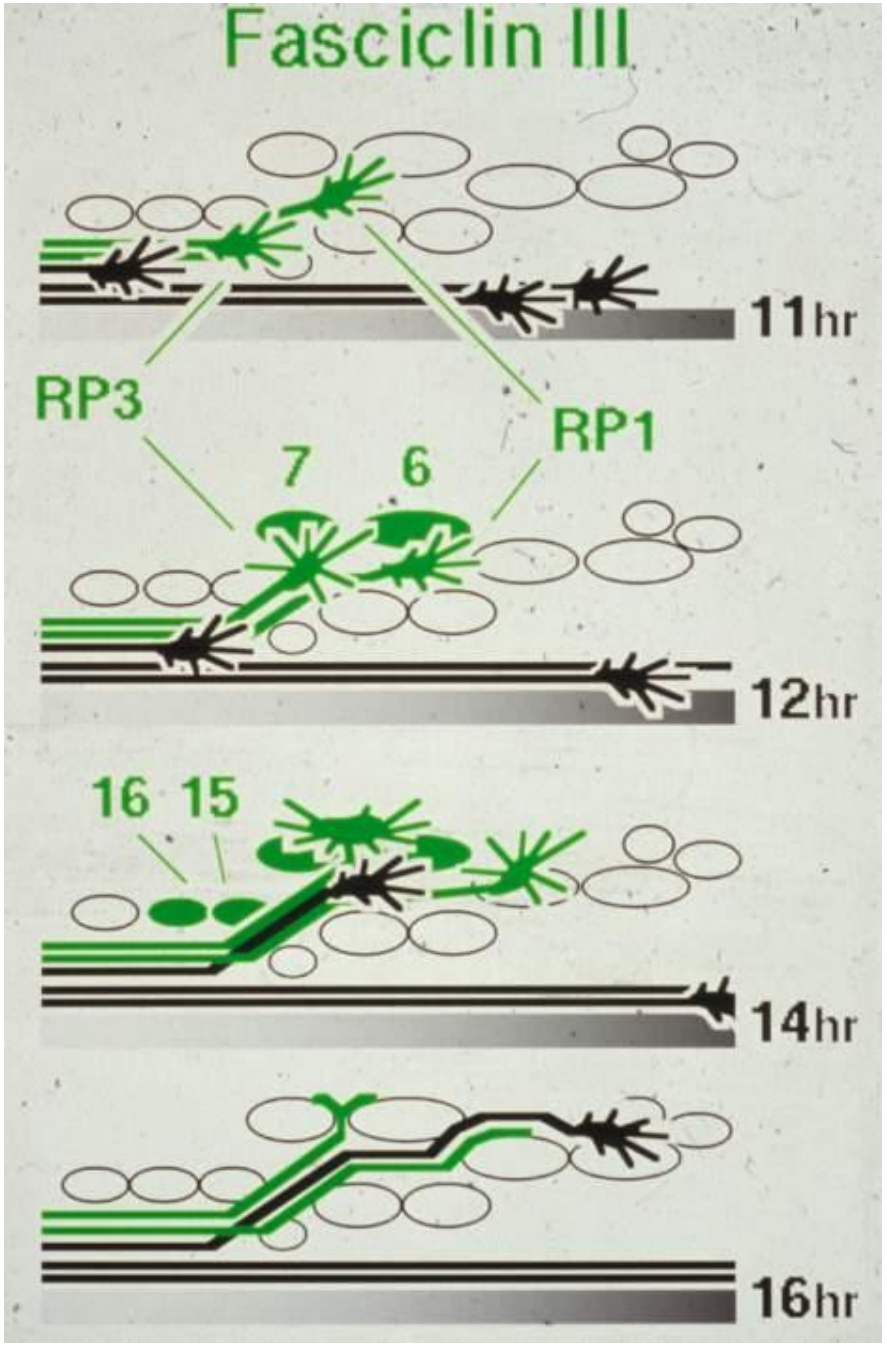








‡ Chiba et al., Nature 374, 6518,166-168, (1995)



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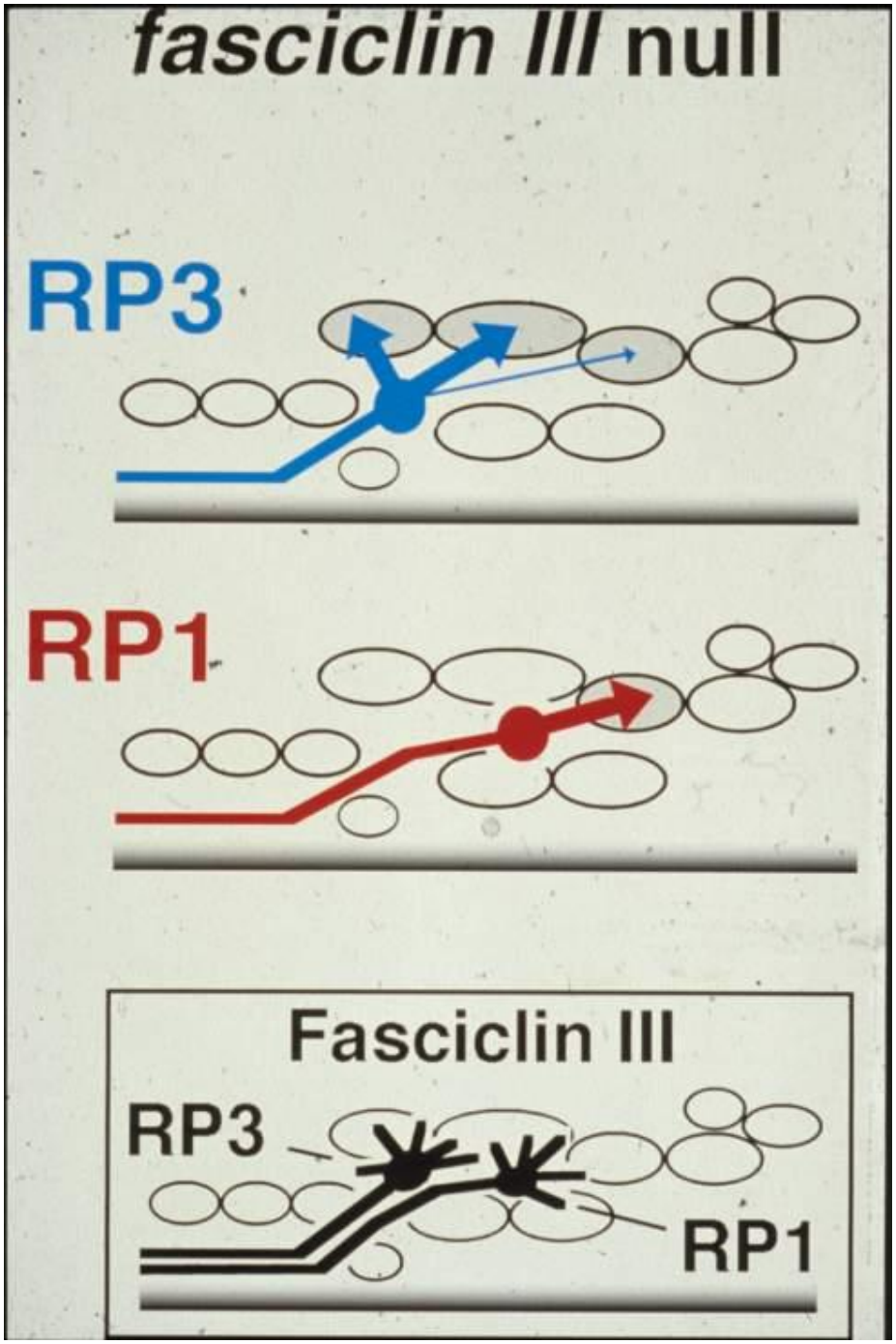

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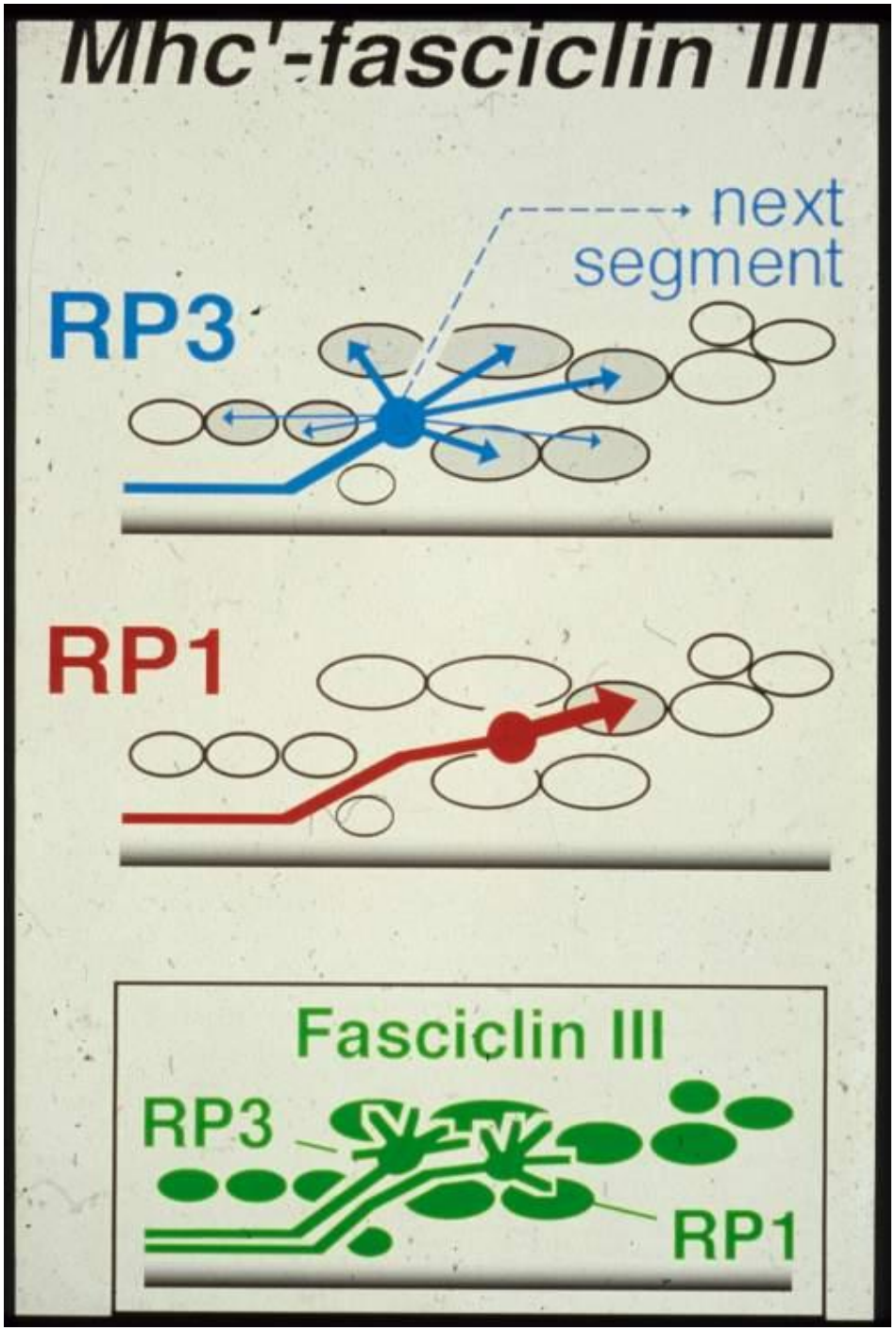

‡ Chiba et al., Nature 374, 6518,166-168,(1995)

The Third Revolution

Early 21st century: Advent of genome era

→ **Decoding the entire genome of organisms**

→ **Comparative genomics, evolution of life**

→ **Fundamental understanding of life**

→ **Social and medical applications**

Traditional common concepts of science

Precise description → Elimination of insignificant details → Abstraction

(Creativity is in the way of Elimination and Abstraction!)

Formulating as a law

(A word is enough to the wise!)

Experiments designed to examine only a part of the system!

Unique feature of genomics

Examining the entire subject all together!

(Quantity and speed are the key!)
(Advancements in computer technology)

Is this a new scientific style?

Challenges in life science research

Unified theory based on DNA

→ Natural history of molecules

Elements → Systems Network

Demands for new methodology

(Mathematics, Information Science, Analysis techniques)

Trend: Basic Science → Application

How far can we go with determinism?

The human brain is good at deterministic thinking

Determinism is used to understand non-deterministic phenomena, too

(for example, advancements in physics)

Newtonian Mechanics → Quantum Mechanics

Non-deterministic properties of organisms are determined by genes, too

Determinism (gene) vs. **Non-determinism (environment)**

Genes determine the non-deterministic scope, too

e.g. "Language"

ability is inherent **content is acquired**

Genes code "Brain Language"

References

Yoshiki Hotta and Kuniyoshi Sakai (2007)
“Gene, Brain, and Language” Fun of Science Café, Chuko Shinsho

A portion of my research references information from books by Takashi Tachibana listed below (although they may be too technical).

Takashi Tachibana
“10 Billion Years of Travel (I. Exploring the brain by genes)”, p.11–26,
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“Science Millennium (Elucidating the mystery of brain development by genes)”,
p.157–186, Chuo Koron Shinsha (1999)