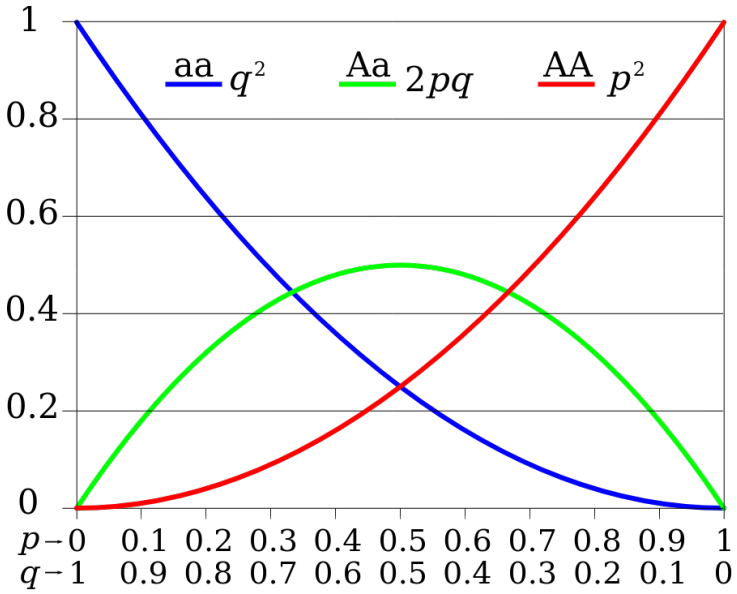


Population and Evolutionary Genetics

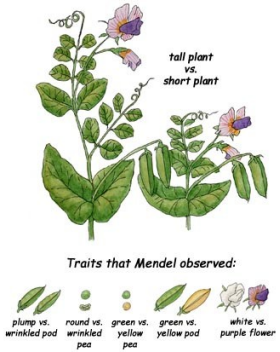
Equilibrium population

Aristotelis C. Papageorgiou, MBG DPTH, apapage@mbg.duth.gr

Gregor Mendel

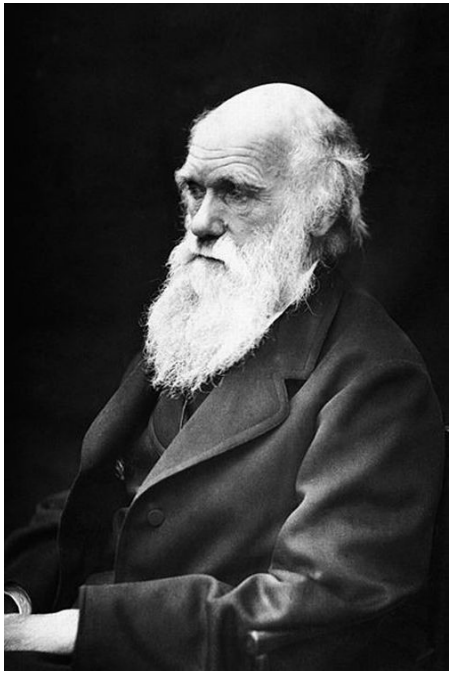
- He discovered the binary nature of heredity
- The probability of carrying an allele to the next generation is ½
- Traits are inherited randomly
- Mendel's work remained unknown until 1900

Gregor Mendel (1822-1884)



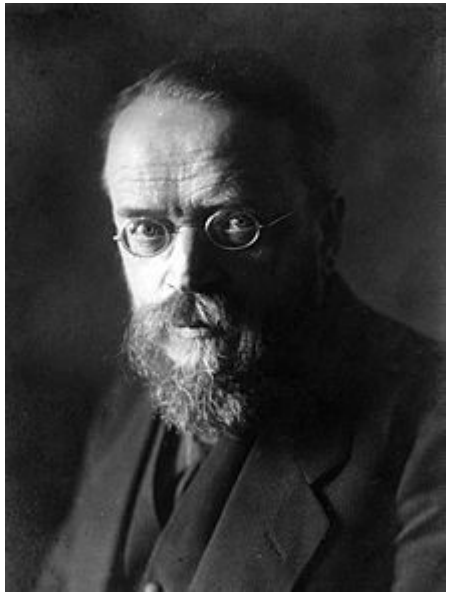
Charles Darwin

- He described the mechanism of natural selection in evolution
- He founded a dynamic evolutionary theory
- He didn't use any math
- He did not explain the mechanism of inheritance



Charles Darwin (1809–1882)

Discovery of Mendel's Laws (1900)



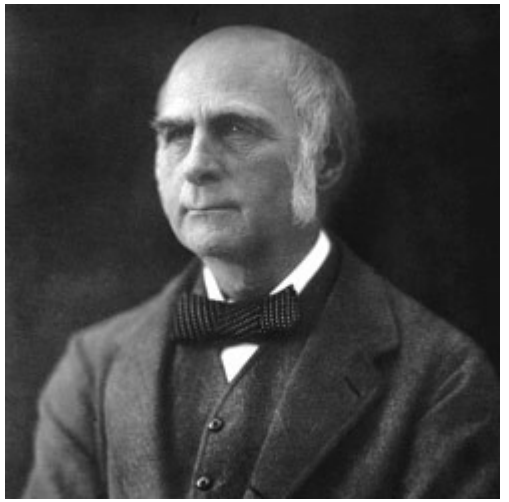
Carl Erich Correns
(1864 - 1933)

Hugo Marie de Vries
(1848 - 1935)[

Erich Tschermak
(1871 - 1962)

Francis Galton

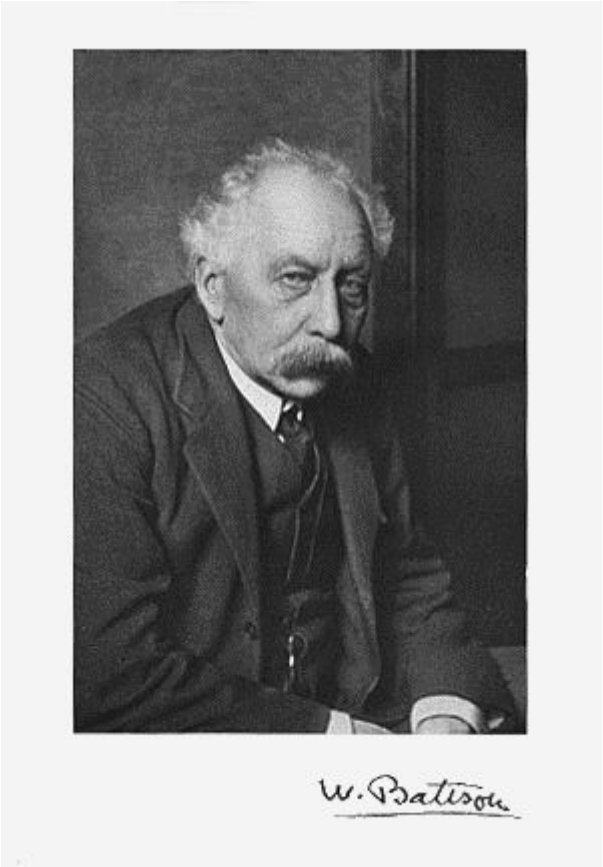
- Statistician, psychologist, sociologist, anthropologist, explorer, geneticist
- Founder of "Eugenics" and "Social Darwinism"
- He studied biometric differences in human populations
- He proposed an alternative theory of inheritance to that of Mendel (**biometric** approach)



Francis Galton (1822–1911)

William Bateson

- He defended **Mendelism** and became the founder of genetics as a science
  - With Charles Davenport and Wilhelm Johannsen
- By the 1930s, Mendelian inheritance was broadly accepted



William Bateson (1861-1926)

Hardy & Weinberg Solve a Paradox (1908)

- It was believed that for distinct Mendelian characters, all pairs of phenotypes in a population would eventually reach a ratio of 3:1 with the dominant allele increasing and the recessive allele decreasing in frequency
  - Yule argued that "since brachydactyly is a prevalent disease, in time we will meet three individuals with brachydactyly and one normal"
    - In fact, brachydactyly is a very rare disease
  - Hardy replied that 'it is utterly untenable to think that a dominant character will tend to spread through the population while a recessive will tend to disappear"

Yule 1902,
Castle 1903,
Pearson 1904

Wilhelm Weinberg
(1862–1937)

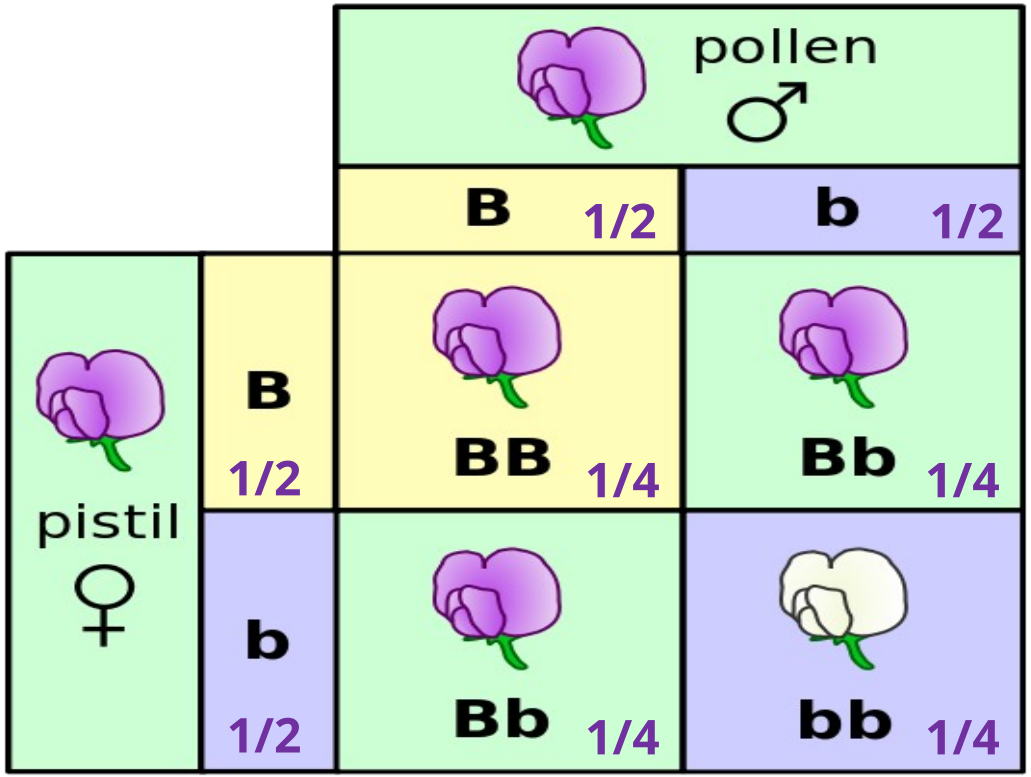
1908

Godfrey Harold Hardy
(1877–1947)

Hardy, GH (1908). "Mendelian proportions in a mixedpopulation".*Science* **28**: 49–50.

Weinberg, W. (1908). "Über den Verebung der Verebung beim Menschen".*Jahreshefte des Vereins für vaterländische Naturkunde in Württemberg* **64**: 368–382.

Estimation of genotype frequencies



- Mendel estimates phenotype and genotype frequencies among the offspring based on the genotype of the parents of a single cross
- Can we estimate the genotype frequencies in a population?
  - Yes, if there is **random reproduction**!

Mendelian, panmictic or random mating population

- A population where mating between adult individuals occurs randomly is called a **Mendelian** population
  - A population with two sexes and adult (sexually mature) individuals
  - All possible mating events are **equally likely**
    - Random mating population
- The probability of interbreeding between individuals with a particular genotype or phenotype is equal to the product of their frequencies in the population

Random play

Female gametes (frequency)

Male gametes (frequency)

	A (p)	a (Q)
A (p)	AA (p^2)	Ah (pq)
a (Q)	Ah (pq)	aa (q^2)

P= p^2

H=pq+pq= 2 pkgQ= q^2

Hardy's approach

Mating pair	Frequency of mating pair	Mendelian probabilities of offspring (zygotes)		
		AA	*Aa*	*aa*
$AA \times AA$	$G_{AA} \times G_{AA} = {G_{AA}}^2$	1	0	0
$AA \times Aa$	$G_{AA} \times G_{Aa} = G_{AA}G_{Aa}$	½	½	0
$Aa \times AA$	$G_{Aa} \times G_{AA} = G_{AA}G_{Aa}$	½	½	0
$AA \times aa$	$G_{AA} \times G_{aa} = G_{AA}G_{aa}$	0	1	0
$aa \times AA$	$G_{aa} \times G_{AA} = G_{AA}G_{aa}$	0	1	0
$Aa \times Aa$	$G_{Aa} \times G_{Aa} = {G_{Aa}}^2$	¼	½	¼
$Aa \times aa$	$G_{Aa} \times G_{aa} = G_{Aa}G_{aa}$	0	½	½
$aa \times Aa$	$G_{aa} \times G_{Aa} = G_{Aa}G_{aa}$	0	½	½
$aa \times aa$	$G_{aa} \times G_{aa} = {G_{aa}}^2$	0	0	1
Total Offspring		G'_{AA}	G'_{Aa}	G'_{aa}

Summing zygotes over all mating types:

$$G'_{AA} = {G_{AA}}^2 + ½\,[2G_{AA}G_{Aa}] + ¼{G_{Aa}}^2 = [G_{AA} + ½G_{Aa}]^2 = p^2$$
$$G'_{Aa} = ½[2G_{AA}G_{Aa}] + 2G_{AA}G_{aa} + ½{G_{Aa}}^2 + ½[2G_{Aa}G_{aa}] = 2[G_{AA} + ½G_{Aa}][G_{aa} + ½G_{Aa}] = 2pq$$
$$G'_{aa} = ¼{G_{Aa}}^2 + ½[2G_{Aa}G_{aa}] + {G_{aa}}^2 = [G_{aa} + ½G_{Aa}]^2 = q^2$$

Note: Female genotypes are indicated first in the mating pair, male genotypes second.

Weinberg's approach

Alan R. Templeton. Population Genetics and Microevolutionary Theory, 2nd Edition (2021)

1st conclusion from HW

- In a randomly mating population, knowing the allele frequencies in one generation, we can calculate the genotype frequencies in the next generation!

$P' = p^2$

$H' = 2pkg$

$Q' = q^2$

Calculate the allele frequencies in the next generation, p' and q'

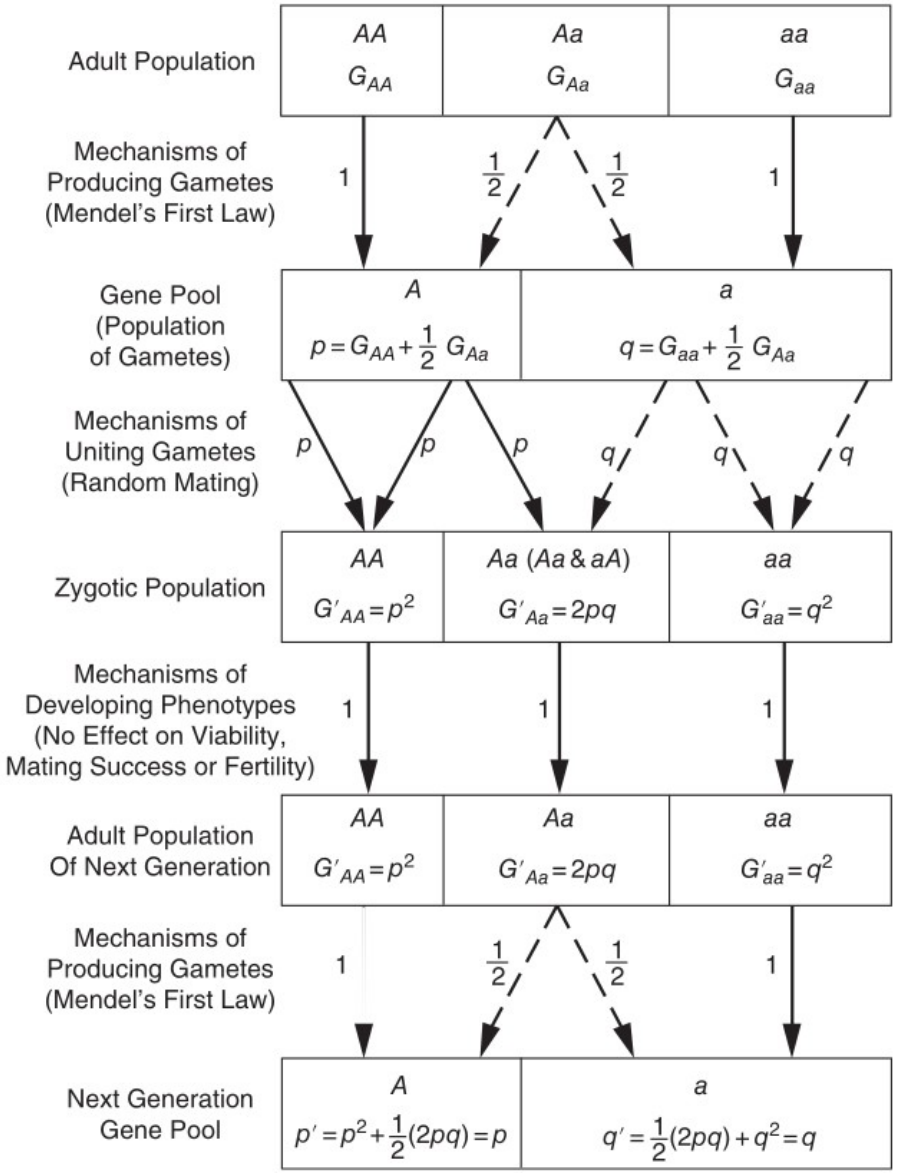
Next generation allele frequencies

$P' = p^2$
$H' = 2pkg$
$Q' = q^2$

$$p' = P' + H'/2 = p^2 + 2pq/2 = p^2 + pq$$
$$= p(p+q) = p$$

$p+q=1$

$$q' = Q' + H'/2 = q^2 + 2pq/2 = q^2 + pq$$
$$= q(p+q) = q$$



In a randomly mating population, allele frequencies from generation to generation do not change!

Alan R. Templeton. Population Genetics and Microevolutionary Theory, 2nd Edition (2021)

2nd conclusion from HW

- In a randomly mating population, allele frequencies from generation to generation do not change!
- This is an **equilibrium population**

p'= p

Q'= q

Calculate the allele frequencies in the next generation, p' and q'

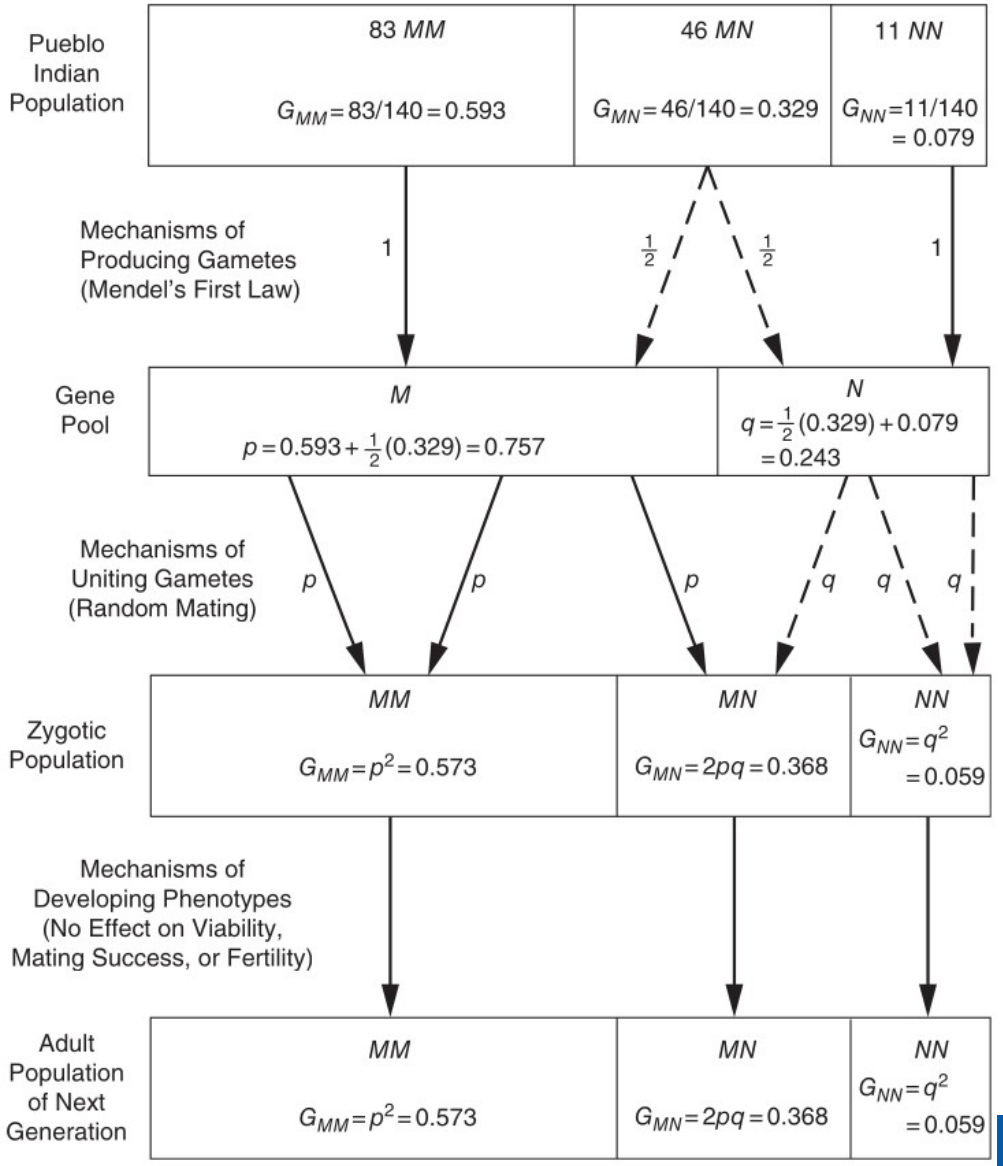
Example

	Σπερματοζωάρια	
	Συχν. (*A*) = 0,7	Συχν. (*a*) = 0,3
Συχν. (*A*) = 0,7	Συχν. (*AA*) = 0,7 × 0,7 = 0,49	Συχν. (*Aa*) = 0,7 × 0,3 = 0,21
Ωάρια		
Συχν. (*a*) = 0,3	Συχν. (*aA*) = 0,3 × 0,7 = 0,21	Συχν. (*aa*) = 0,3 × 0,3 = 0,09

P'= p^2

H'=2 pkg

Q'= q^2



Example

Application of the Hardy–Weinberg model to a sample of Pueblo Indians scored for their genotypes at the autosomal **MN blood group l**ocus.

P'= p^2

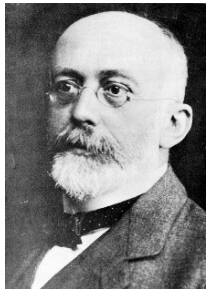
H'=2 pkg

Q'= q^2

Alan R. Templeton. Population Genetics and Microevolutionary Theory, 2nd Edition (2021)

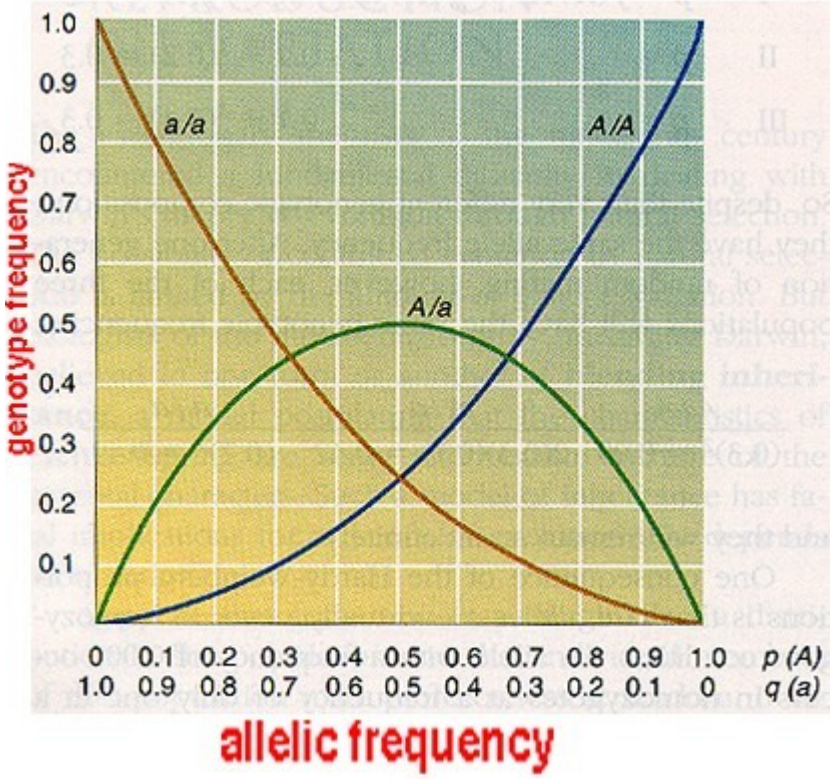
Hardy-Weinberg Law

- The most basic model in population genetics
  - When we have random reproduction, after one generation we can calculate the genotype frequencies of a population as a binomial function of the allele frequencies
  - If other evolutionary factors (e.g. selection) are absent, and reproduction remains random, then these frequencies do not change from generation to generation



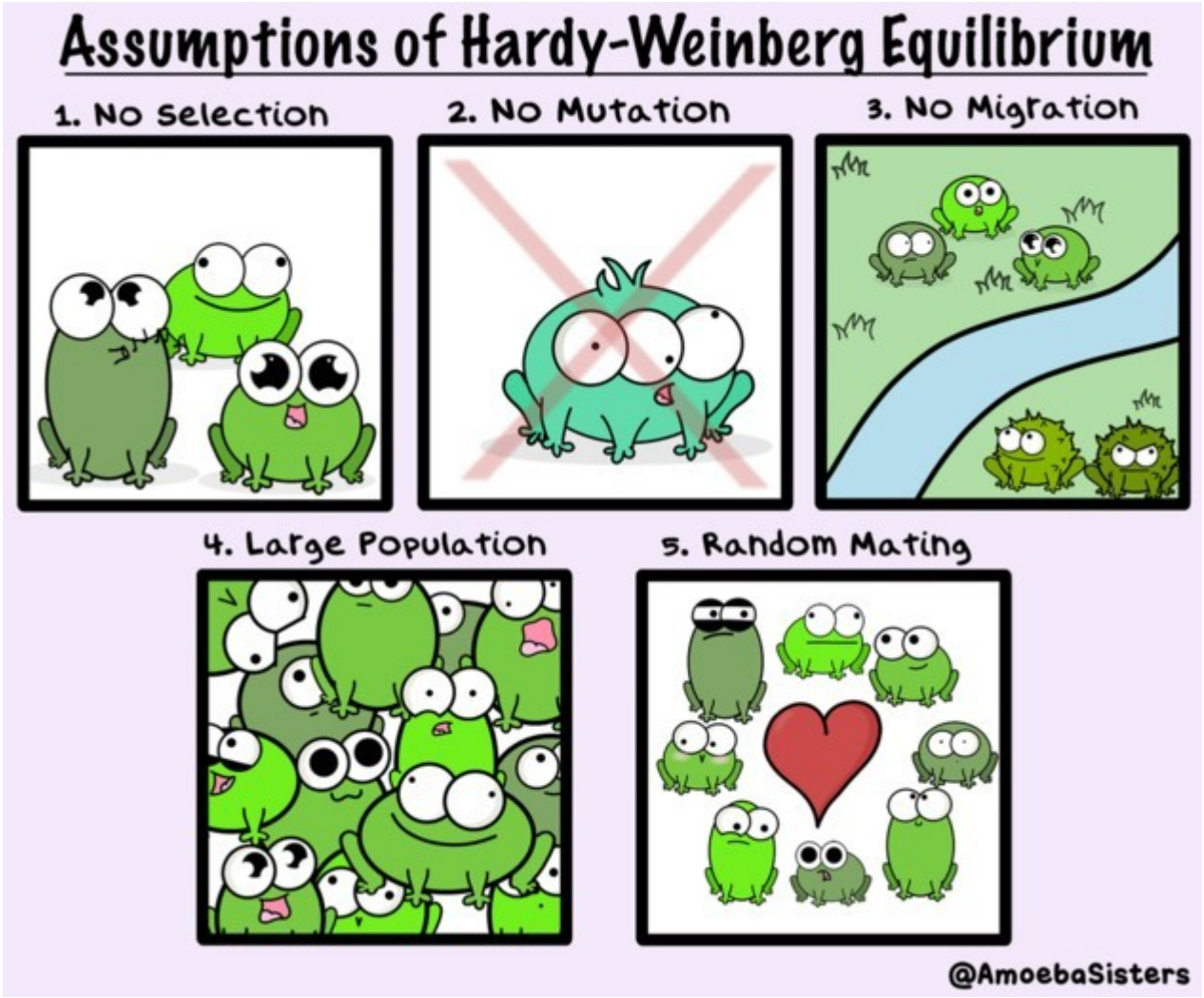
Binomial development

- $p^2+2pq+q^2= (p+q)^2$
- It means that with random reproduction, alleles A and a with frequencies p and q are randomly combined in pairs
  - Why every two?



Conditions for the validity of the HW theorem

- Diploid organism
- Sexual reproduction
- Non-overlapping generations
- Population size infinite
- Same allelic frequencies in males and females
- Random pairing of individuals (mixture)
- No Selection
- No influx of alleles into the population (immigration or mutation)



Conditions for the validity of the HW theorem

Understanding Mendel's and Hardy-Weinberg's laws

- The relationship (dominant or recessive) between the alleles does not matter
- For a population in Hardy-Weinberg equilibrium, there is no tendency for an allele to become extinct or dominant
- This ability to maintain genetic diversity is one of the most important features of Mendelian genetics in contrast to older theories of blended inheritance.

Genetic diversity

- Based on the HW law, genetic diversity has an inherent (mathematical) tendency to be conserved
- An equilibrium population does not change over time
  - Evolution, however, concerns changes in the genetic composition of populations
  - The equilibrium population is the "null" hypothesis of evolution
- By breaking the equilibrium population conditions one by one, we can study evolutionary forces at the genetic level!

More than 2 alleles

- Hardy Weinberg's law also applies in the case that we have 3 alleles (A, B, and C) with frequencies p, q, and r:
  - $(p + q + r)^2 = p^2 + 2pq + q^2 + 2pr + 2qr + r^2$
- For 4 alleles (A, B, C, and D) with frequencies p, q, r, and s respectively are:
  - $(p + q + r + s)^2 = p^2 + 2pq + q^2 + 2pr + 2qr + r^2 + 2ps + 2qs + 2rs + s^2$
- Generally: $\boldsymbol{P_{ii} = P_i^2}$ $\boldsymbol{P_{ij} = 2p_ip_j}$

The HW theorem for sex-linked genes

Sex-linked locus A (A,a), equal allelic frequencies between males and females, equal number of males and females:

		Male gametes - X		Male gametes - Y
		$X^A(p)$	$X^a(Q)$	
Females gametes	$X^A(p)$	$X^AX^A(p^2)$	$X^AX^a(pq)$	X^AY (p)
	$X^a(Q)$	$X^aX^A(q.p.)$	$X^aX^a(q^2)$	X^aY (q)

Genotypic frequencies of females equal H-W frequencies, while males equal allele frequencies

Inquiry

- In some African population, 4% of the (equilibrium) population is born with a severe form of sickle cell disease. What percentage of the population (roughly) has the greatest susceptibility to contracting malaria?

Inquiry

- A microsatellite has five alleles that each occur at a frequency of 0.2. What percentage of the (equilibrium) population will be heterozygotes?

Inquiry

- A disease is caused by a recessive sex-linked gene. In a large (equilibrium) population where mating is random, the disease affects one man in 10. What is the frequency of affected women?

Inquiry

- An autosomal recessive disease has a carrier frequency of 1/50. What is the probability that the first child of a random couple will have the disease?

Inquiry

- In a sample of 990 individuals from a European population the following frequencies were found for the MN blood group system genotypes:
- 439 MM, 421 MN, 130 NN
  - What is the observed and what is the expected heterozygosity?

Inquiry

- You have sampled from a population in which you know that the frequency of the recessive homozygous genotype (aa) is 36%. Using this 36%, calculate the following:
  - the frequency of genotype “aa”,
  - the frequency of the allele “a”,
  - the frequency of the "A" allele,
  - the frequencies of the genotypes "AA" and "Aa" and the frequencies of the two possible phenotypes if "A" is dominant.

Inquiry

- If in an admixed population (equilibrium) the frequency of phenotype A (A dominant against recessive α) is 0.19, what is the frequency of heterozygous genotypes?

Inquiry

- The HALn recessive allele of the HAL gene (HALN, HALn) is responsible for the positive reaction of pigs to halothane. In a population of 1000 Large White pigs one in 400 pigs was found to react positively to halothane.
  - Estimate the number of normal pigs that are carriers of the recessive allele.