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Welcome to "Genes - How They Were Discovered and What They Do"

I've changed the title of this seminar to something more provocative…

"All About Genes - A Seminar for Very Smart, but ~~Ignorant~~ Uninformed, Elderly Folks"

Please don't hesitate to interrupt me to ask questions or to offer comments

(we're not on a schedule)

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Course Outline

Gregor Mendel: How a monk came to discover the basic rules of inheritance

Genes and chromosomes - the fly in the ointment

Microbiologists discover that most genes are made of DNA

How two amateurs beat the A team to solve the structure of DNA

The genetic code. Again an obscure team of players beats the pros.

How genes are controlled. The French connection.

***Gregor Mendel**, a monk, the "father" (pun intended) of Genetics, didn't have any notion about the nature of genes.*

He never used the word 'gene' or 'genetics'

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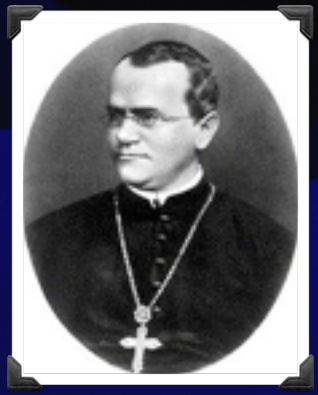
G. Mendel

G. Mendel

1822 - 1884

He discovered the basic rules of genetics in the 1860's in what is now the Czech Republic while a monk in the Augustinian Monastery at Brno.



Gregor Johann Mendel

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A map for those geographically challenged

In 2011, I made a pilgrimage to the Czech Republic in pursuit of an answer to an issue that haunted me since I was a student.

How is it that a monk working in a monastery in Eastern Europe came to discover the fundamental principles of genetics?

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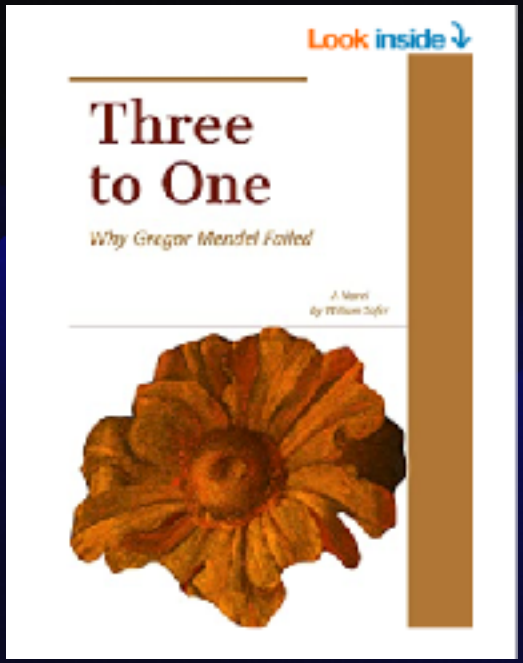
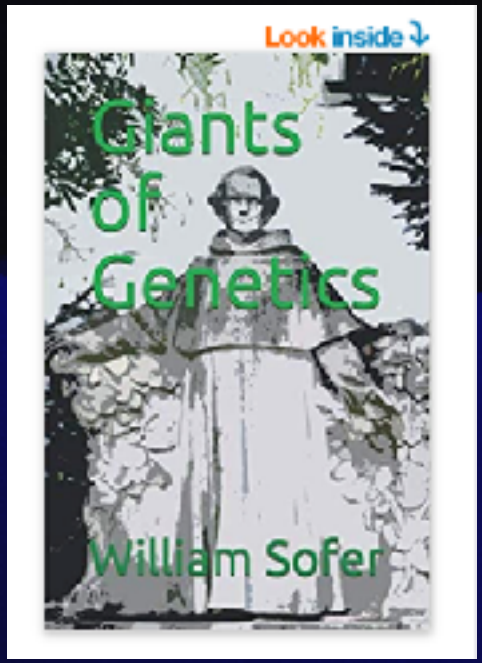
It led me to write two books about Father Mendel.





Available on Amazon

Here's what I found.

Johann Mendel was born in July 1822 in the tiny hamlet of Heinzendorf (Hynčice).

He was the only son of a peasant farmer.

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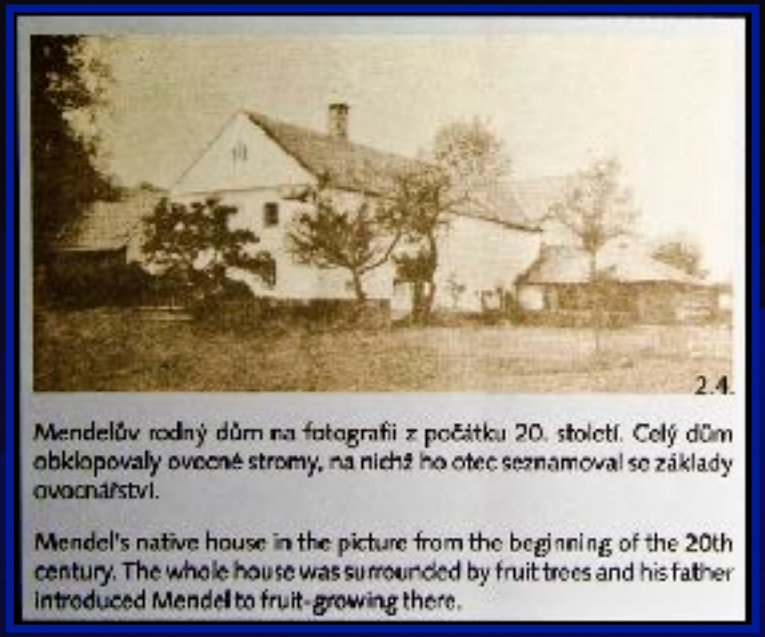
My photos of the Mendel farm and the house where Mendel was born.



2.4.

Mendelův rodný dům na fotografii z počátku 20. století. Celý dům obklopovaly ovocné stromy, na nichž ho otec seznamoval se základy ovocnářství.

Mendel's native house in the picture from the beginning of the 20th century. The whole house was surrounded by fruit trees and his father introduced Mendel to fruit-growing there.

It's now a cycling hostel and a museum.

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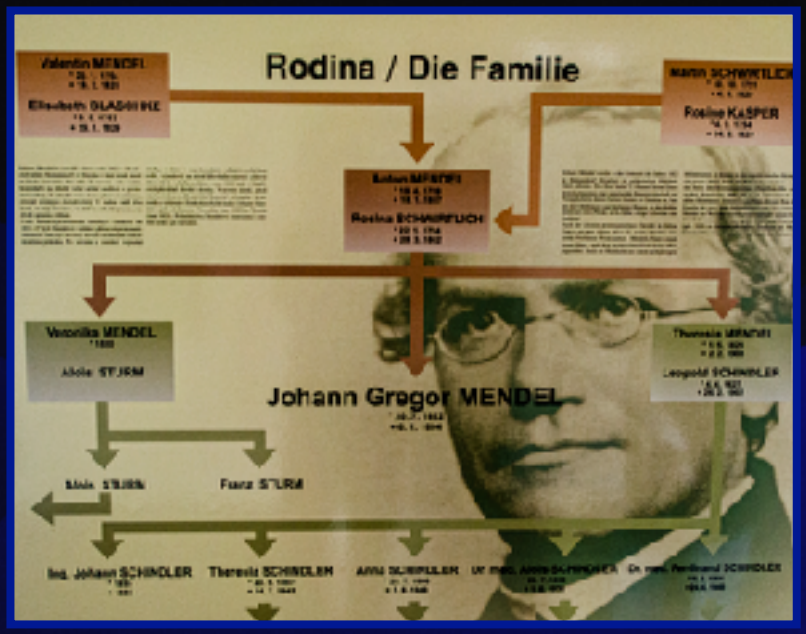

A guide took us around the museum and showed us a graphic of the Mendel family history.

Mendel's sisters and brother-in-law.

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Mendel showed considerable intellectual promise early in his schooling. His family (at a substantial financial burden) sent him away to further his education, first to Leipnik for middle school,

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and then to Opava for high school (gymnasium).

Because his family couldn't afford it, he had to earn extra money on his own by tutoring.

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Olomouc

Despite some health problems, his grades at every level were excellent.

To complete his education, he attended the Philosophical Institute in Olomouc.

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Olomouc

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Because his father had been injured while at work, the family farm had to be sold.

The little financial aid that his parents had been giving him was now not forthcoming. He became ill. He withdrew from school.

His younger sister, Theresia, came to his rescue, and gave part of the proceeds of her inheritance to Johann. With these funds and others earned by tutoring, he began his studies again and graduated two years later at the age of 21.

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Last year his body was dug up and his DNA sequenced. Investigators found a genetic mutation associated with mental illness.

"He suffered throughout his life from some sort of a psychological or neurological disorder that caused him to have very severe nervous breakdowns. That may well have been an inherited condition"

After graduating, he had to decide what to do for the rest of his life.

He chose the clergy.

Here's what he had to say about this choice:

" ... having finished my philosophical studies, I felt compelled to enter a station in life that would free me from the bitter struggle for existence. ***My circumstances decided my vocational choice****. I requested and received in the year 1843 admission to the Augustinian Monastery of St. Thomas in Brno." (Orel, p 43-44; Some changes made by me).*

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The monastery offered stability, freedom from having to earn a living by farming, and a chance for contemplation and study.
There's no evidence that there was any religious motivation in his choice.

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Abbot Franz Cyrill Napp accepted Mendel upon the recommendation of Mendel's Olomouc physics teacher, Fredrich Franz, and he became a novice.
He took the name "Gregor".

He took a further four years of religious instruction at the Brno Theological College (including classes in agriculture), and was ordained a priest.

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Fig. 6.1 Members of the Augustinian monastery in Brno in about 1862. Standing, from left to right: Benedikt Fogler, Anselm Rambousek, Antonín Alt, Tomáš Bratránek, Joseph Lindenthal, Gregor Mendel, and Václav Šembera. Seated, from left to right: Pavel Křižkovský, Baptist Vorthey, Cyrill Napp, and Matouš Klácel.

Benedikt Fogler, professor of Romance languages; Tomas Bratranek, natural scientist; Pavel Krizkovsky, musician; and Matous Klacel, philosopher, are shown alongside Mendel and Napp.

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At first, Mendel was assigned parish duties. Here's what Abbott Napp had to say:

" ... he is very diligent in the study of the sciences; ... he is much less fitted for work as a parish priest, the reason being that he is seized by an unconquerable timidity when he has to visit a sick-bed or to see anyone ill and in pain. Indeed, this infirmity of his made him dangerously ill, and that was why I found it necessary to relieve him of service as a parish priest"

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Since Mendel couldn't perform his regular priestly duties, Napp had him appointed a substitute teacher for first through fifth graders at a school in the town of Znain.

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Mendel was, by all accounts, an excellent teacher, well liked by both students and administrators

However, government regulations interposed. In order for teachers to hold a permanent teaching position, they were required to pass a certification examination.

Mendel took the exam in Vienna and failed.

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Despite performing badly (especially on the biology part of the exam), the head of the examination committee recommended that he be sent to a university to make up for his deficiencies.

Abbott Napp agreed, and sent the following note to his superiors:

"In view of the fact that Pater Gregor Mendel has proved unsuitable for work as a parish priest, but has on the other hand shown evidence of exceptional intellectual capacity and remarkable industry ... it would seem necessary and desirable to send him to Vienna University where he will have full opportunities for study ... "

Mendel went to Vienna.

Over a two year period, he took courses in physics, zoology, botany, and math.
The University (founded in 1365!) had a distinguished faculty.

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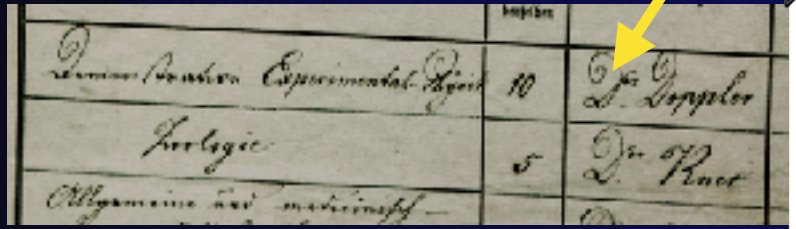
Here's a record of some of the classes he took.

Notice the name of his physics instructor, "Christian Doppler".



Upon leaving the University, he was offered a position as a substitute teacher of natural history and physics at the Brno Modern School. He remained at this post for 14 years.


Mendel
Faculty of the Brno Modern School
Courtesy of the Mendelianum, Moravian Museum, Brno.
Noncommercial, educational use only.

He took the certification examination once more, two years after assuming his teaching post (1853).

He failed again!

It isn't clear why. But the only practical effect was that he was paid half the normal wages of a full time teacher, and that he taught fewer hours.

Most of the monks at the school were engaged in some kind of scholarly activity.

Many were carrying on research in a variety of areas.

Mendel decided to begin a scientific research project.

He began to study peas in approximately 1856, after having failed his second teaching examination.

He completed his experiments in 1863/4.

He presented a paper (in two parts) on his results in 1865 at the Brno Society for the Study of Natural Sciences.

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He published his results in 1866.

Versuche

über

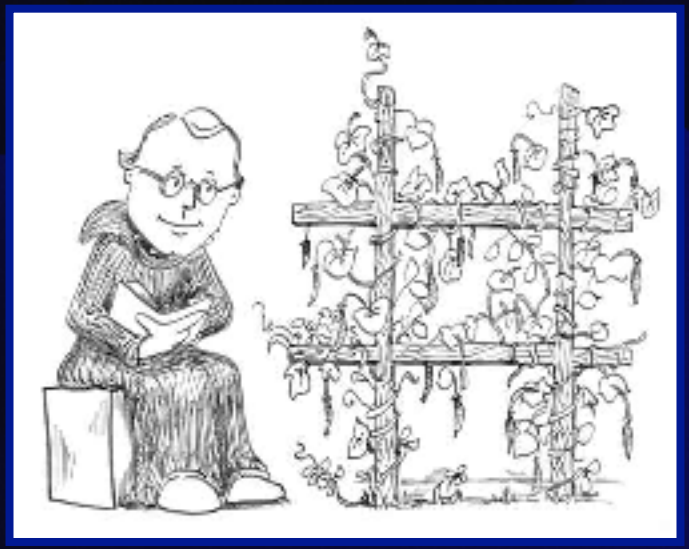
Pflanzen-Hybriden,

von

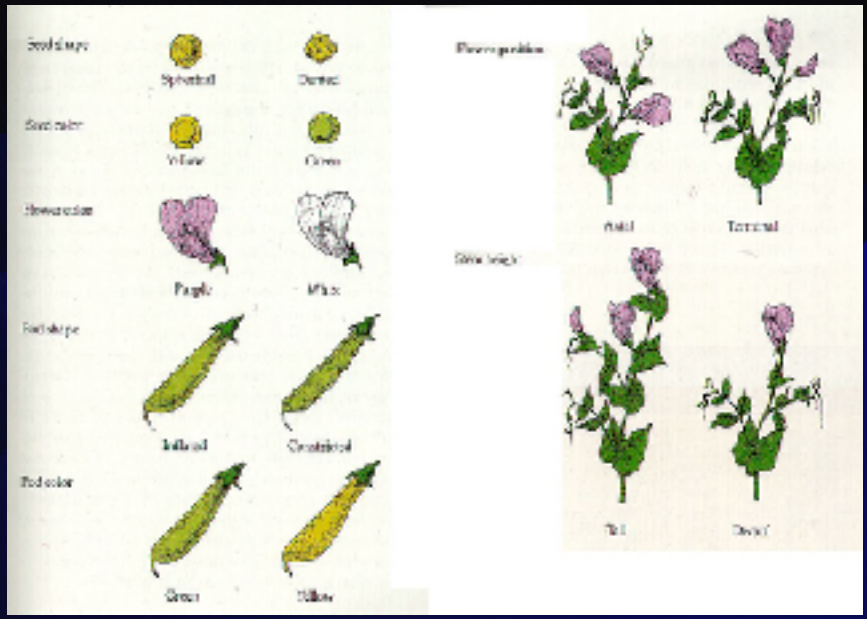
Gregor Mendel.

Brünn, 1866.

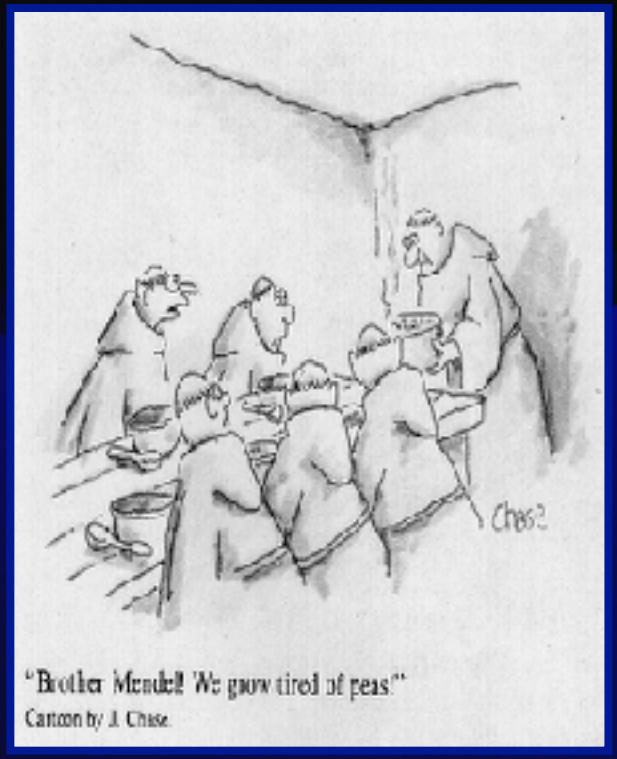
What had he done?



Mendel worked with 14 pea varieties; seven pairs of traits.



He chose peas because they have a short growing season, could be raised in pots, and were available in many easily obtained varieties which could be crossed to produce fertile hybrids.



"Brother Mendel! We grow tired of peas."
Cartoon by J. Chase.

For simplicity sake, I'm going to focus on his results with only one pair of traits, the one having to do with seed shape.

We'll call the two varieties, ***round*** *and* ***wrinkled****.*

Mendel showed that both these varieties of peas were "true breeding". That is, rounds produced rounds, and wrinkleds produced wrinkleds for many generations without exception.

Then he asked, what would happen if you crossed a round true breeding pea to a wrinkled true breeding pea?

What would the offspring look like?

Can you guess what type of peas resulted from Mendel's cross?

a. All wrinkled
b. All round
c. Intermediates
d. mostly wrinkles, some rounds
e. mostly rounds, some wrinkleds
f. rounds and wrinkleds, equally
g. no progeny at all

Here's what he found:

a. All wrinkled
b. All round
c. Intermediates
d. mostly wrinkles, some rounds
e. mostly rounds, some wrinkleds
f. rounds and wrinkleds, equally
g. no progeny at all

The results were dramatic, but puzzling.

Mendel had shown that crossing rounds to rounds, always produced rounds.

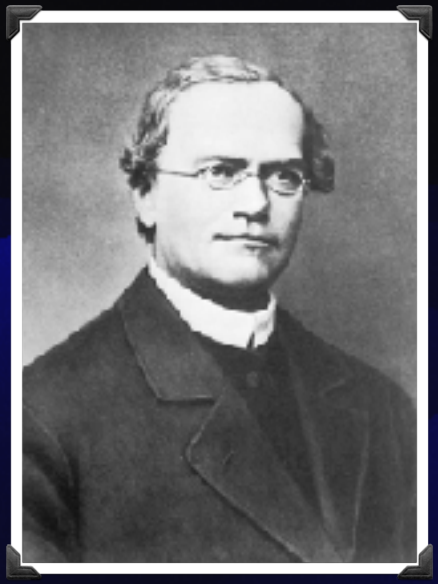
Now, amazingly, crossing rounds with wrinkleds also produced rounds.

Mendel said:

"What the heck!"

"Are these hybrid rounds true breeding like their true breeding round parents?

They certainly look just like regular rounds."



"But, if you cross these hybrid rounds with each other, do they always produce rounds like their parents?"

What do you think?

Do hybrid rounds produce only rounds when crossed with each other?

Or are there occasional wrinkleds?

What happens if you cross hybrid rounds to each other?

a. All wrinkled
b. All round
c. Intermediates
d. mostly wrinkles, some rounds
e. mostly rounds, some wrinkleds
f. rounds and wrinkleds, equally
g. no progeny at all

Here's what he found

a. All wrinkled
b. All round
c. Intermediates
d. mostly wrinkleds, some rounds
e. mostly rounds, some wrinkleds
f. rounds and wrinkleds, equally
g. no progeny at all

The answer turns out to be:

Hybrid rounds, when crossed with each other produce

rounds

and

wrinkleds.

To summarize…
There appear to be two kinds of rounds.

1. *True breeders*
2. *Hybrid rounds that result from crossing with wrinkleds.*

They look the same, but differ in what happens when crossed with each other.

At this point, Mendel did something no one else had done previously (or if they had, they hadn't realized the significance of their results).

He counted

Here are his results:

There were 1,850 wrinkled peas and 5,474 round ones.

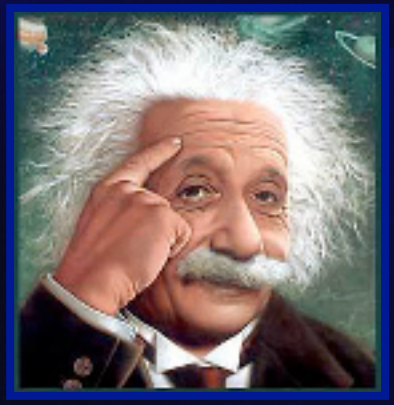
About three rounds for every wrinkled.

(Actually 2.96)

*It's also important to note that some pods contained **all** rounds, a few **all** wrinkleds, and every possibility in between.*

Only when you summed up all the numbers, did you find this 3:1 ratio.

What did these numbers mean?



He generated the following theory:

First, whatever is causing wrinkledness or roundness is some solid entity that he called a "genetic determinant" (what today we'd call a gene).

(He had no idea what these determinants were or how they acted)

Second, he theorized that these genetic determinants come in ***pairs****.*

determinants

Third, only one member of each pair from each parent gets randomly passed on to the next generation.

Just one gets inherited

Now put these ideas together and you get...

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Round true breeders, have two round determinants.

r r

Wrinkled true breeders have two wrinkled determinants.

w w

They are true breeders because they can't pass on anything else to their offspring.

Hybrids have two <u>different</u> determinants.

(Mendel didn't explain why they looked round despite having two different determinants. But he did give the phenomenon a name: dominance).

Each hybrid parent randomly passes one or the other determinate in its sex cells to its offspring.

What's the chance that any given offspring will get two wrinkled determinants?

(one from each parent)

25%

What's the chance that an offspring will get two round determinants

(one from each parent)?

25%

What's the chance that an offspring will get two different determinants?

(one from each parent)

50%

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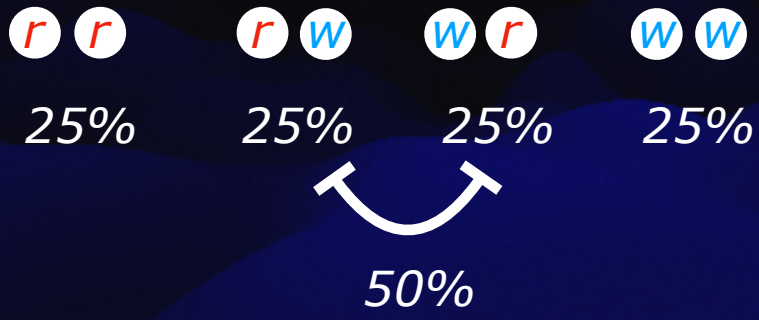


Round to wrinkled

3:1

Great ideas are great because they not only explain an observed phenomenon (in this case, the 3:1 ratio), but also because they can accurately predict future ones.

What does Mendel's theory predict for the following cross:

Hybrid Round x wrinkled?

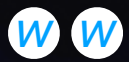
Anyone want to guess?

Hybrid to wrinkled.

What ratio do you get?

a. All wrinkled
b. All round
c. Intermediates
d. wrinkled:rounds, 3:1
e. rounds:wrinkleds, 3:1
f. rounds and wrinkleds, 1:1

50%:50%, Wrinkled:Round



This parent has a 50:50 chance of passing on a round or a wrinkled

This parent can only contribute wrinkleds to the next generation

Therefore you get a one to one ratio of wrinkleds to rounds

Let’s summarize

Mendel is responsible for the idea that genetic determinants, genes, come in pairs, and one of each pair is randomly passed on to one's descendants.

His work also suggested that genes are solid entities of some sort that retain their integrity from generation to generation

He found that when two alternative versions of a trait occur in a hybrid, one can predominate - the concept of 'dominance'

These laws largely hold today, for most familiar organisms (including humans), although there are many exceptions

We'll deal with a major one next week

Mendel published his results in 1866, a year after presenting his discoveries in two lectures at the Brno Natural History Society.

He sent out reprints of work to some of the prominent scientists of his day.

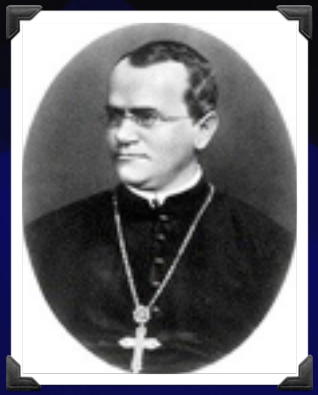
40 reprints were ordered.

The whereabouts of eight copies are known.

He expected to receive the accolades of the scientific community.

He's still waiting...

On August 15, 1868, Mendel was elected Abbot of the Bruno Monastery.



Abbot Mendel

Soon, he became involved in a dispute with the authorities concerning taxation.

G. Mendel

His health suffered.

His research ended.

He died in 1884, beloved as a priest, Abbot, and teacher; forgotten as a scientist.

It wasn't until 1900, 35 years after publishing his seminal paper, was Mendel's work rediscovered.

Hugo DeVries, Carl Correns and Erich von Tschermak - independently rediscovered Mendel's work in 1900

Soon, a bevy of scientists were finding Mendelian ratios (and exceptions) in all manner of organisms.

TH Morgan

We'll look at one of these exceptions and the scientist that discovered it next time.