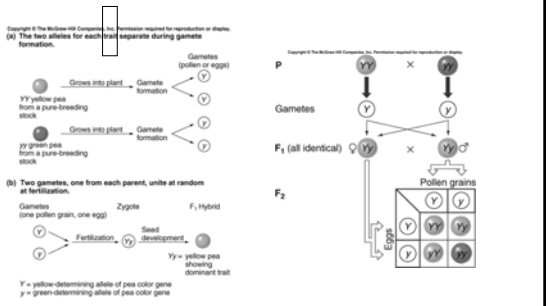
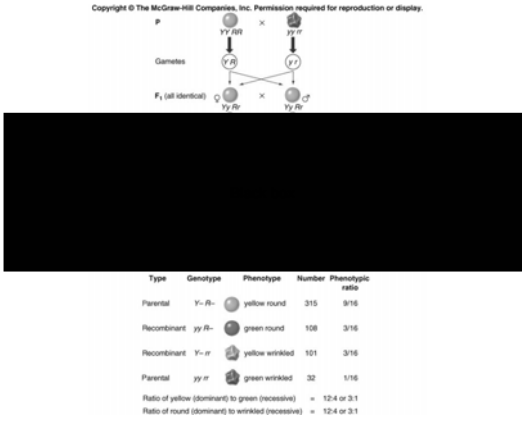


Gregor Mendel
Versuche über Pflanzenhybriden

The Second Law



Type	Genotype	Phenotype	Number	Phenotypic ratio
Parental	Y– R–	yellow round	315	9/16
Recombinant	yy R–	green round	108	3/16
Recombinant	Y– rr	yellow wrinkled	101	3/16
Parental	yy rr	green wrinkled	32	1/16
Ratio of yellow (dominant) to green (recessive)		=	12:4 or 3:1	
Ratio of round (dominant) to wrinkled (recessive)		=	12:4 or 3:1	

"The offspring of hybrids in which several differing traits are associated"

"In the experiments above described plants were used which differed only on one essential character. The next task consisted in ascertaining whether the law of development discovered in these applied to each pair of differentiating characters when several diverse characters are united in the hybrid by crossing." → **dihybrid cross**

"Two experiments were made with a considerable number of plants. In the first experiment the parental plants differed in the form of the seed and in the color of the albumen; in the second in the form of the seed, in the color of the albumen, and in the color of the seed-coats. Experiments with seed characters give the result in the simplest and most certain way.

In order to facilitate study of the data in these experiments, the different characters of the seed plant will be indicated by **A**, **B**, **C**, those of the pollen plant by **a**, **b**, **c**, and the hybrid forms of the characters by **Aa**, **Bb**, and **Cc**."

In order to facilitate study of the data in these experiments, the different characters of the seed plant will be indicated by *A*, *B*, *C*, those of the pollen plant by *a*, *b*, *c*, and the hybrid forms of the characters by *Aa*, *Bb*, and *Cc*.

Expt. I. — *AB*, seed parents. *ab*, pollen parents
A, form round. *a*, form wrinkled
B, albumen yellow. *b*, albumen green

The fertilized seeds appeared round and yellow like those of the seed parents. The plants raised therefrom yielded seeds of four sorts, which frequently presented themselves in one pod. In all, 556 seeds were yielded by 15 plants, and of these there were

315 round and yellow,
101 wrinkled and yellow,
108 round and green,
32 wrinkled and green.

All were sown the following year. Eleven of the round yellow seeds did not yield plants, and three plants did not form seeds. Among the rest

38 had round yellow seeds *AB*
65 round yellow and green seeds *ABb*
60 round yellow and wrinkled yellow seeds *AaB*
136 round yellow and green, wrinkled yellow and green seeds *AaBb*

From the wrinkled yellow seeds 96 resulting plants bore seed, of which

29 had only wrinkled yellow seeds *aB*
68 wrinkled yellow and green seeds *aBb*

From 108 round green seeds 102 resulting plants fruited, of which

35 had only round green seeds *Ab*
67 round and wrinkled green seeds *Aab*

The wrinkled green seeds yielded 30 plants which bore seeds all of like character; they remained constant *ab*.

The offspring of the hybrids appeared therefore under nine different forms, some of them in very unequal numbers. When these are collected and coordinated we find

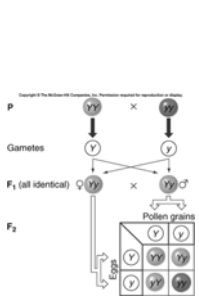
38	plants with the sign	*AB*		
29	"	"	"	*aB*
30	"	"	"	*Ab*
65	"	"	"	*ABb*
68	"	"	"	*aBb*
60	"	"	"	*AaB*
67	"	"	"	*Aab*
136	"	"	"	*AaBb*

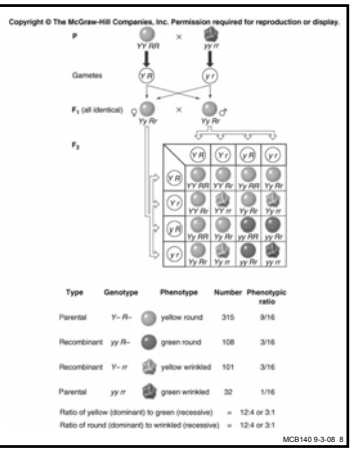
characters. Consequently, the offspring of the hybrids, if two kinds of differentiating characters are combined therein, are represented by the expression

$$AB + Ab + aB + ab + 2ABb + 2aBb + 2AaB + 2Aab + 4AaBb$$

This expression is indisputably a combination series in which the two expressions for the characters A and a, B and b are combined. We arrive at the full number of the classes of the series by the combination of the expressions:

$$A + 2Aa + a$$
$$B + 2Bb + b$$





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2.11

Ta-daaa! The second law

"There is therefore no doubt that for all of the traits involved in the experiments this statement is valid: *the offspring of the hybrids in which several essentially different characters are combined exhibit the terms of a series of combinations, in which the developmental series for each pair of differentiating traits are combined.*

It is demonstrated at the same time that *the relation of each pair of different traits in hybrid union is independent of the other differences in the two parental plants*."

"Es unterliegt daher keinem Zweifel, dass für sämmtliche in die Versuche aufgenommenen Merkmale der Satz Giltigkeit habe: *die Nachkommen der Hybriden, in welchen mehrere wesentlich verschiedene Merkmale vereinigt sind, stellen die Glieder einer Combinationsreihe vor, in welchen die Entwicklungsreihen für je zwei differirende Merkmale verbunden sind.*

Damit ist zugleich erwiesen, dass *das Verhalten je zweier differirender Merkmale in Hybrider Verbindung unabhängig ist von den anderweitigen Unterschieden an den beiden Stammpflanzen."*

Mendel's laws

1. For any given autosomal locus, a diploid organism makes an equal number of gametes carrying one allele and the other allele – the two alleles segregate equally to the gametes – **law of equal segregation**. For example, an organism heterozygous for a given locus (Aa) will make 50% **A** and 50% **a** gametes
2. Mendel's first law holds for each locus if we study two separate, unlinked autosomal loci. The alleles at each locus sort themselves to the gametes according to Mendel's first law independently of the way alleles for the other locus segregate – **law of independent assortment**. For example, an organism double-heterozygous (AaBb) will make AB, aB, Ab, and ab gametes in equal proportion – because the A locus and the B locus each obey Mendel's first law without regard for what alleles for the other locus are doing.

Gasp

"Even the validity of the law formulated for *Pisum* requires still to be confirmed, and a repetition of the more important experiments is therefore desirable … In the meantime we may assume that no basic difference could exist in important matters, **since unity in the developmental plan of organic life is beyond question**."

"Indessen dürfte man vermuthen, dass in wichtigen Puncten eine principielle Verschiedenheit nicht vorkommen könne, **da die Einheit im Entwicklungsplane des organischen Lebens ausser Frage steht**."

Gregor Mendel to Carl Nägeli, Dec. 31, 1866

"Highly esteemed Sir:

The acknowledged preeminence your Honor enjoys in the detection and classification of wild-growing plant hybrids makes it my agreeable duty to submit for your kind consideration the description of some experiments in artificial fertilization."

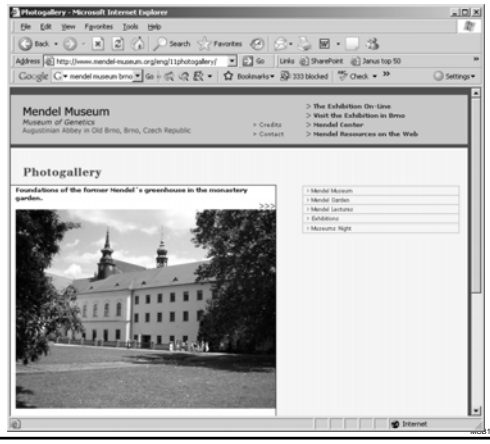
Gregor Mendel to Carl Nägeli, Dec. 31, 1866

"I am not surprised to hear your honor speak of my experiments with mistrustful caution. … I knew that the results I obtained were not easily compatible with our contemporary scientific knowledge, and that under the circumstances publication of one such isolated experiment was doubly dangerous; dangerous for the experimenter and for the cause he represented. Thus I made every effort to verity, with other plants, the results obtained with *Pisum*."

Apomixis

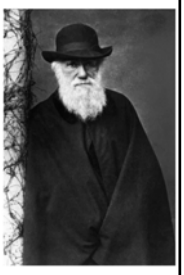
"In botany, apomixis is asexual reproduction, without fertilization and modified meiosis.The modified meiosis yields seeds that are genetically identical to the one of the parental plants."

In zoology, the cognate phenomenon is known as *parthenogenesis*.



Charles Darwin (1859)
The Origin of Species by Means of Natural Selection

1. Living organisms multiply; resources are limited.
2. Organisms vary. Some variation affects survival and reproduction.
3. Like begets like.
4. Populations of organisms will *evolve*: those organisms with characteristics most favourable for survival and reproduction will not only have more offspring, but will pass their characteristics onto those offspring.



→ the characteristics seen in the population will change

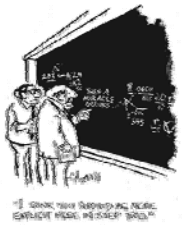
heritable change in animals → selection by environment → adaptation to environment

The problem with step 2

"What was missing from Darwin's theory was a source for the variations on which natural selection acted.

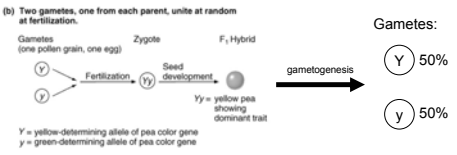
… Darwin addressed the problem of heredity. He believed that smalled units, which he called gemmules, were produced by the cells, and them migrated through the body, and some of them would be retained in the … gonads." EA Carlson, *Mendel's Legacy*

"The most unfortunate of the assumptions underlying Darwin's mechanism of evolution was that of blending heredity; i.e., that parental differences are merged in the offspring of bisexual reproduction so that variation is constantly being diminished. The basis for this assumption wsa the so-called intermediacy of hybrids which Koelreuter regarded as a law for all "true" hybrids." R. Olby *Origins of Mendelism*

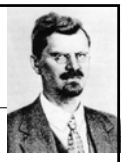


Charles – talk to Gregor. PLEASE, pretty please.

"With Pisum it was shown by experiment that the hybrids form egg and pollen cells of *different* kinds, and that herein lies the reason of the variability of their offspring.With regard to those hybrids whose progeny is *variable* we may perhaps assume that between the differentiating elements of the egg and pollen cells there … occurs a compromise…; **but, nevertheless, the arrangement between the conflicting elements is only temporary…** we must further assume that it is only possible for the differentiating elements to **liberate themselves** from the enforced union when the fertilizing cells are developed."



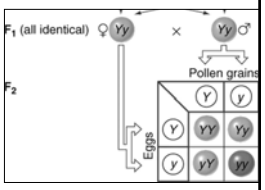
Sergei Chetverikov (1926)
On certain aspects of the evolutionary process from the standpoint of modern genetics



"mutational load"

1. Trap 239 *Drosophila melanogaster* near Moscow.
2. Self their offspring (brother-sister).
3. 32 recessive loci (=186 in humans).

"… A species, like a sponge, soaks up heterozygous mutations, while remaining phenotypically homozygous."



Chromosome "theory" of inheritance

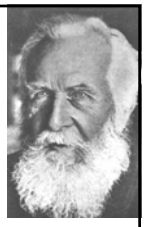
Other "theories"

- Darwin's "theory" of evolution
- Crick's central "dogma" of molecular biology
- Galileo's "theory" that the Earth rotates around its axis, and revolves around the Sun

The chromosome fact of inheritance:
Mendel's "Particles of Inheritance" (the Genes) Lie on Chromosomes:

From Theory in the 1900s to Firmly Established Fact by ~1920

Ernest Häckel



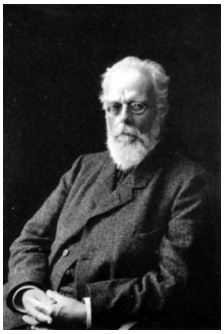
1866:

General Morphology of the Organisms

"The nucleus is the part of the cell that is responsible for heredity"

Nice idea, but not based on data of any sort (at the time).

August Weissman, 1883



CHAPTER VI

THE FORMATION OF GERM-CELLS

1. The Continuity of the Germ-plasm

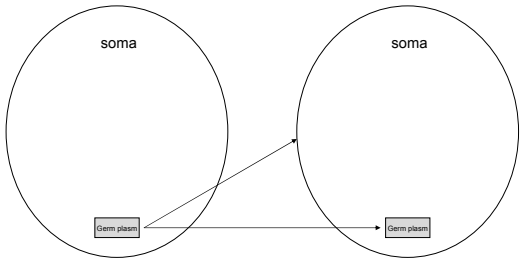
If heredity depends on the presence of a substance, the germ-plasm, which causes the production of the new individual by directing the process of division in ontogeny, in the course of which it becomes changed in a regular manner, the question arises as to how unaltered germ-plasm can nevertheless reappear in the germ-cells of the new individual. The transmission of characters from parent to child can only depend on the germ-cell from which the offspring arises containing ids of germ-plasm precisely similar to those of the germ-cell from which the parent was developed. The germ-plasm, however, undergoes an enormous number of changes during the development of the ovum into the parent: how is it possible therefore that this substance can reappear in the germ-cells of this parent?

There are obviously two possible solutions of this problem. The changes which the germ-plasm undergoes during the construction of the body must either be of such a kind that they can take place in the reverse order when the idioplasm of all, or at least of a portion of, the somatic cells is re-transformed into the germ-plasm from which it was, in fact, *indirectly* derived; or, if such a reversal is impossible, the germ-plasm of the germ-cells must be handed on *directly* from parent to offspring. This latter hypothesis was suggested by me some years ago under the name of the *continuity of the germ-plasm*.* A third solution of the problem is impossible, for it is quite out of the question that the germ-plasm can be entirely formed anew.

The hypothesis of the continuity of the germ-plasm depends on the assumption of a contrast between the *somatic* and the *reproductive* cells, such as can be observed, in fact, in all multicellular plants and animals, from the most highly differentiated forms to the lowest heteroplastids amongst the colonial Algæ.

* 'Die Continuität des Keimplasma's als Grundlage einer Theorie der Vererbung.' Jena, 1885 (English translation, and ed., p. 163).

Recall Darwin's "gemmules"…

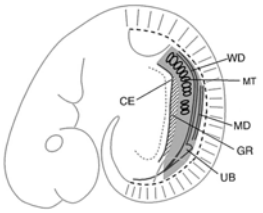


Weissman's somewhat gruesome but, well, persuasive experiment

1. Cut off the tail of some mice.
2. Breed the tailless mice.
3. Get children with tails.
4. Cut off their tails.
5. Breed them.

Repeat 21 times.

"Experiments" done by others and cited by Weissman as supporting evidence: centuries and centuries of foot-binding by the Chinese and circumcision by the Jews have not led to the inheritance of either trait.



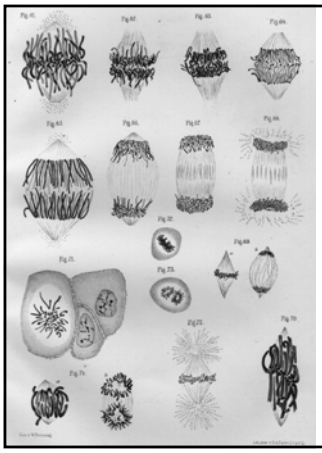
Walther Flemming, 1879

Salamander tail fin cells – living cells.

Gills – fixed cells.

"Beitrage zur kentniss der Zelle und ihre Lebenserscheinungen"

"Contributions to knowledge about the cell and of aspects of its appearance that have to do with the fact that it is alive."



"Mitosis" – a process with threads
a process with threads = mitosis

The object that acquires a color **after** we stain it: the chromosome

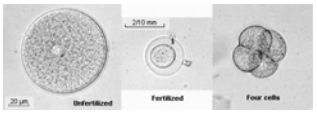
Flemming stained the cell with a dye and found that something inside the nucleus stained quite vigorously. He called it "chromatin" ("stainable material").

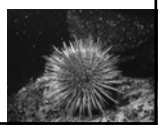
In 1888, Waldeyer renamed Flemming's "threads" – "chromosomes."

A question

What – if anything – do the chromosomes have to do with the process of heredity?

Theodor Boveri, 1895





Boveri, expt 1

1. Enucleate sea urchin egg by agitation.
2. Fertilize this "cytoplasm only" egg with sperm.
3. To his surprise, get a larva, but a much smaller one.

"… It is not a given number of chromosomes as such that is required for normal development, in as much as these fragments, although they contained only half the normal amount of chromatin and half the number of elements, namely the chromosomes of one sperm nucleus, still give rise to normal plutei."

Pluteus = easel.

222 *The American Naturalist.* [March,

AN ORGANISM PRODUCED SEXUALLY WITHOUT CHARACTERISTICS OF THE MOTHER.

By Th. Boveri.

[In offering a translation of Dr. Th. Boveri's paper, entitled Ein geschlechtlich erzeugter Organismus ohne mütterliche Eigenschaften, I have been guided by two motives. First, to make this paper, which will certainly become a classic in Biological literature, accessible to American students, since the journal in which it appeared "Sitz. d. Gesellschaft für Morphologie und Physiologie zur München" v. Sitzung am 16 Juli, 1889, has a very limited circulation in this country.

In the second place, to point out the new avenues of research that such work opens. Results of this kind are of the utmost importance, inasmuch as they touch the very heart of the question of Heredity. Each advance in our knowledge gained by experimental work of this sort, carries forward rapidly our understanding of the most vital phenomena of life.

Results of this importance must be verified over and over again, until all chances of error (by no means small) are eliminated. Dr. Boveri writes that during the present Winter it is his hope to carry forward this work at Naples.

Three small wood cuts were given in the original paper. Dr. Boveri has most generously placed at my disposal the original drawings as well as five additional figures. These are added to the present account. The original figures gave side views of the Echinus larva, the Sphaerechinus larva, and the side view of the bastard larva (Echinus ♂, Sphaerechinus ♀). Three of the new figures give posterior views of the same larvæ and two of the *Dwarf Larvæ*.

Wilson, referring to Boveri's work, in his essay on Amphimixis affirms that *two spermatozoa enter the enucleated* egg to form the segmentation nucleus. I wish to call attention to the foot note in Boveri's paper, where it is positively stated that only a *single spermatozoon enters the enucleated egg.*

T. H. Morgan.]

Boveri, expt. 2

Enucleate the egg of one species of sea urchin, and fertilize with a sperm of a different species.

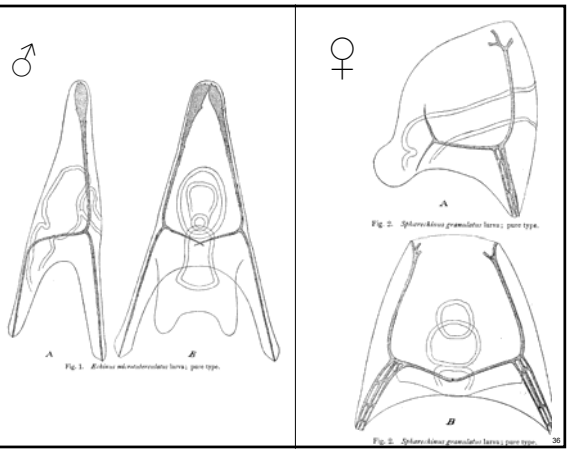
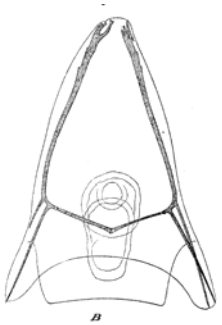


Fig. 1. *Echinus microtuberculatus* larva; pure type.

Fig. 2. *Sphaerechinus granularis* larva; pure type.

Fig. 2. *Sphaerechinus granularis* larva; pure type.



B

Fig. 3.

Larva of bastard of *Echinus microtuberculatus* ♂ and *Sphaerechinus granularis* ♀.

E.B. Wilson, 1896

"… the maternal cytoplasm has no determining effect on the offspring, but supplies only the material in which the sperm nucleus operates. Inheritance is, therefore, affected by the nucleus alone."

Boveri, expt. 3

Let's make a triploid sea urchin embryo by fertilizing an egg with two sperm.

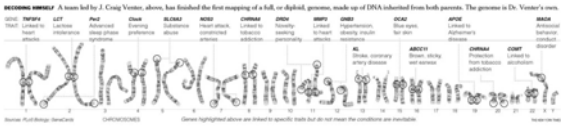
The resulting zygote does divide, but the mitotic spindles are multicentric. Sometimes, this triploid entity even produced a 4-cell embryo. The resulting blastomeres, when separated, invariably failed to develop further. In contrast, the 4 blastomeres from a diploid embryo went on to form 4 plutei.

Boveri expt. 3 ctd.

"… the next question was whether this unequal distribution of the chromatin is of any influence upon the properties of the four cells. … While the four blastomeres of a normally divided egg are absolutely equivalent to each other, it is seen that the properties of the blastomeres of a doubly fertilized one are different from each other in diverse ways, and to varying extent.

All that remains is that not a definite number, but a *definite combination of chromosomes* is necessary for normal development, and this means nothing other than that the *individual chromosomes* must possess different qualities."

J. Craig Venter's genome
S. Levy et al.
PLOS Biology 2007



Next time

A *synthesis* – Mendel's laws finally meet the chromosomes.

→ chromatids, chromosomes, sisters, homologs …