Principles of Inheritance & Variation

Genetics - branch of biology dealing with heredity & variation among organisms.

Father of Genetics = ~~Darwin~~ Gregor J. Mendel (1822-84).

Father of Modern Genetics - T.H. Morgan (Drosophila)

Mendel worked on garden pea (Pisum sativum).

Heredity vs Variation

Heredity - transmission of traits from parent to offspring.

Variation - differences among individuals (within a species).

Why Pea?

1. Short life cycle, easy to grow
2. Many distinct, stable, contrasting traits
3. Bisexual flowers; can be self / cross-pollinated
4. Large, easy to ~~crossed~~ emasculate
5. Large progeny - statistical analysis possible

Mendel's Method

(i) Selected pure-breeding lines

(ii) Crossed contrasting parents

(iii) Recorded results numerically

(iv) Statistical analysis -> ratios

Mendel's 7 Contrasting Traits

Character	Dominant	Recessive
Stem height	tall	dwarf
Flower colour	violet	white
Flower position	axial	terminal
Pod shape	inflated	constricted
Pod colour	green	yellow
Seed shape	round	wrinkled
Seed colour	yellow	green

Important Terms

Allele	alternate forms of same gene (T / t)
Homozygous	same alleles (TT or tt)
Heterozygous	different alleles (Tt)
Phenotype	expressed appearance (Tall)
Genotype	genetic makeup (TT, Tt, tt)
Dominant	expressed in heterozygote
Recessive	masked in heterozygote
P, F1, F2	Parent, 1st filial, 2nd filial gen

Gene Symbols

Capital letter = dominant (T) ; small = recessive (t)

Monohybrid Cross

- Cross involving ONE pair of contrasting traits.
Tall (TT) x Dwarf (tt) -> F1 all Tall (Tt)
Self F1 -> F2 : 3 Tall : 1 Dwarf
1 TT : 2 Tt : 1 tt (ge

Punnett Square. (Tt x Tt)

	T	t
T*	TT	Tt
t	Tt	tt

Fig. Monohybrid F2 = TT : Tt : Tt : tt

Law of Dominance

- When two alleles are present in heterozygous individual, only the DOMINANT one is expressed.

Law of Segregation

- During gamete formation, two alleles of each gene SEGREGATE cleanly so that each gamete carries only one allele.
(Law of purity of gametes).

Test Cross

Cross of dominant phenotype (TT or Tt?) with homozygous RECESSIVE (tt) to determine genotype.

Case 1 : TT x tt

All offspring TALL (Tt)

=> parent was homozygous (TT).

	T	T
t	Tt	Tt
t	Tt	Tt

TT x tt -> all Tt

	T	t
t	Tt	tt
t	Tt	tt

Tt x tt -> 1:1

Case 2 : Tt x tt

Half offspring Tall (Tt), half dwarf (tt) -> 1:1

=> parent was heterozygous (Tt).

Back Cross

Cross of F1 hybrid with one of its PARENTS.

If parent is homozygous recessive, back cross = test cross.

Uses

Dihybrid Cross (9 : 3 : 3 : 1)

Cross involving TWO pairs of contrasting traits.

Round Yellow (RRYY) x wrinkled green (rryy)

F1 - all Round Yellow (RrYy)

Self F1 -> F2 = 9 RY : 3 Ry : 3 rY : 1 ry.

4 x 4 Punnett (RrYy x RrYy)

	RY	Ry	rY	ry
RY	RRYY	RRYy	RYYr	RYry
Ry	RRYy	RRyy	RYry	Rryy
rY	RYYr	RYry	YYrr	Yrry
ry	RYry	Rryy	Yrry	rryy

Fig. 16-cell dihybrid Punnett square

F2 Phenotypes (9 : 3 : 3 : 1)

9 Round-Yellow : 3 Round-green :

3 wrinkled-Yellow : 1 wrinkled-green.

Confirms ~~dominance~~ law of independent assortment.

Mendel's Three Laws

Law I - Law of Dominance

(a) Characters are controlled by units called FACTORS (now called genes).

(b) Factors occur in pairs.

(c) In dissimilar pair, ONE factor dominates the other.

Law II - Law of Segregation

Alleles do not show blending; both characters recovered in F2 generation.

Gametes are PURE - each carries only one allele.

Universal law - ~~only sometimes~~ ALWAYS true.

Law III - Independent Assortment

When two pairs of traits are combined in a hybrid, segregation of one pair is INDEPENDENT of the other.

Explains 9 : 3 : 3 : 1 ratio in dihybrid.

Limitation - true only for genes on DIFFERENT chromosomes (or far apart on same chromosome).

Why Mendel was right

(a) Used pure-breeding parents

(b) Picked traits controlled by SINGLE gene

(c) Traits had clear dominance

(d) Genes were on different chromosomes

Incomplete Dominance

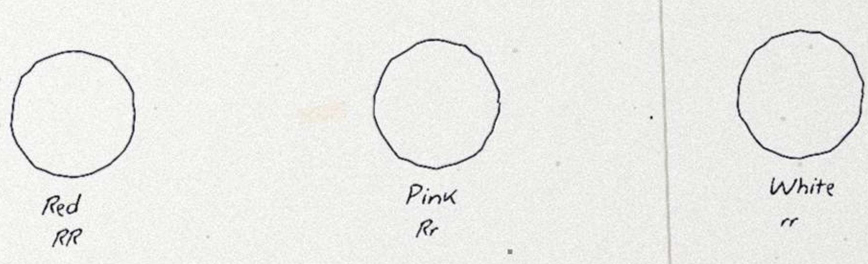
Heterozygote shows PHENOTYPE intermediate between the two homozygotes. Neither allele fully dominant.

Snapdragon (Mirabilis jalapa)

RR (Red) x rr (white) -> F1 = Rr (PINK)

F2 = 1 Red : 2 Pink : 1 white (1:2:1)

Genotype ratio = Phenotype ratio (no masking).



Mode of Inheritance

Neither allele is fully dominant -> blending.

Other examples - hair texture (curly + straight), flower colour in Antirrhinum.

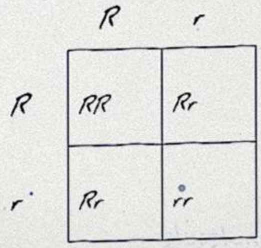


Fig. Rr x Rr -> 1 RR : 2 Rr : 1 rr

Co-dominance & ABO Blood Groups

Co-dominance

BOTH alleles expressed independently in heterozygote (no blending).

ABO Blood Group (Karl Landsteiner)

Gene I has 3 alleles - I^A, I^B, i

I^A and I^B - CO-DOMINANT

Both are DOMINANT over recessive i.

Blood Group Table

Genotype	Phenotype	Antigen	Antibody
$I^A I^A$ or $I^A i$	A	A	Anti-B
$I^B I^B$ or $I^B i$	B	B	Anti-A
$I^A I^B$	AB	A + B	None
ii	O	None	Anti-A + Anti-B

Universal Donor / Recipient

O - Universal donor (no antigen)

AB - Universal recipient (no antibody)

Multiple Alleles

More than 2 alleles for same gene in a population (but ~~each individual~~ any individual has only 2).

Pleiotropy & Polygenic Inheritance

Pleiotropy

ONE gene -> MULTIPLE phenotypic effects.

Eg. Sickle-cell anaemia gene (HbS) :

- -> anaemia (chronic)
- -> joint pain
- -> spleen damage
- -> resistance to malaria (heterozygotes only!)

Eg. Phenylketonuria (PKU) - mental retardation, reduced hair + skin pigmentation.

Polygenic Inheritance

Trait controlled by THREE OR MORE genes.

Each gene contributes additively to phenotype.

Eg. Human skin colour (3 genes: A, B, C)
Allele combinations -> continuum (very dark to very fair).

Other examples : Height, eye colour, weight.

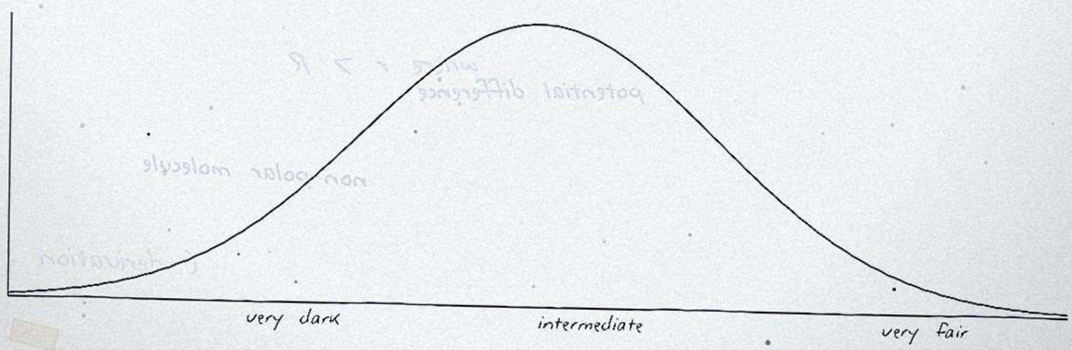


Fig. Polygenic trait -> bell-curve distribution

Chromosomal Theory of Inheritance

Sutton & Boveri (1902) - independently noted that chromosome behavior in meiosis parallels Mendel's *factor behavior.

Parallels

Chromosomes	Genes / Factors
In pairs	In pairs
Segregate in meiosis	Segregate in gametes
Assort independently	Independent assortment
One from each parent	One from each parent

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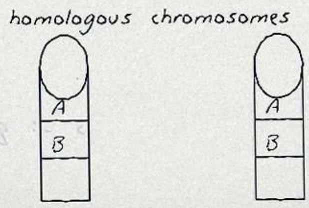
Verification - T. H. Morgan

Drosophila melanogaster used as model.

Yellow body + white eye genes -> located on X chromosome -> Morgan's sex-linked discoveries.

Nobel Prize 1933.



Linkage & Recombination

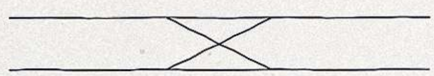
Linkage

Genes on the SAME chromosome tend to be inherited together - do NOT assort independently.

Morgan (1910) demonstrated linkage in Drosophila :
yellow body (y) + white eye (w) genes always inherited together (on X chromosome).

Recombination - Crossing Over

Linked genes can still RECOMBINE through crossing over in meiosis I (pachytene of prophase-I).
Frequency proportional to ~~number~~ DISTANCE between genes.



<- chiasma

Frequency = Distance

Recombination frequency = % recombinants in offspring
1 % recombination = 1 centi-Morgan (cM)
Used by Alfred Sturtevant to make first ~~phylogenetic~~ GENETI
of Drosophila X chromosome.

Sex Determination Mechanisms

Genetic Methods

Type	Female	Male	Examples
XX-XY	XX	XY	Humans, Drosophila
XX-XO	XX	XO	Grasshopper, cockroach
ZZ-ZW	ZW	ZZ	Birds, butterflies
ZZ-ZO	ZO	ZZ	Some insects

Honeybee - Haplodiploidy

Female (queen + worker) = diploid ($2n = 32$)

Male (drone) = haploid ($n = 16$)

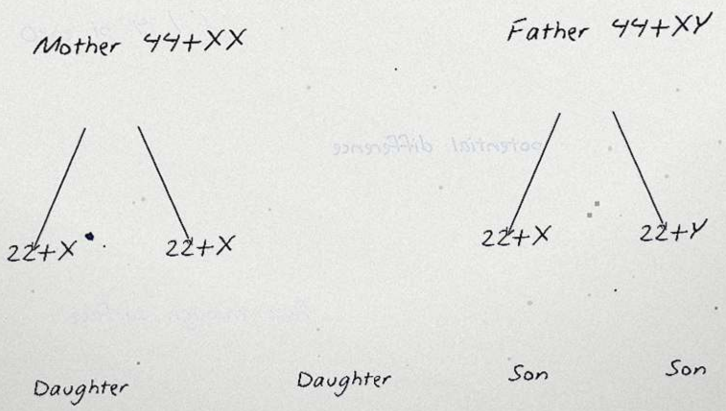
Males develop from unfertilised eggs (parthenogenesis).

Human Sex Determination

44 autosomes + 2 sex chromosomes (XX or XY).

Heterogametic sex = MALE (produces X or Y sperms).

Mother always gives X; father determines sex.



Sex-Linked Inheritance

Genes located on SEX chromosomes (X or Y).

Inheritance pattern differs from autosomal.

X-Linked Recessive

Males have only ONE X -> if affected allele present, they DEFINITELY express disease (hemizygous).

Females are carriers in heterozygous state.

Examples - Haemophilia, Colour blindness, Duchenne muscular dystrophy.

Haemophilia (Royal Disease)

Defective clotting factor -> non-stop bleeding from minor cuts.

Famous case - Queen Victoria's descendants.

~~Females~~ Males much more affected.

Carrier mother x Normal father

$X^h X \times XY$

=> 1/4 $X^h X$ (carrier daughter)

1/4 XX (normal daughter)

1/4 $X^h Y$ (haemophilic son)

1/4 XY (normal son)

Colour Blindness

Mendelian Disorders

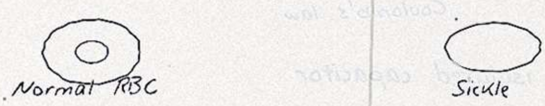
(1) Sickle Cell Anaemia

Autosomal recessive (Chr 11; HbS allele).

Mutation : Glu (6th aa of beta-globin) -> Val (GAG -> GUG; missense / point mutation)

RBCs become SICKLE-shaped under low O2.

Heterozygotes (Hb A Hb S) are CARRIERS, partial resistance to malaria - pleiotropic effect.



(2) Phenylketonuria (PKU)

Autosomal recessive.

Defective phenylalanine hydroxylase -> Phe builds up -> phenylpyruvate accumulates -> mental retardation.

(3) Thalassemia

Autosomal recessive defect in synthesis of alpha or beta globin chains.

alpha-thal on ~~Chr 11~~ Chr 16 ; beta-thal on Chr 11.

Causes ANAEMIA - chronic, severe.

Chromosomal Disorders

Due to missing / extra / abnormal chromosomes.

Caused by NON-DISJUNCTION ~~during mitosis~~ in meiosis.

*__Aneuploidy vs Polyploidy__

Aneuploidy - loss / gain of CHROMOSOMES.

Monosomy (2n - 1), Trisomy (2n + 1)

Polyploidy - increase in CHROMOSOME SET

Triploid (3n), Tetraploid (4n) - common in plants

(a) Down's Syndrome

Trisomy 21 -> 47, 21+

Slanting eyes (Mongolian fold), broad face, short stature, palm crease, retarded mental development.

First described by Langdon Down (1866).

Risk ~~constant~~ increases with mother's age (>35).

(b) Klinefelter's Syndrome

47, XXY - Male with extra X

Feminine traits, gynaecomastia, sterile.

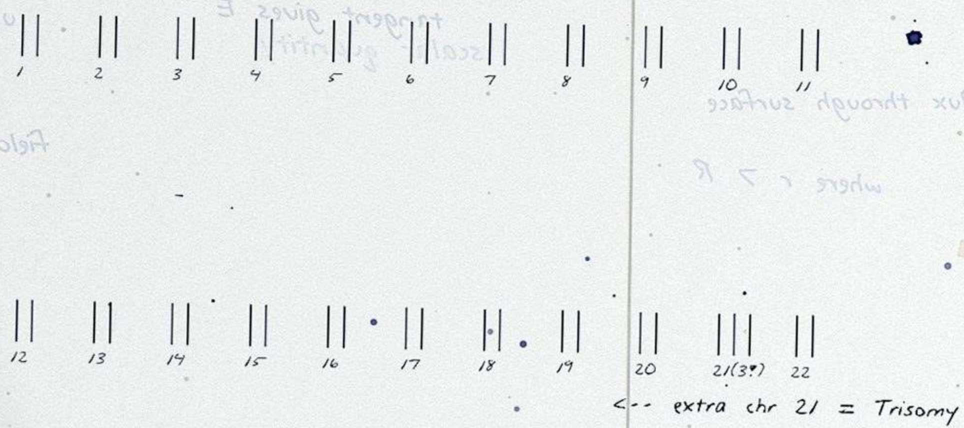
(c) Turner's Syndrome

45, XO - Female with only one X

Short stature, webbed neck, no breast dev., rudimentary ovaries (sterile).

Karyotype - Trisomy 21

Karyotype - organised display of all chromosomes of an individual in homologous pairs.
Used to diagnose chromosomal disorders.



Other Trisomies

Trisomy 13 - Patau syndrome
Trisomy 18 - Edward's syndrome
Both are very serious; few survive beyond a year.

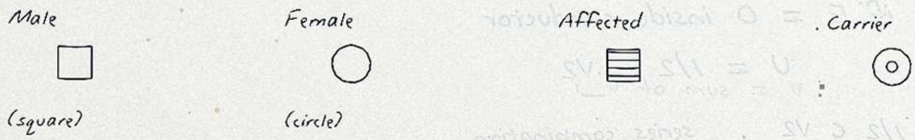
Sex-Chromosome Aneuploidy

Klinefelter (XXY), Turner (XO), Triple X (XXX)

Pedigree Analysis

Pedigree chart - family tree showing inheritance of a trait through multiple generations.

Symbols



Pedigree Conventions

Horizontal line between square + circle = mating
Vertical line below mating = offspring
Roman numerals (I, II, III) = generations
Arabic numerals = individuals in a generation

Uses

(i) Trace ancestry of a trait
(ii) Predict trait expression in future offspring
(iii) Identify carriers
(iv) Determine if trait is dominant / recessive, autosomal / X-linked.

Genetic Counselling

Recap - Why Mendel was Lucky

Mendel's 7 genes happened to fall on different chromosomes (or very far apart) => no linkage to spoil independent assortment ratio.

Modern View - Gene = DNA segment

Each Mendelian factor = a stretch of DNA (usually coding for a single protein / RNA).

Concepts Summary

Mendel's experiment	1856-1865
Rediscovery	1900 (de Vries, Correns, Tschermak)
Chromosomal theory	Sutton + Boveri 1902
Linkage	Morgan 1910
Genetic map	Sturtevant 1913
DNA structure	Watson + Crick 1953
Genetic code	Nirenberg + Khorana
Human Genome	Completed 2003

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Indian Contributions

M. S. Swaminathan - Father of Green Revolution

Har Gobind Khorana - cracked genetic code

P. Maheshwari - embryologist

Vasudev Sahni - paleobotanist

Important Terms - Glossary

Allele	- alternate forms of a gene
Locus	- position of gene on chromosome
Homologous	- matching pair of chromosomes
Karyotype	- ordered display of chromosomes
Autosomes	- chromosomes other than sex (1-22)
Heterogametic	- produces 2 types of gametes (XY)
Homogametic	- produces 1 type (XX)
Crossing over	- exchange of segments in meiosis-I
Chiasma	- visible point of crossing over
Test cross	- X recessive homozygote
Back cross	- F1 X parent
Co-dominance	- both alleles expressed
Pleiotropy	- one gene -> many traits
Polygenic	- one trait -> many genes
Aneuploidy	- wrong number of chromosomes
Polyploidy	- extra full sets of chromosomes
Lethal genes	- kill organism in homozygous form
Epistasis	- one gene masks another
Penetrance	- % of carriers expressing trait
Expressivity	- extent of expression

Practice Problems

Q1 Blood Groups

Father - AB ; Mother - O. Possible children?

I A I B x i i -> I A i (A) ; I B i (B)

Children can only be A or B; NEVER AB or O.

Q2 Carrier Mother

Haemophiliac father x carrier mother.

X h Y x X h X

Daughters : 1/2 X h X h (haemo) + 1/2 X h X (carr

Sons : 1/2 X h Y (haemo) + 1/2 X Y (normal)

Q3 Dihybrid

AaBb x aabb -> ?

1 AaBb : 1 Aabb : 1 aaBb : 1 aabb (1:1:1:1)

Q4 Sickle Cell

Both parents heterozygous (Hb A Hb S).

F1 ratio : 1 normal : 2 carriers : 1 anaemic

Q5 Polyploid Plant

Banana, watermelon - triploid (3n) seedless varieties.

Wheat - hexaploid (6n).

Q6 Sex of Bee

Lethal Alleles & Epistasis

Lethal Alleles

Genes that kill the organism in homozygous form.

Example - yellow body in mice (AY).

AY AY -> embryo lethal

AY a -> yellow live mouse

a a -> black live mouse

AY a x AY a -> ratio = 2 yellow : 1 black (not 3:1).

Epistasis

One gene masks the expression of another gene.

Example - Albino (cc) masks all coat colours.

Modified Mendelian dihybrid ratios :

12 : 3 : 1 (dominant epistasis)

9 : 3 : 4 (recessive epistasis)

13 : 3 (dominant-recessive)

9 : 7 (duplicate recessive)

Hybrid Vigour (Heterosis)

F1 hybrid often shows traits SUPERIOR to either parent (taller, healthier, more yield).

Eg. hybrid corn yields 2x parent yield.

Inbreeding Depression

Repeated selfing -> homozygosity -> weak progeny.

Notable Scientists - Quick Recap

Mendel (1822-84)	Laws of inheritance ; pea plants
Sutton & Boveri	Chromosomal theory (1902)
T.H. Morgan	Linkage, sex linkage in Drosophila
Sturtevant	Genetic mapping (1913)
Garrod	Inborn errors of metabolism
Beadle & Tatum	One gene - one enzyme (Neurospora)
Karl Landsteiner	ABO blood groups (1900)
Watson & Crick	Double-helix DNA (1953)
Khorana	Genetic code (Nobel 1968)
Nirenberg	Cracked codon table
Hardy + Weinberg	Population genetics (1908)

Numbers to Remember

Human chromosomes - 46 (44 + XX or 44 + XY)

Mendel's pea traits - 7

Monohybrid F2 ratio - 3:1

Dihybrid F2 ratio - 9:3:3:1

Test cross ratio - 1:1

Incomplete dominance F2 - 1:2:1

End of Chapter 4