Chapter 3: The Chromosomal Theory of Inheritance

I. A prelude to the chromosomal theory of inheritance (genes/Mendel's factors are part of cellular structures called chromosomes)

A. Discoveries leading up to the CTI

1. Early on it was realized that hereditary material carried by sperm and egg.

a) Sperm from mammals seen by van Leeuvenhook in late 17th-early 18th. Mammalian egg not found until 1827.

b) Usually, the egg and sperm cell were usually greatly different in size, but it was noted that the nuclei were very nearly the same size. This suggested that the cytoplasm was not the source of the hereditary material - rather that the nucleus is.

2. The microscope continued to improve, and the microtome (cutting device for make very thin sections of tissue for observation under the microscope) was improved so that sections made were thinner and more even.

3. The processes of <u>mitosis</u> (nuclear division accompanied by cell division that produces two daughter nuclei identical to the parental nuclei) and <u>meiosis</u> (two successive nuclear divisions accompanied by cell division that produces products that have one-half of the genetic material of the parental cell) were visualized.

B. Let's look at the process and behavior of chromosomes during mitosis and meiosis to see how they qualify for the designation of hereditary material. These are the observations that led to the CTI.

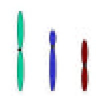
II. SOME DEFINITIONS

A. Chromosome sets. Higher organisms contain two similar sets of chromosomes in somatic cells. One set came from the male parent and the other set came from the female parent. Each member of a set has a <u>homologous</u> partner, and two members of a pair are called <u>homologues</u> (meaning same shape).

In humans: 23 <u>pairs</u> of chromosomes = 46 chromosomes <u>total</u>

In Drosophila: 4 <u>pairs</u> of chromosomes = 8 chromosomes <u>total</u>

B. Haploid: a cell or organism having only one set of chromosomes



C. Diploid: a cell or organism having two complete sets of homologous chromosomes (referred to as 2n where n = the number of chromosomes in a set)

Mendel's peas: 2n = 2(7 chromosomes in one set) = 14
Humans: 2n = 2(23 chromosomes in one set) = 46
Drosophila: 2n = 2(4 chromosomes in one set) = 8

D. Genome: the total complement of genes contained in a cell.

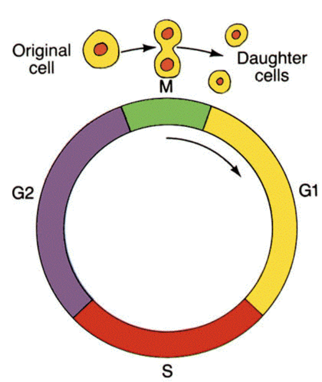
III. MITOSIS

Nuclear division accompanied by a cell division that produces 2 daughter cells having genetic material identical to the parent

A. General info

1. Mitosis occurs in the somatic cells (all the cells of the body that do not become sex cells)
2. In mitosis, the chromosomes make copies of themselves and the copies split apart from each other to form genetically identical chromosomes that go to genetically identical daughter cells.
3. The cell cycle: Divided into four periods: M (mitosis), G1 (gap 1), S (DNA synthesis), and G2 (gap 2). G1, S, and G2 referred to as Interphase. Length of time involved varies with cell type, but with higher organisms 18-24 hours is usual. M usually only 1/2-2 hrs.

(from An Introduction to Genetic Analysis, 6th ed. By Griffiths et al. W. H. Freeman and Company)

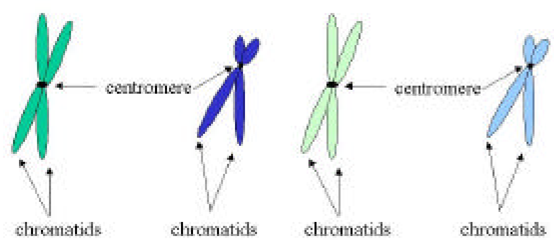


B. Mitosis

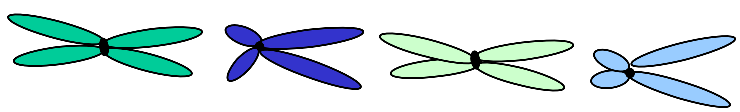
Mitosis period of the cell cycle is divided into four stages:

Prophase, metaphase, anaphase, telophase. (mnemonics: Peas make awful tarts or Pay Me Anytime)

1. Prophase
    a) Marked by the thickening and coiling (condensation) of the chromosomes which makes them visible.
    b) As the coiling and condensation continue, it can be seen that the chromosomes are doubled. During mitosis, each chromosome is composed of two halves along their length. Each of the halves are called chromatids.
    c) They are attached to each other at their centromeres.
    d) Nucleolus (plural, nucleoli) a nuclear organelle containing rRNA and amplified multiple copies of genes for rRNA, disappear.
    e) Nuclear membrane breaks down. Nucleoplasm and cytoplasm become one.
    f) Important point: the homologous chromosomes do <u>not</u> pair.



2. Metaphase:
    a) Assembly of the <u>nuclear spindle</u>. Parallel spindle fibers that point to and are attached to each of two cell poles.
    b) Chromosomes move to the center of the cell (<u>equatorial plane</u>)
    c) Centromeres become attached to spindle fibers from each pole.
    d) Once again, homologous chromosomes do not pair.



3. Anaphase:

Each centromeres divides into 2 and begins to move to separate poles. Each sister chromatid seems to be pulled by centromere. Once centromere splits, the chromatids are referred to as <u>daughter chromosomes</u>.

4. Telophase:

a) Nuclear membrane reforms around each set of chromosomes to form daughter nuclei.
b) The chromosomes uncoil in the two new daughter nuclei which are identical genetically.
c) Nucleoli reappear
d) Spindle disappears
e) Cytoplasm divides (<u>cytokinesis</u>)
f) New cell membrane forms

IV. Meiosis

Q: How were organisms able to produce offspring with exactly the same number of chromosomes as the parents when two parental cells were joined during fertilization?
A: The process of <u>meiosis</u>.

46 chromosomes + 46 chromosomes = 46 chromosomes

A. General

1. Meiosis occurs in specific cells. In animals, called <u>meiocytes</u>, general term for primary spermatocytes and oocytes. In plants, called <u>meiospores</u>. In animals the final products are gametes, eggs and sperms that unite to form zygote. In plants there is somewhat more complication. We will talk about plant life cycle, along with other life cycles a little later.
2. Process is much longer than mitosis, may require days or even weeks.
3. G1, S, and G2 phases of the cell cycle are similar to mitosis
4. Meiosis consists of two nuclear divisions; therefore meiosis is divided into Meiosis I and Meiosis II. First division is <u>reduction division</u>. Second division is <u>equational division</u> and is nearly like mitosis.
Each division is divided into four stages that are similar to mitosis: prophase, metaphase, anaphase, telophase.

B. Meiosis I

Reductional division: Diploid to haploid or # of centromeres is halved.

1. Prophase I:

Prophase I is the lengthiest and most complex and is divided into 5 stages: leptotene, zygotene, pachytene, diplotene, diakinesis (Little Zelda packs diplomats diapers OR Lewd zebras practice dirty dialogues)

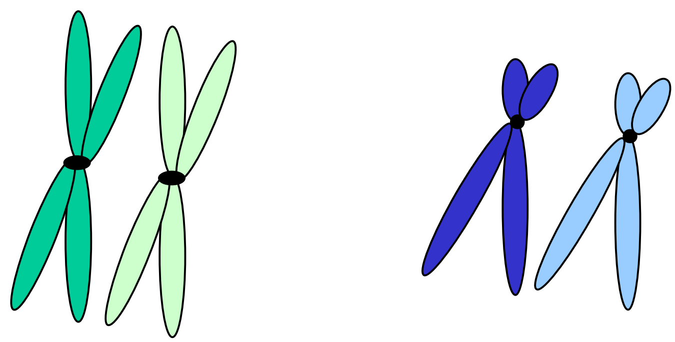
a) Leptotene: (thin thread stage)

(1) Chromosomes begin to condense and coil and become visible as thin threads.

(2) Small areas of localized condensation along length called chromomeres.

b) Zygotene: (yolk thread)

(1) Each chromosome set pairs up with its homologous chromosome to form a homologous pair. This does not happen in mitosis. They are progressively joined or synapsed.



(2) The synaptonemal complex (an elaborate structure of protein and DNA) holds the homologs together. The complex is also thought to help the homologues find each other.

c) Pachytene: (thick thread)

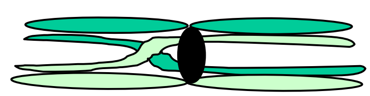
(1) Chromosomes have thickened even more and are fully synapsed along their length.

(2) Nucleoli still present

d) Diplotene: (double thread)

(1) Chromosomes now appear as a bundle of four homologous chromosomes.

(2) The synapsis becomes less secure, even seem to repel each other, but are connected at the chiasmata, cross-shaped structures where crossing over (a break and reunion event in the DNA) has occurred. This is a major difference from mitosis where rarely is there crossing over and the chromosomes do not synapse.

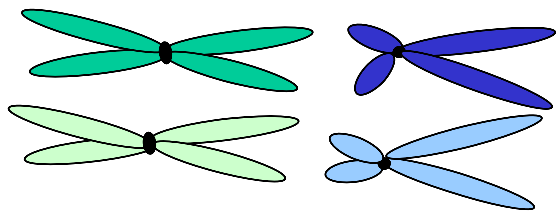


(3) Nucleolus disappears

e) Diakinesis:

(1) Further condensation and thickening of chromosomes.

2. Metaphase I:
    a) Nuclear membrane and nucleoli have disappeared.
    b) The chromosomes line up along the equatorial plane.
    c) The two centromeres of a homologous gene pair attach to the spindle fibers.



3. Anaphase I:
    a) Chromosomes begin moving to the two poles. The centromere holding the two sister chromatids together does <u>not</u> divide.
    b) Members of homologous pairs move to different poles.
4. Telophase I: variable for different organisms.
    a) Some go immediately into MII without stopping, with no nuclear membrane being formed.
    b) Some have the chromosomes become diffuse, form a nucleus.
    c) Period is brief between MI and MII and <u>there is no DNA synthesis</u>.

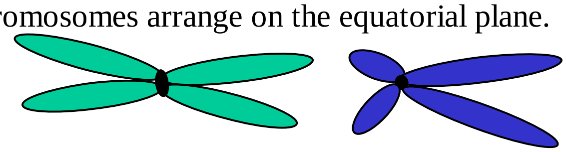
C. Meiosis II

1. Prophase II:

Contracted chromosomes,

2. Metaphase II:

Chromosomes arrange on the equatorial plane.



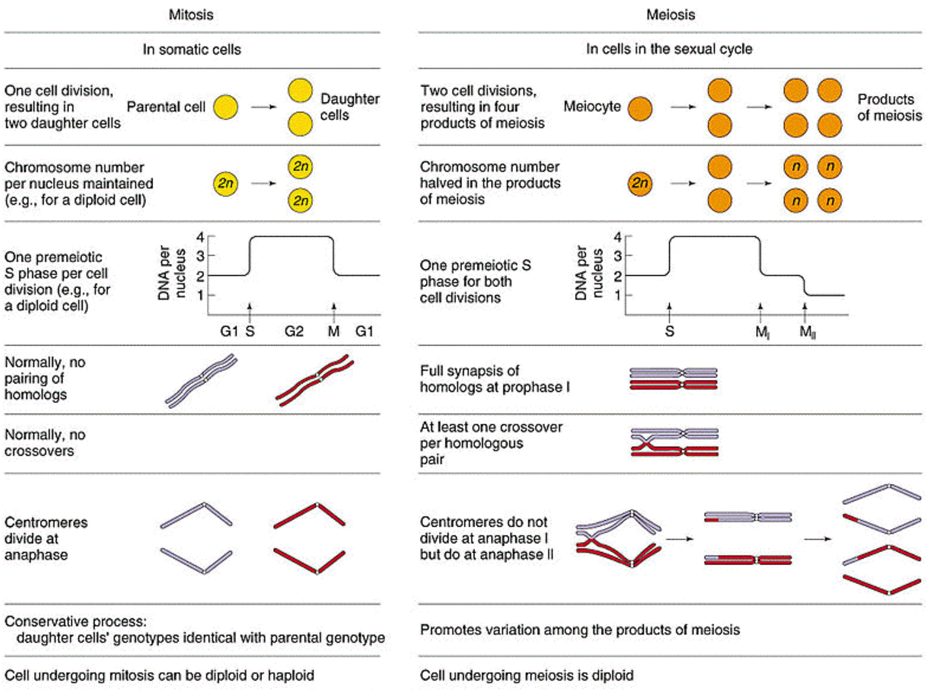
3. Anaphase II:

Centromeres split, chromatids move to opposite poles.

4. Telophase II:

Nuclear membranes form around the nucleus

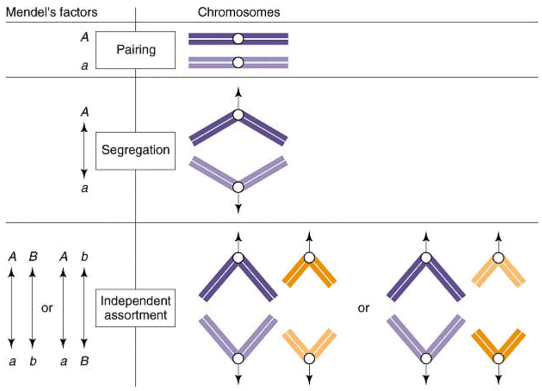
V. Summary:



(from An Introduction to Genetic Analysis, 6th ed. By Griffiths et al. W. H. Freeman and Company)

VI. The chromosomal theory of inheritance

1902 - With evidence presented by other researchers of the behavior of chromosomes, Walter Sutton (an American graduate student) and Theodor Boveri (German biologist) recognized independently that the factors described in Mendel's paper could be explained by consideration of the behavior of chromosomes during meiosis. Known as the Sutton-Boveri chromosome theory of heredity.



(from An Introduction to Genetic Analysis, 6th ed. By Griffiths et al. W. H. Freeman and Company)

VII. Objections and counter objections to the chromosome theory of inheritance.

A. Objections:

1. chromosomes could not be detected during interphase

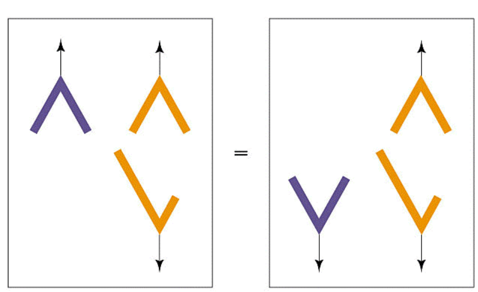
Boveri did careful cytological studies of chromosome position before and after interphase to reinforce his position that chromosome structure remained intact.

2. In some organisms all the chromosomes were identical so how could you tell that homologous chromosomes were specifically pairing.

Boveri observed that sea urchin eggs chromosomes were very different and like ones paired.

3. In some organisms all the chromosomes were identical so how could you tell that non-homologous chromosomes were sorting independently.

1913 Elinor Carothers found unusual grasshopper chromosomes in testes. One pair that were different shape/size that regularly synapsed (heteromorphic pair) and one chromosome without a partner. She found equal number of the following patterns; therefore, Non homologous chromosomes assort independently.



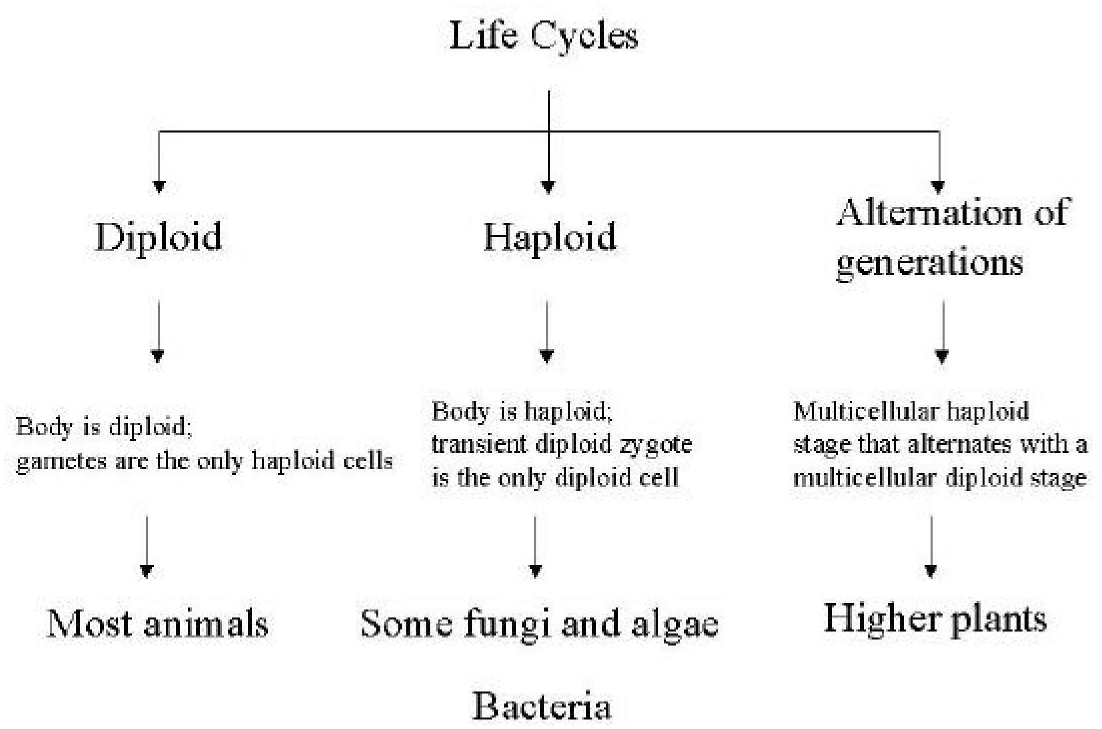
4. Chromosomes were "stringy structures" with no real difference between them.

    1922 Alfred Blakeslee worked on the plant jimsonweed (12 chromosomes). For plants that had an extra chromosome set, the plant had a different phenotype and each phenotype was different depending on which chromosome pair was duplicated.

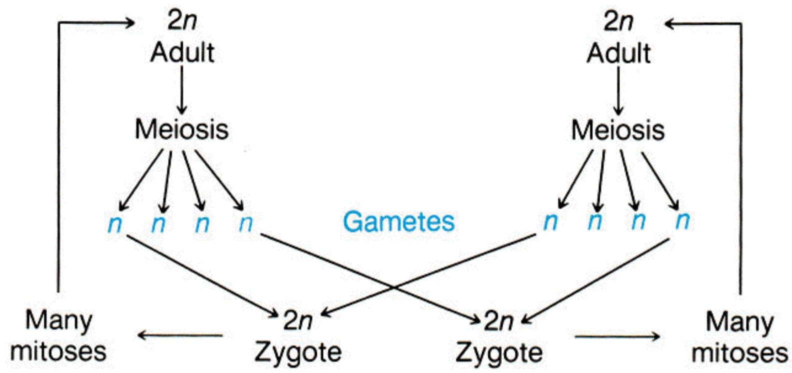
5. Definitive proof for the CTI was provided with the discovery of sex linkage which will be discussed later.

VIII. LIFE CYCLES

A. Overview

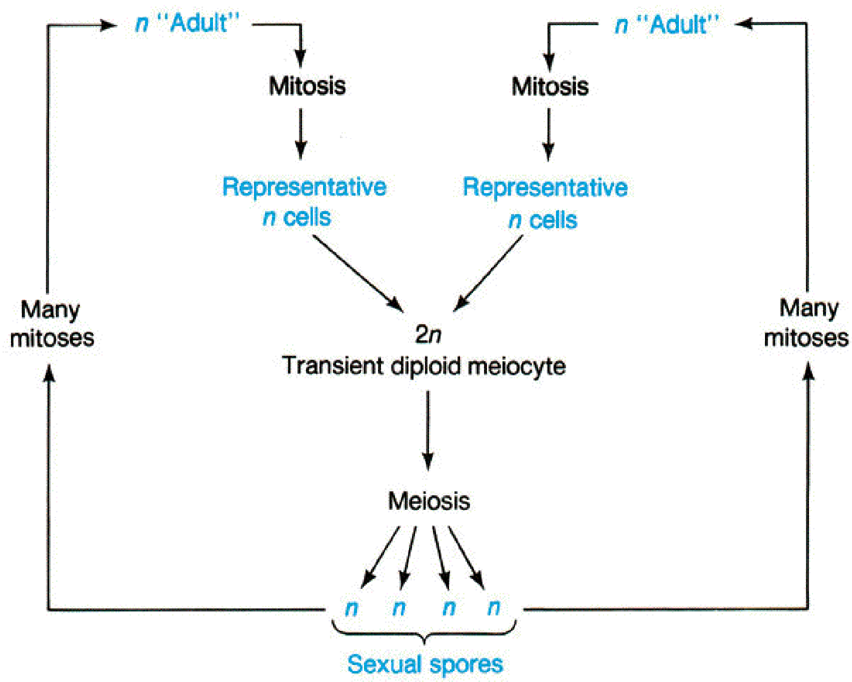


B. Diploid



(from An Introduction to Genetic Analysis, 6th ed. By Griffiths et al. W. H. Freeman and Company)

C. Haploid



(from An Introduction to Genetic Analysis, 6th ed. By Griffiths et al. W. H. Freeman and Company)

Example of Mendelian rations in a haploid organism

Neurospora crassa is a multicellular haploid fungus that causes bread mold.
They can bear asexual spores (conidia).   These are identical to parent, but can disperse and form new colonies Also, can act as male gametes, with a cell within a hyphae developing as female gamete. Requires two different mating types A x a, so cannot self -- but can reproduce asexually.

Wild type = pink color (al^+) and spreading morphology (col^+)

Mutant = albino color (al) and colonial morphology (col)

Cross col al   X col^+ al^+

Halploid cells fuse to form a transient diploid

Transient diploid undergoes meiosis to generate haploid ascospores

Obtain the ascospores and grow to determine phenotype of the offspring.

1/4 col al
1/4 col al^+
1/4 col^+ al
1/4 col^+ al^+

This shows that Mendel's laws of equal segregation and independent assortment apply to haploid organism too. However, note that we had no need to worry about dominance and recessiveness because the progeny were haploid.

D. Alternating Haploid/Diploid

Multicellular haploid stage that alternates with a multicellular diploid stage. Usually one stage is predominant.

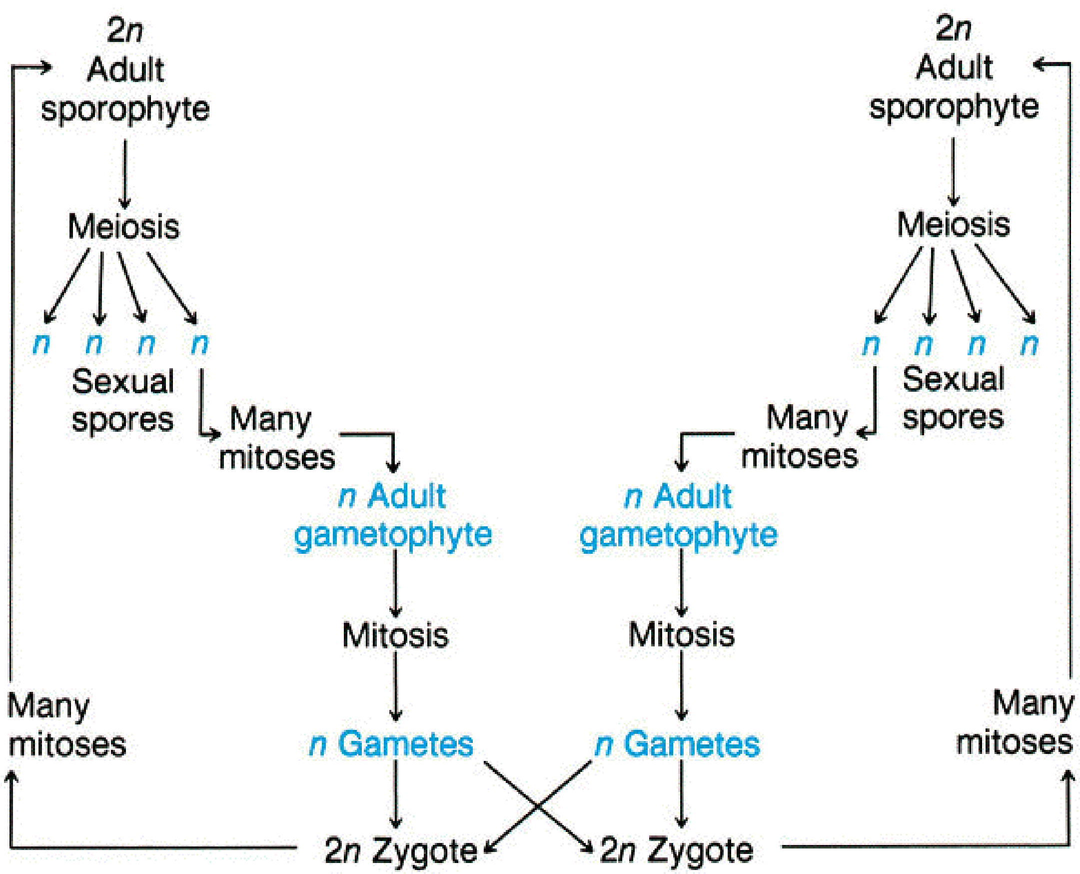
meiosis   fertilization

Sporophyte ⟶ spore ⟶ gametophyte ⟶ gamete ⟶ zygote ⟶ sporophyte

Example: Fern plant is diploid, but has inconspicuous haploid stage that grows and photosynthesizes

Mosses the green part is haploid and the brown stalk is diploid -- so diploid is dependent - even parasitic on haploid.

Flowering plants: diploid predominant and haploid dependent on the diploid. Haploid products are called spores. These undergo mitosis and form haploid stage called a gametophyte. Male gametophyte is the pollen.



.

(from An Introduction to Genetic Analysis, 6th ed. By Griffiths et al. W. H. Freeman and Company)