

Model Organisms and the Rise of *Drosophila*

Model Organisms and the Rise of *Drosophila*

1. What is a model organism?
2. What are the primary model organisms and their characteristics?
3. How did *Drosophila* become a model organism?
4. What is the current status of *Drosophila* as a model organism?

A **model organism** is a species that is extensively studied to understand particular biological phenomena, with the expectation that discoveries made in the model organism will provide insight into the workings of other organisms.

This is possible because fundamental biological principles such as metabolic, regulatory, and developmental pathways, and the genes that code for them, are conserved through evolution.

What are the characteristics of a model organism?

1. **Short life cycle**
2. **Small adult size**
3. **Readily available**
4. **Tractable**
5. **Cost effective**

The major model organisms:

1. *Escherichia coli*
2. *Saccharomyces*
3. *Caenorhabditis elegans*
4. *Drosophila melanogaster*
5. *Mus musculus*
6. *Brachydanio rerio*
7. Human cell lines
8. *Arabidopsis thaliana*
9. *Brassica rapa*
10. *Zea mays*

Escherichia coli (*E. coli*) is one of the main species of bacteria that live in the lower intestine of warm-blooded animals and are necessary for the proper digestion of food.

When?

1950's after DNA confirmed as genetic material, structure, etc

Advantages?

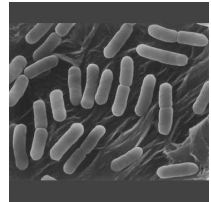
Single, simple chromosome
Cheap, fast generation time, easy to manipulate

Types of biological problems?

Gene regulation, transcription, translation

Resources?

Genome sequenced
E. coli stock center-Yale



THE WORM

Caenorhabditis elegans is a small (about 1 mm long) soil nematode found in temperate regions.

WHEN ?
1960's

Advantages?

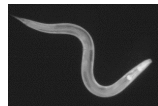
959 cells in the adult hermaphrodite;
1031 cells in the adult male

Types of biological problems

Development, neurogenetics, aging

Resources?

Sequenced genome, Wormbase,
Stock centers (1000 strains)



THE MOUSE

•When ?

William Castle 1902
inbred strains of mice

•Advantages?

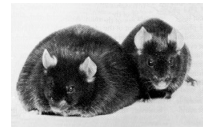
mammal, short generation time

•Types of biological problems?

cancer, diabetes, aging, development,
immune disorders, neurological disorders

•Major resources for mouse research ?

Jackson Laboratories-Maine
3000 strains of mice
2 million mice shipped/year



Important dates in the history of genetics

1859 Darwin

1865 Mendel

1900 Rediscovery of Mendel

1902-3 Sutton: Chromosome Theory of Inheritance

What was the important scientific question at the time?

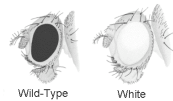
C.W. Woodworth - Harvard University

Bred *Drosophila*, in his laboratory, suggested it would be a good organism for heredity studies 1902

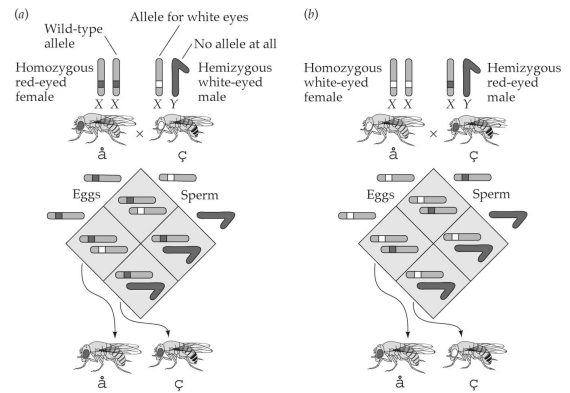
Thomas Hunt Morgan (1866 - 1945)

1890 Ph.D. Johns Hopkins University experimental embryology marine organisms
 1904 Faculty position at Columbia University in New York City.
 1909 Started working with *Drosophila*, looking for a cheap and easy system

What did Morgan do?



1. Looked for mutants by inbreeding and by using X-rays
2. Finally in 1910, white eyed mutant was found.
3. Bred white eyed males to females and crossed the progeny he noticed that only males displayed the white-eyed trait.



In 1902, Walter Sutton (1877–1916) and Theodor Boveri (1862–1915) realized that the behavior of chromosomes during meiosis – the cell division that produces gametes (sex cells) – is similar to the behavior of Mendel's factors. The idea that chromosomes carry the factors came to be known as the chromosome theory of inheritance. In 1910, Thomas Hunt Morgan (1866–1945) provided the first good evidence to support this theory.

MORGAN'S EXPERIMENT

Morgan knew that normal female fruit flies have two X chromosomes and males have an X and a Y chromosome.

1 Parental (P) generation
He mated a white-eyed male with a red-eyed female. White eyes and red eyes are phenotypes (expressions) of the gene for eye color.

2 First (F₁) generation
All the F₁ generation had red eyes.

3 Second (F₂) generation
When the F₁ generation flies were mated, there was a 3:1 ratio of red-eyes to white-eyes. Although half of the male flies had white eyes, however, none of the females did.

MORGAN'S CONCLUSION
The gene for eye color was on the X (a) but not the Y (b) chromosome.

Eye color
W is the gene for eye color. It has two alleles (forms): W (red eyes) and w (white eyes). W is dominant – expressed in preference to recessive ("weaker") w.

4 Parental (P) generation
The original male fly had a single copy of the gene for white eyes (w). The female had two alleles of the gene for red eyes, giving her the genotype (genetic constitution) WW.

5 First (F₁) generation
All of the female offspring had one red-eye gene and one white-eye gene (Ww). All of the male flies had a single red-eye gene (W). All of these genotypes give red eyes.

6 Second (F₂) generation
Half of the F₁ males had the white-eye gene and half the red-eye gene, so half had red eyes and half had white eyes. None of the females could have had two white-eye genes, so all the females were red-eyed.

PHENOTYPES

GENOTYPES

Key: Male Female

What did Morgan do?

Wild-Type White

1. Looked for mutants by inbreeding and by using X-rays
2. Finally in 1910, white eyed mutant was found.
3. Bred white eyed males to females and crossed the progeny he noticed that only males displayed the white-eyed trait.
4. Morgan also discovered a pink-eyed mutant that showed a different pattern of inheritance.
5. 1911 Science: concluded that
 - (1) some traits were sex-linked
 - (2) the trait was probably carried on one of the sex chromosomes,
 - (3) other genes were probably carried on specific chromosomes

V:U

Clarity

Figure 23 Brittle phenotypes: + wild, f. linked (1-56.7), m. angled (1-21.9), m. apical (1-58.3), Ss, Shobbs (1-59.2), cv. shaven (1-61). Brittle phenotype can be readily distinguished with the magnification of a stereomicroscope.

The Thomas Hunt Morgan group at Columbia University 1910 - 1928 "FLY ROOM"

1. Chromosomes as the hereditary material
2. Discovery of crossing over, or genetic recombination
3. Creation of genetic maps

The Thomas Hunt Morgan group
 Moved to the California Institute of Technology 1928



Calvin Bridges
 (Chromosome maps,
 sex determination)



Alfred Sturtevant
 (additional *Drosophila*
 species)



Herman J. Muller
 (Indiana University
 radiation genetics)

The Thomas Hunt Morgan group
 Moved to the California Institute of Technology 1928

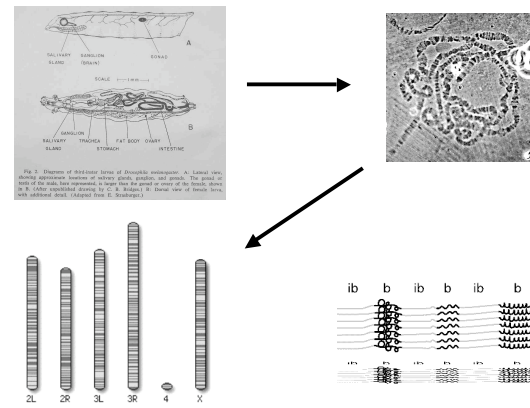


THEODOSIUS DOBZHANSKY



The basic *Drosophila* karyotype is five rods and a "dot" all referred to as "Muller Elements", six of them in all

D. melanogaster has an acrocentric X (one arm), metacentric second (two arms) metacentric third (two arms) and a small fourth, the dot.



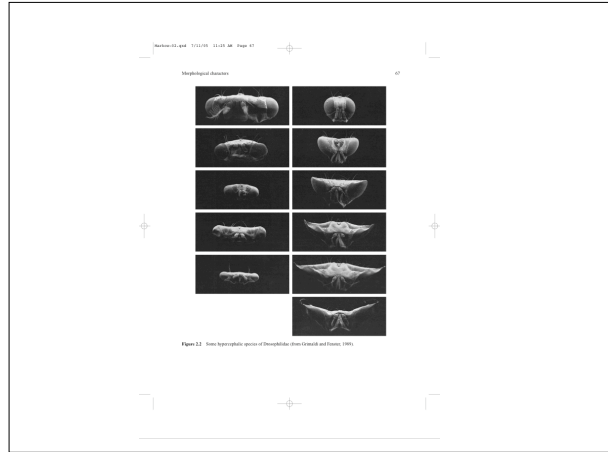
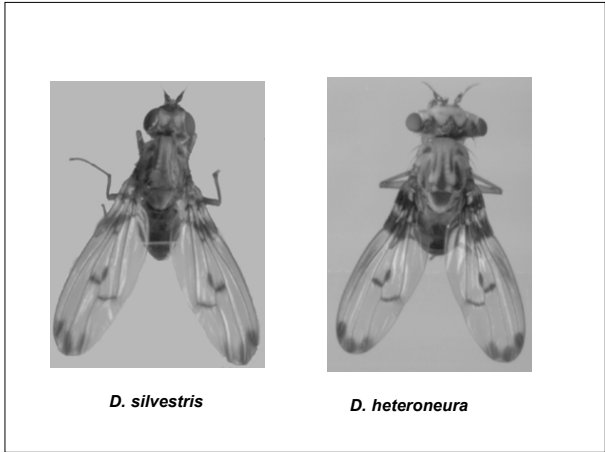
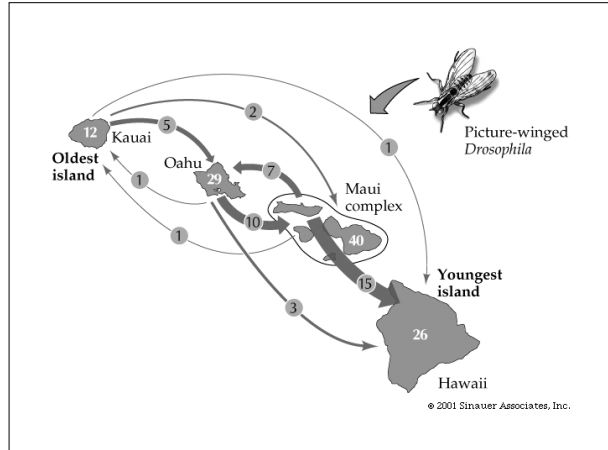
Other *Drosophila* species (about 2000 of them):

- Sturtevant: *Drosophilidae* of North America
- Patterson and Stone: Evolution in the genus *Drosophila* (*The Texas group*) 1940s- 1970
- Hawaiian *Drosophila* Project
- Russian and Japanese *Drosophila* projects pre - WW2

D. virilis



D. ananassae



Examples of traits with significant interspecific variation in *Drosophila*

Body size, morphology

Coloration

Growth rate

Longevity

Reproduction

egg production

sperm production

copulation duration

seminal "feeding" or ejaculatory donation to eggs

female remating

Stress tolerance

heat

cold

desiccation

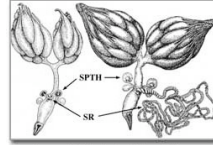
starvation

toxic chemicals

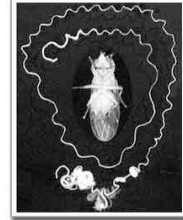
Immunity

Locomotor activity

Ecology

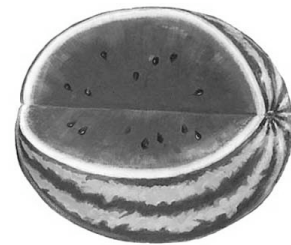
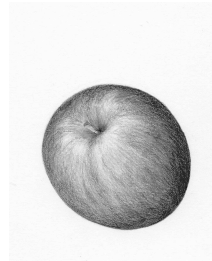
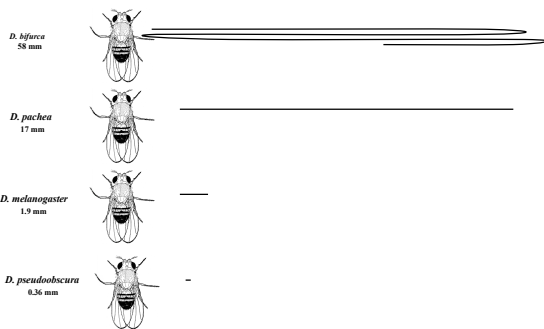


Female reproductive tract of *Drosophila pseudoobscura* (left), which has 0.56 mm long sperm, and of *D. bifurca* (right), which has 58.3 mm long sperm. SR = seminal receptacle, SPTH = spermathecae. Drawings by J. C. Paterson. See Finnick et al. 1990 for details.

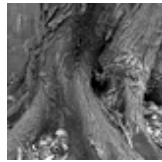


Male *Drosophila bifurca* surrounded by one of his testes (reproductive tract dissected after imaging male then photographed at same magnification). The energetic demand of such massive testes underlies many life history costs. See Finnick 1990 for details.

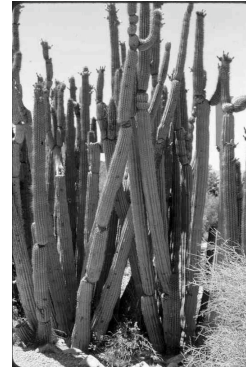
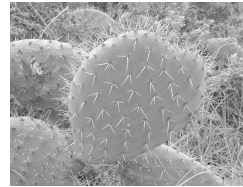
Tamaño del espermatozoide en varias especies de *Drosophila*



Fruits



Slime flux



Genome related traits showing interspecific variation in *Drosophila*:

Karyotype

Chromosome number (centric fusions)
Inversion polymorphism

Levels of variation

Codon Bias

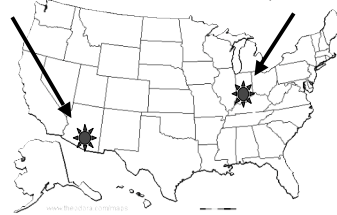
Transposable elements

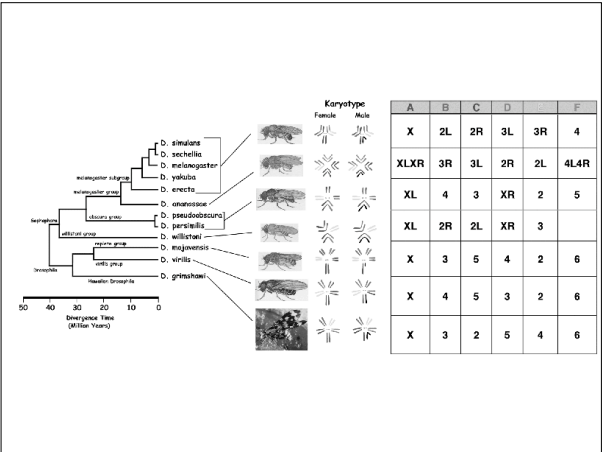
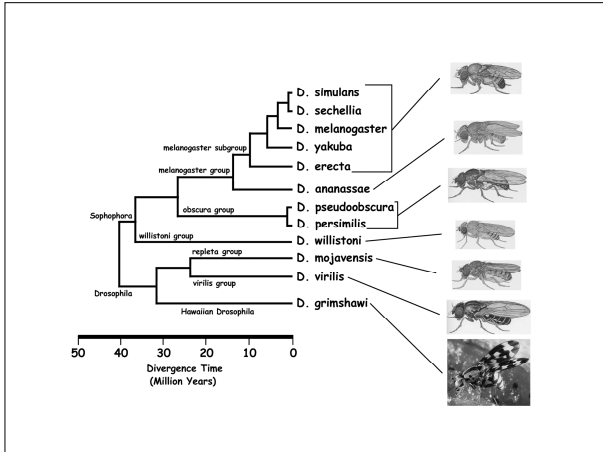
Genome size

Heterochromatin

Other *Drosophila*
Tucson Stock Center
250 species,
1600 stocks


D. melanogaster
Bloomington Stock Center
15,000 stocks





DROSOPHILA AS A MODEL SYSTEM

- *D. melanogaster* and early studies in genetics
- Other *Drosophila* species
- *Drosophila* Stock centers
- Sequencing projects
- Other resources



What are the important questions that *Drosophila* can be used to address?

How do new species form?

What are the genetic bases of:

- Insecticide and drug resistance?
- Cancer and the control of cell division?
- Aging?
- Developmental defects?
- Stress resistance?