Recognised as one of the greatest and most influential composers of the Western classical tradition

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Ludwig van Beethoven

Composer

Overview Compositions Listen Videos

Encyclopedia Britannica

Ludwig van Beethoven | Biography, Music, & Facts | Britannica

Ludwig van Beethoven, (baptized December 17, 1770, Bonn, archbishopric of Cologne [Germany]—died March 26, 1827, Vienna, Austria), German composer, ...

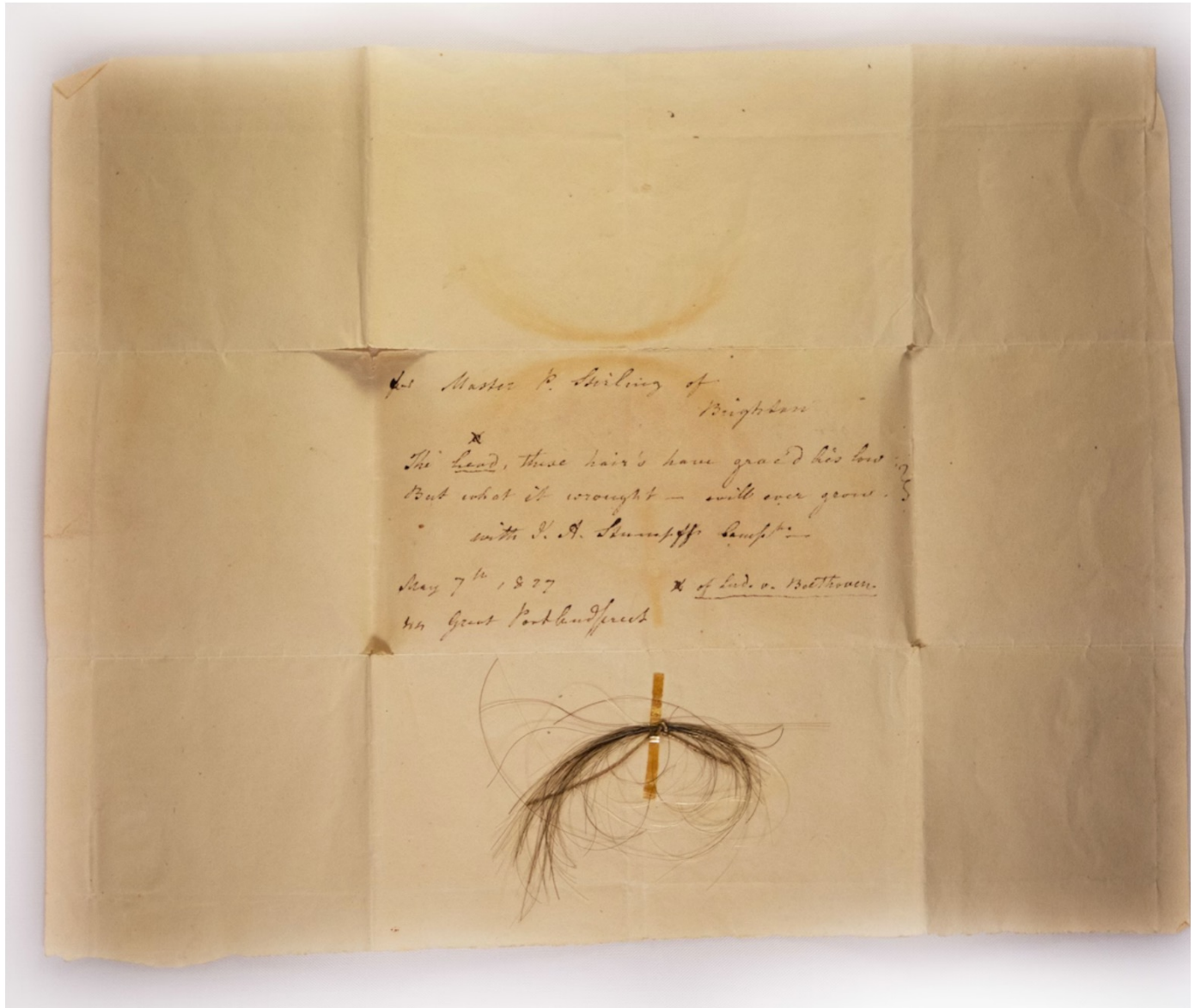
Place of burial	Height
Central Cemetery, Vienna, Austria	1.62 m

Beethoven's DNA decoded from locks of hair saved by his fans

By Carolyn Y. Johnson

March 22, 2023 at 11:00 a.m. EDT

The Washington Post
Democracy Dies in Darkness



The Stumpff lock came attached to an inscription by its former owner Patrick Stirling. (Kevin Brown)

https://www.washingtonpost.com/science/2023/03/22/beethoven-genome-hair/

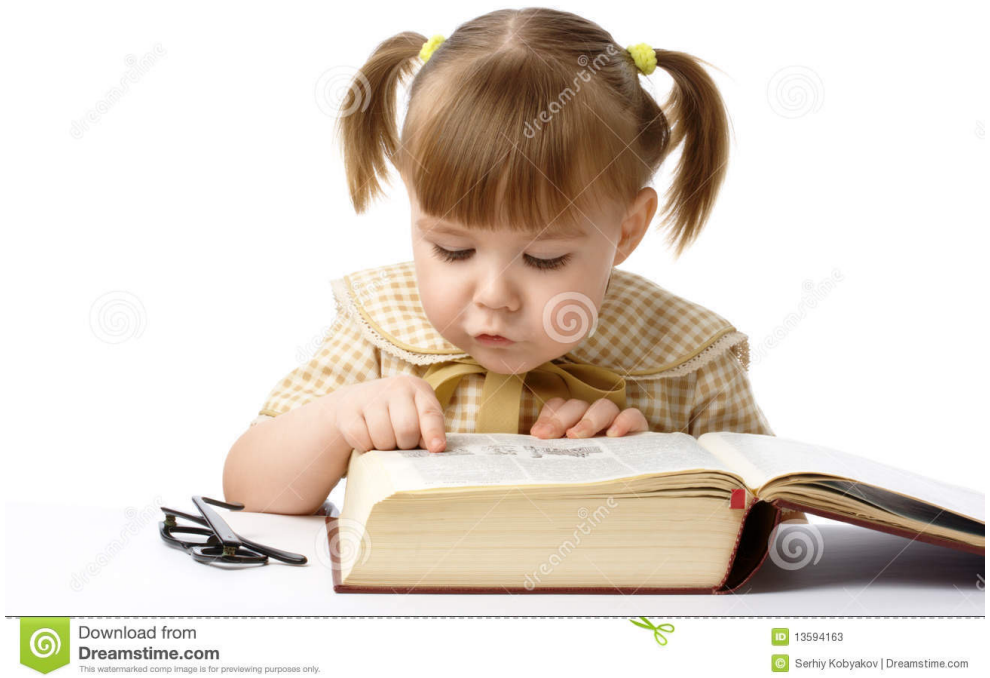
- Beethoven became deaf at the age of 28
- Scientists did not discover a clear explanation for Beethoven's deafness.
- But they identified genetic risk factors for liver disease
  - They found signs he had a hepatitis B infection that could have contributed to his cirrhosis

https://www.washingtonpost.com/science/2023/03/22/beethoven-genome-hair/

- The study was published Wednesday (i.e., 22nd March 2023) in the journal Current Biology
- It illustrates the power of DNA to explore fundamental questions about life in the distant past
- Most diseases are not purely genetic, so the data is limited in what it can reveal

https://www.washingtonpost.com/science/2023/03/22/beethoven-genome-hair/

This lecture is not about technical details but about the underlying basis



How is the manual of life “read” by the cell to create organisms?

https://www.dreamstime.com/stock-photos-cute-little-girl-reading-books-back-to-school-image13594163

Today's topics

- DNA, RNA, and proteins
- DNA to protein – Central Dogma
- The genetic code and mutations
- Inherited DNA leads to specific traits
- Elucidating arginine biosynthesis pathway
- Stem cells

Letters of the English alphabet

$\mathcal{A}$ $\mathcal{B}$ $\mathcal{C}$ $\mathcal{D}$ $\mathcal{E}$ $\mathcal{F}$ $\mathcal{G}$

$\mathcal{H}$ $\mathcal{I}$ $\mathcal{J}$ $\mathcal{K}$ $\mathcal{L}$ $\mathcal{M}$ $\mathcal{N}$

$\mathcal{O}$ $\mathcal{P}$ $\mathcal{Q}$ $\mathcal{R}$ $\mathcal{S}$ $\mathcal{T}$ $\mathcal{U}$

$\mathcal{V}$ $\mathcal{W}$ $\mathcal{X}$ $\mathcal{Y}$ $\mathcal{Z}$

We form words and sentences by joining letters of the alphabet

Letters of the DNA and RNA alphabet

- 4 “letters”
  - A, C, G, and T in case of DNA
  - A, C, G, and U in case of RNA
  - A, C, G, T, and U are 1-letter symbols of specific chemical compounds
- Each letter is called as a nucleotide
- We form DNA/RNA – both are polymers – by joining nucleotides

A long continuous string of letters

dierkalkdfjbeirowejldsmvladmnvoaiuroewjldmvlamvaioeruweodlm
nveihjweoipur**Deoxyribonucleic acid is the material that exi
sts in every cell of an organism**lsmnvksdlvKdierkalkdfjbeiro
wejldsmvladmnvoaiuroewjldmvlamvaioeruweodlmnveihjweoipurlsm
nvksdldierkalkdf**a gene is made of DNA**jbeirowejldsmvladmnvoa
iuroewjldmvlamvaioeruweodlmnveihjweoipurlsmn**A gene can be s
een as a protein encoded in the alphabet of DNA**svksdlvdierk
alkdfjbeirowejldsmvladmnvoaiuroewjldmvlamvaioeruweodlmnveih

- String of letters has meaningful sentences
- Letters interspersing sentences are gibberish
  - "gibberish" part is not really true in case of DNA

Chromosome, DNA, genes, polynucleotide, …

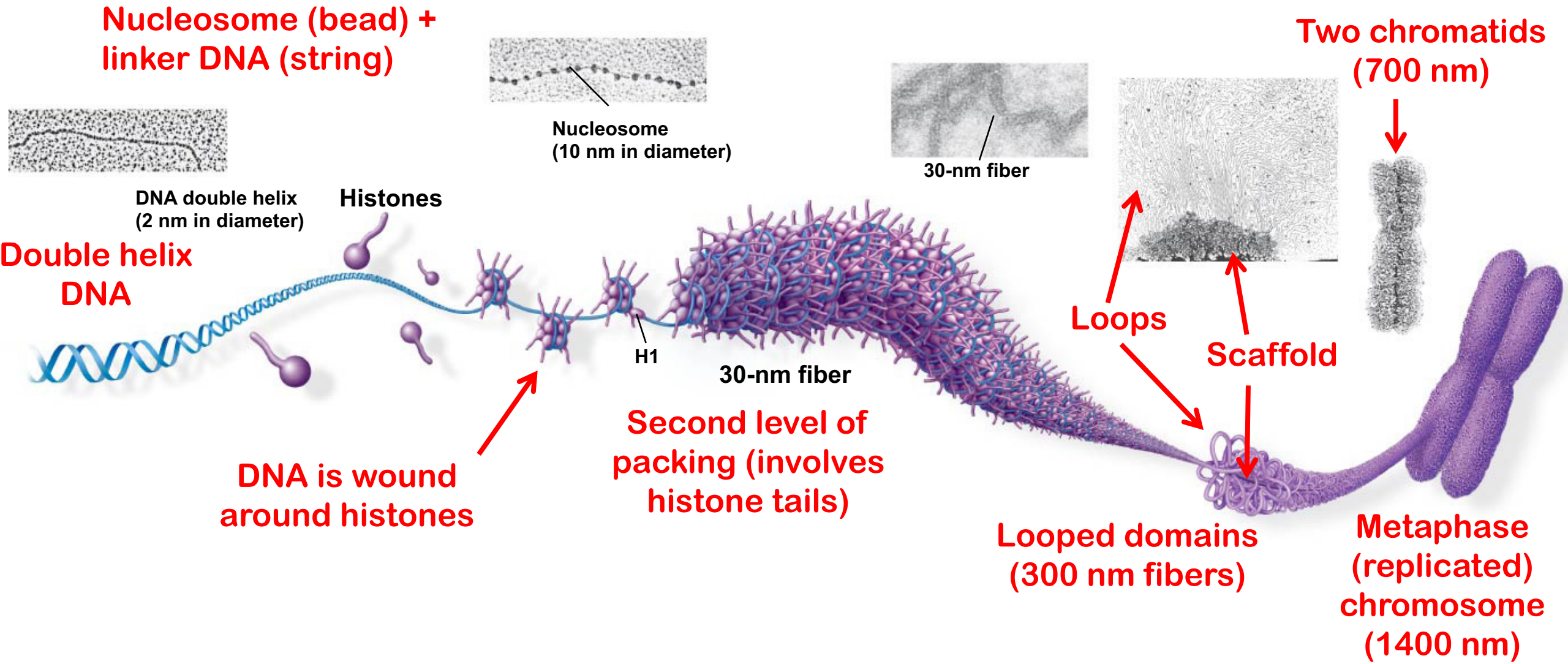
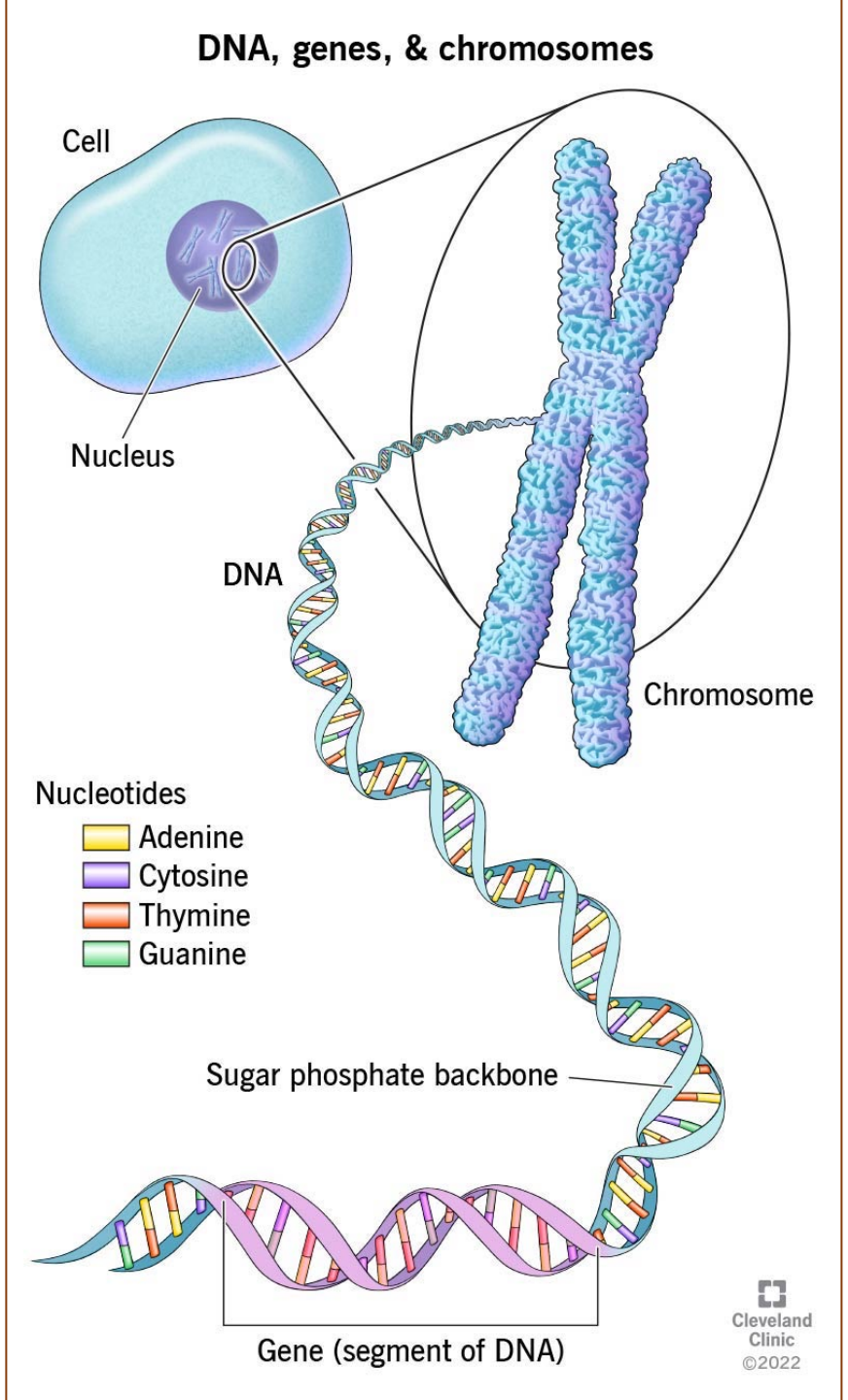


Figure 16.22. Biology. A global approach

Genes



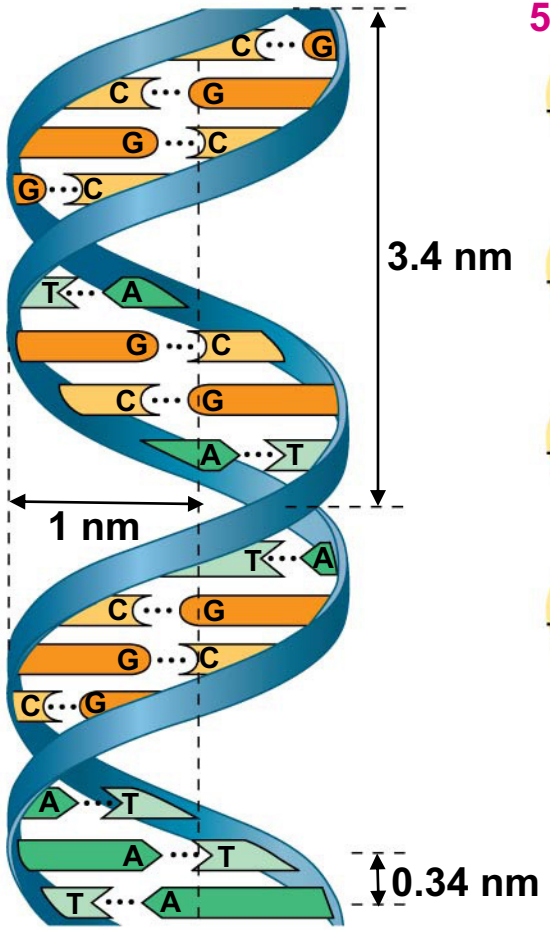
Gene is a stretch of DNA in a chromosome that encodes a protein

https://my.clevelandclinic.org/health/body/23064-dna-genes--chromosomes

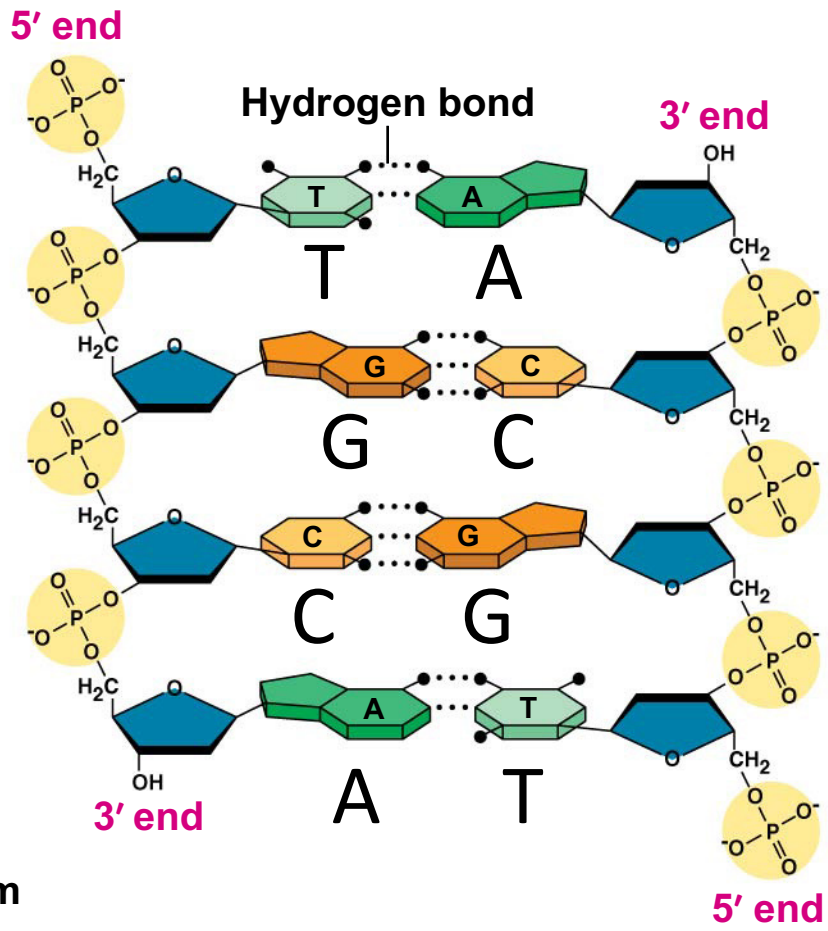
Specifying DNA and RNA "structure"

- A word is spelt by writing the letters of the alphabet in a certain sequence
  - C O M P U T E R H U N G R Y L A N D S C A P E
- Structure of a DNA is specified by writing the sequence of monomers that make up this DNA
  - 5' – A A C G G T A A C C T G T A C T G – 3'
  - Similarly for RNA

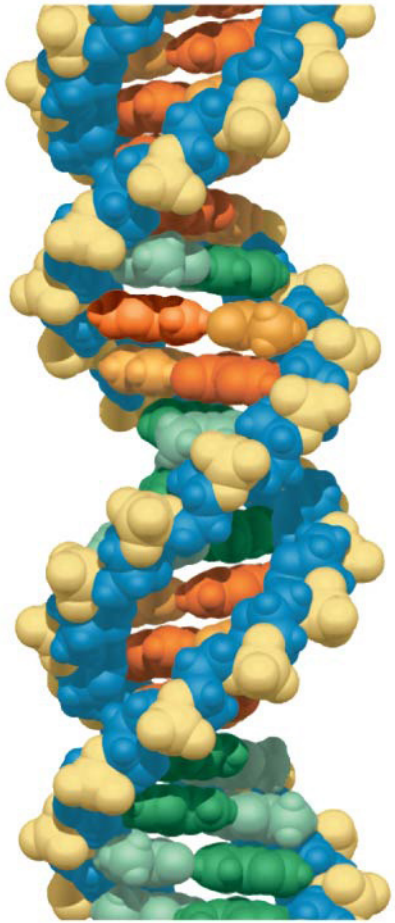
Chromosome, DNA, genes, polynucleotide, …



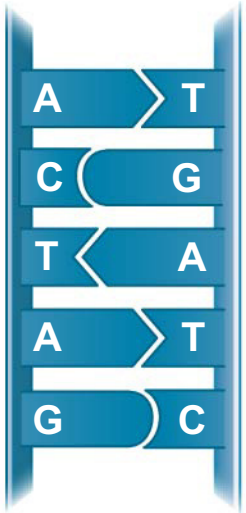
(a) Key features of DNA structure



(b) Partial chemical structure



(c) Space-filling model



Figures 16.7 and 16.9. Biology. A global approach

Letters of the Protein alphabet

- 20 “letters”
- Each letter is called as an amino acid
- We form proteins – a polymer – by joining amino acids
- One such amino acid is arginine

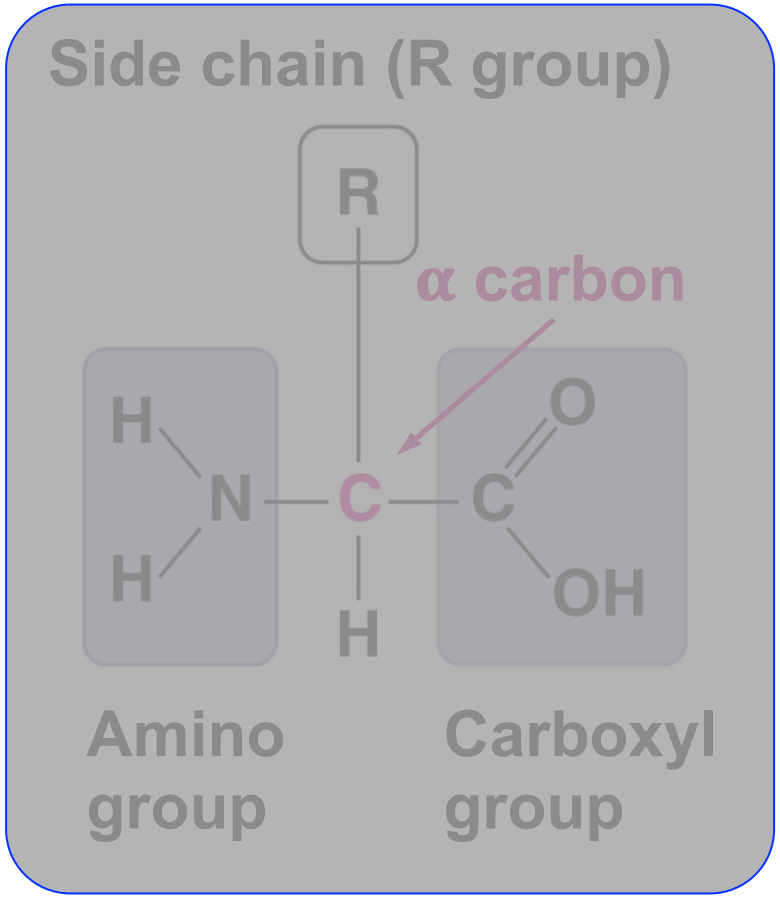


Figure 5.UN01 in Biology. A global approach by Campbell et al., Global Ed.

Amino acid sequence of a protein

P02144 · MYG_HUMAN

Myoglobin · **Homo sapiens (Human)** · **Gene:** MB · 154 amino acids · Evidence at protein level · **Annotation score:** 5/5

Sequence[i]

Tools ▾ Download Add Highlight ▾ Copy sequence

Length 154
Mass (Da) 17,184

Last updated 2007-01-23 v2
Checksum[i] F6A41F19A525F09C

```
        10         20         30         40         50         60         70         80
MGLSDGEWQL VLNVWGKVEA DIPGHGQEVL IRLFKGHPET LEKFDKFKHL KSEDEMKASE DLKKHGATVL TALGGILKKK

        90        100        110        120        130        140        150
GHHEAEIKPL AQSHATKHKI PVKYLEFISE CIIQVLQSKH PGDFGADAQG AMNKALELFR KDMASNYKEL GFQG
```

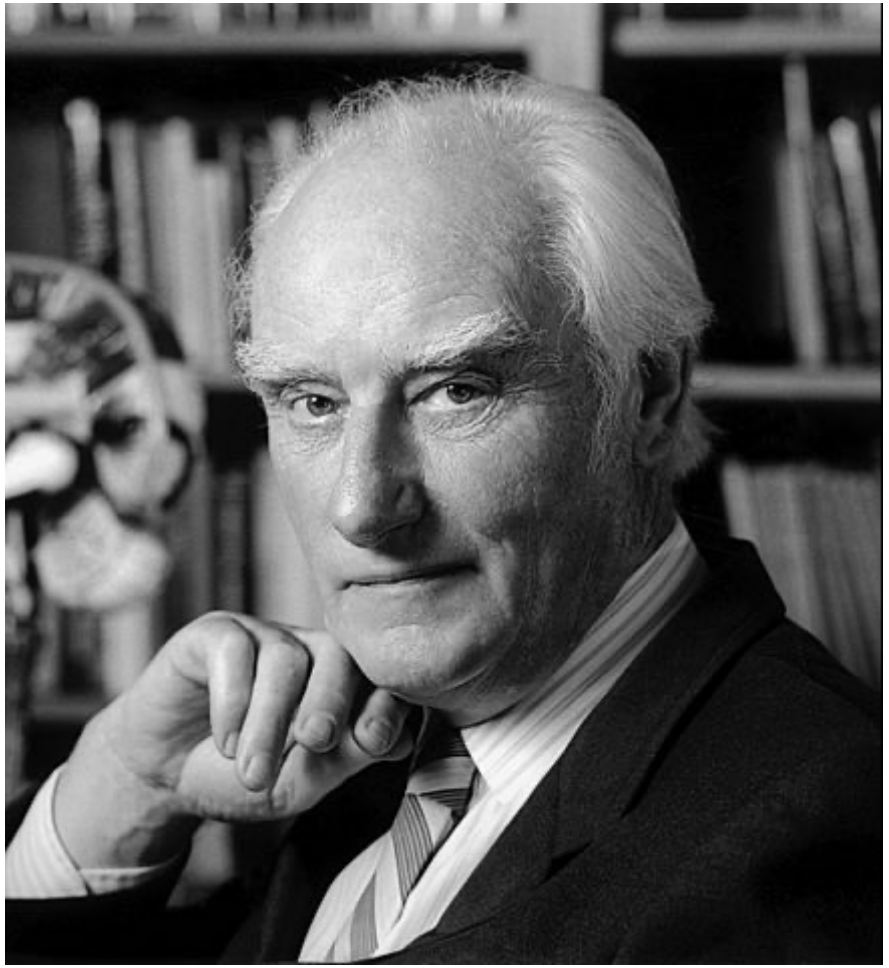
Myoglobin is a protein

https://www.uniprot.org/uniprotkb/P02144/entry#sequences

Today's topics

- DNA, RNA, and proteins
- DNA to protein – Central Dogma
- The genetic code and mutations
- Inherited DNA leads to specific traits
- Elucidating arginine biosynthesis pathway
- Stem cells

Central Dogma



Francis Crick

DNA double helix: 1953
Central dogma: 1956

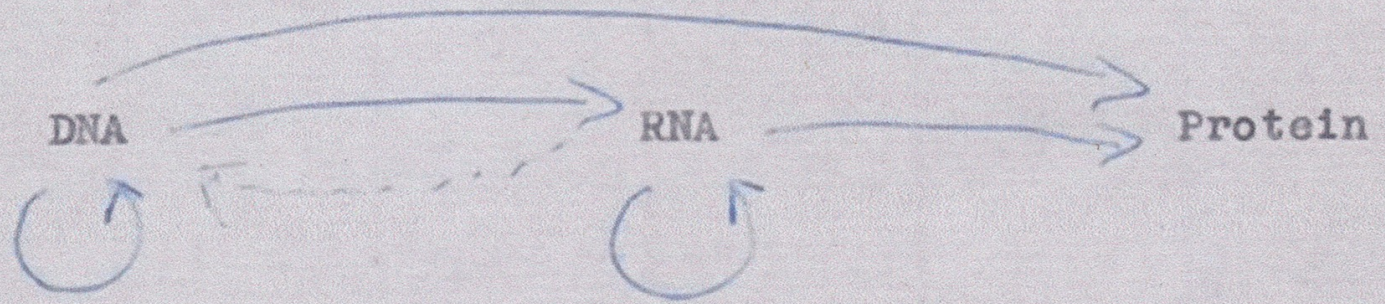
Nobel prize in Physiology or Medicine (1962)
For the discovery of the molecular structure of DNA
With James Watson and Maurice Wilkins

Central Dogma

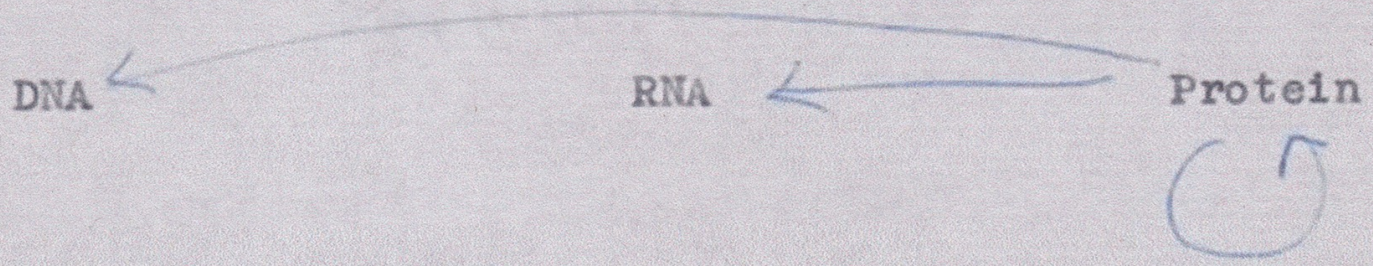
Central dogma is the concept that cells are governed by a cellular chain of command

Crick's original outline

The Central Dogma: "Once information has got into a protein it can't get out again". Information here means the sequence of the amino acid residues, or other sequences related to it. That is, we may be able to have



but never

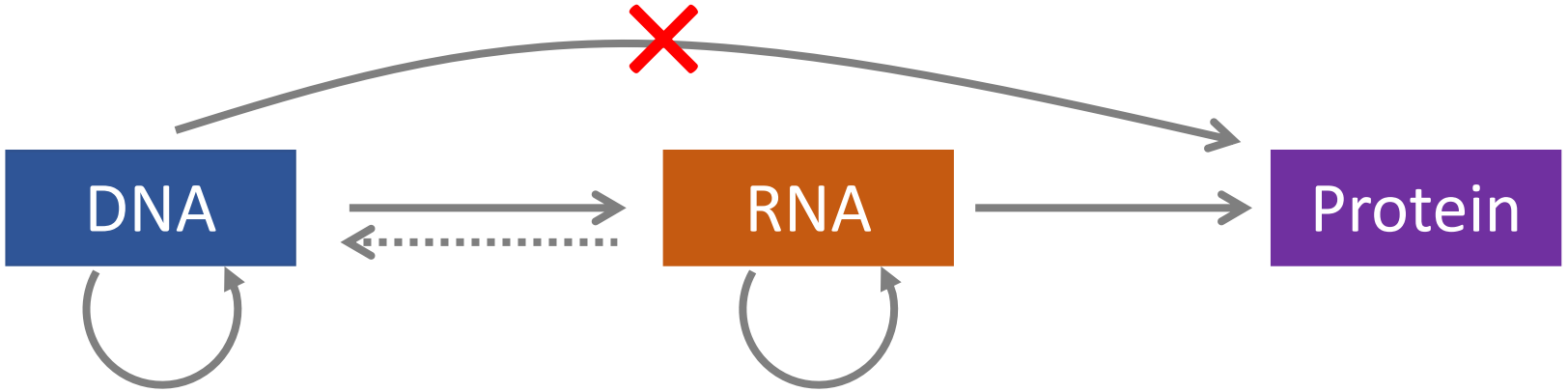


where the arrows show the transfer of information.

https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.2003243

The Central Dogma

- Once information has got into a protein, it can't get out again
- Information here means the sequence of the amino acid residues, or other sequences related to it



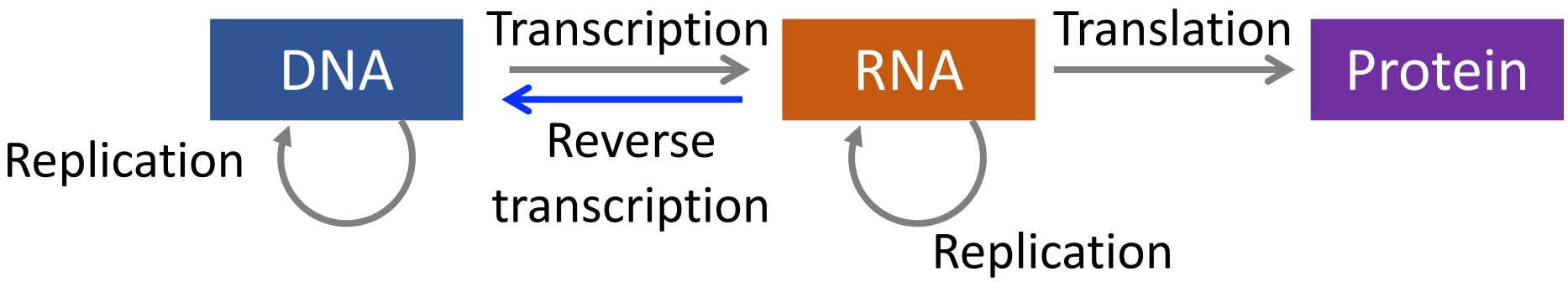
Arrows show the transfer of information

The Central Dogma

- ... but never

Arrows show the transfer of information

The Central Dogma



Central dogma

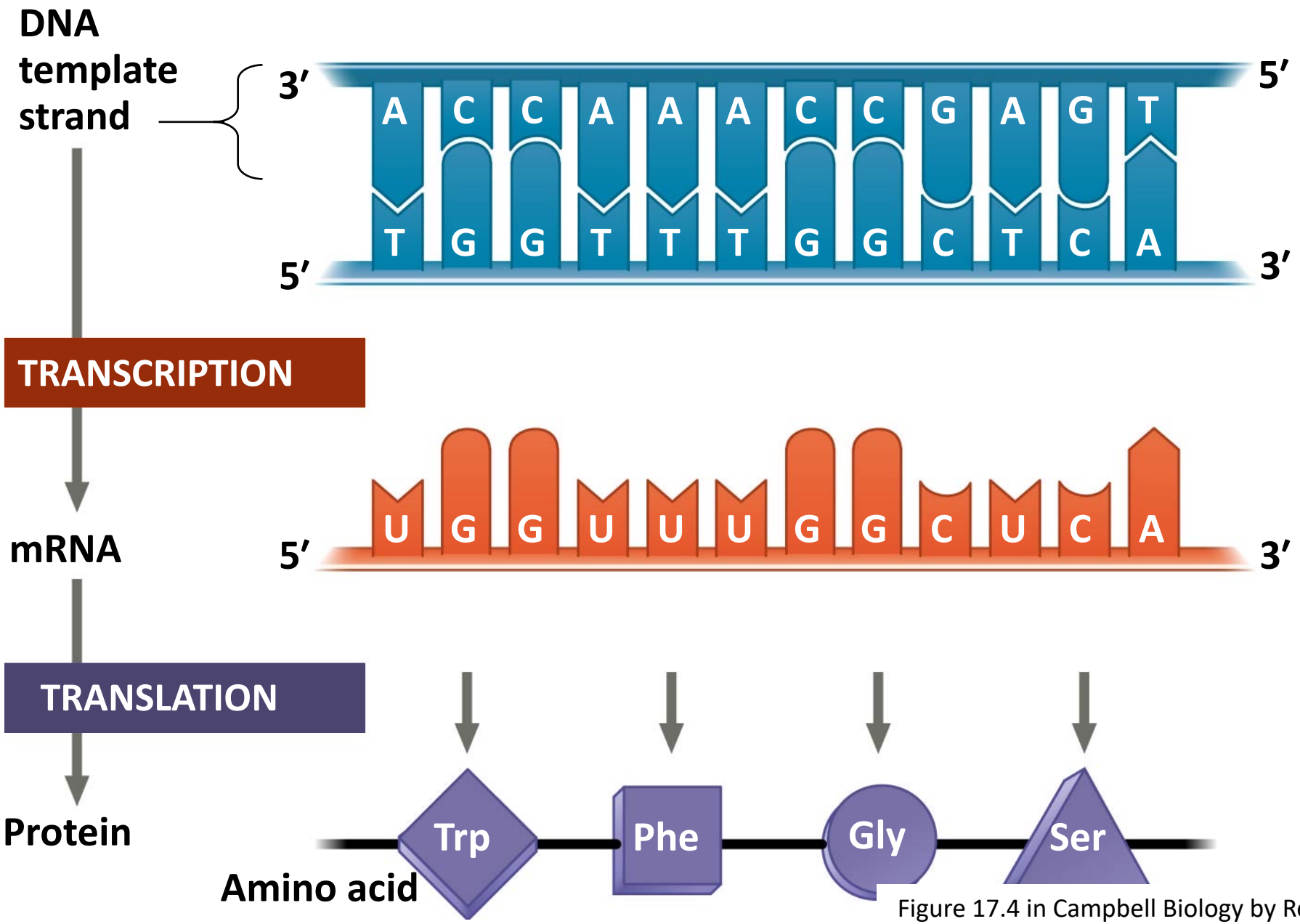


Figure 17.4 in Campbell Biology by Reece et al., (10th edition)

Today's topics

- DNA, RNA, and proteins
- DNA to protein – Central Dogma
- The genetic code and mutations
- Inherited DNA leads to specific traits
- Elucidating arginine biosynthesis pathway
- Stem cells

The Adventure of the Dancing Men

24 languages

From Wikipedia, the free encyclopedia

The Adventure of the Dancing Men is a Sherlock Holmes story written by Sir Arthur Conan Doyle as one of 13 stories in the cycle published as *The Return of Sherlock Holmes* in 1905. It was first published in *The Strand Magazine* in the United Kingdom in December 1903, and in *Collier's* in the United States on 5 December 1903.

Doyle ranked "The Adventure of the Dancing Men" third in his list of his twelve favorite Holmes stories.[1] This is one of only two Sherlock Holmes short stories where Holmes' client dies after seeking his help.[2] Holmes's solution to the riddle of the dancing men rests on reasoning that closely resembles that of Legrand in Poe's "The Gold Bug."

The original title was "**The Dancing Men**," when it was published as a short story in *The Strand Magazine* in December 1903.[3]

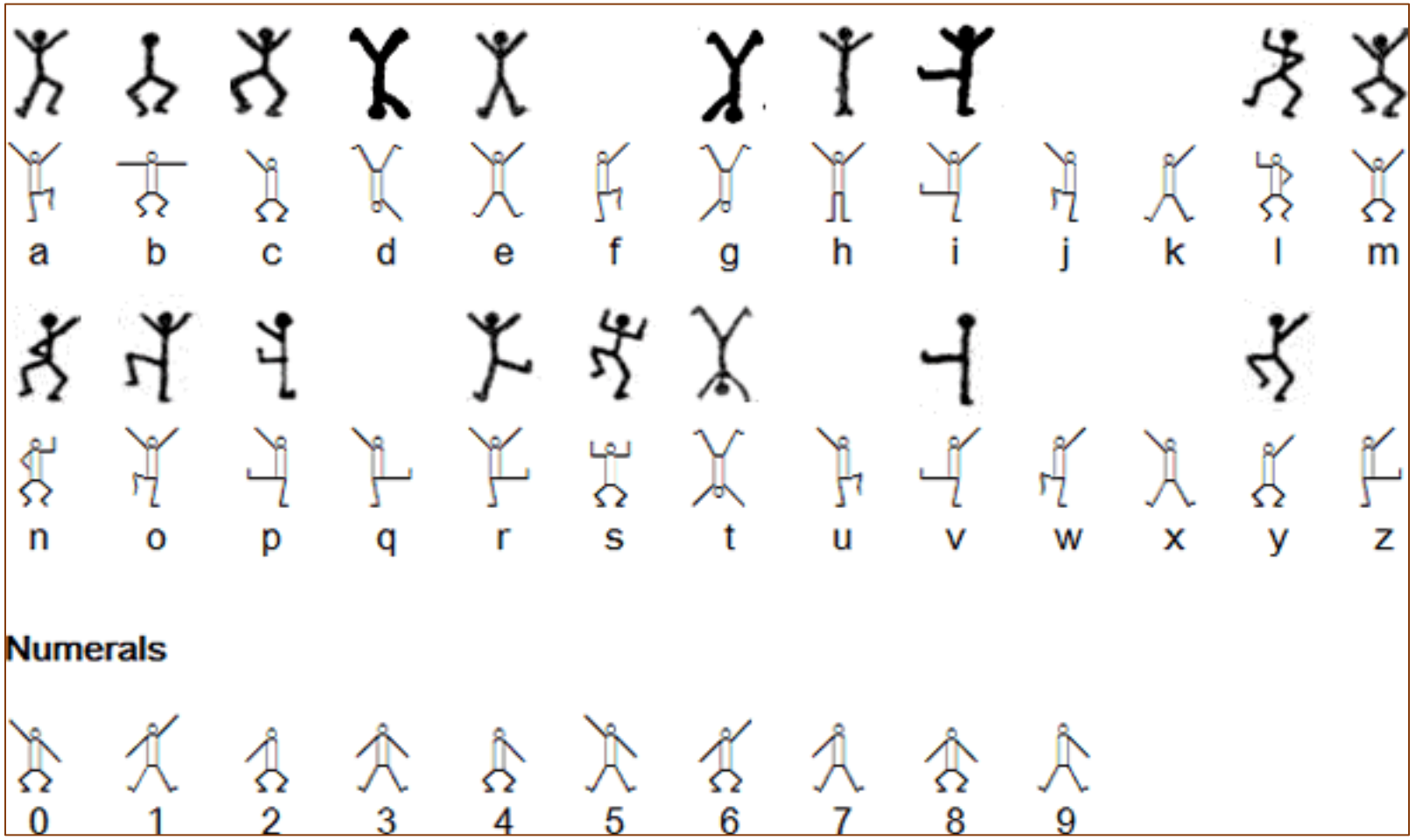
"The Adventure of the Dancing Men"

by Arthur Conan Doyle

Plot [edit]

The story begins when Hilton Cubitt of Ridling Thorpe Manor in Norfolk visits Sherlock

“Dancing men” decoded



https://omniglot.com/conscripts/dancingmen.htm

Decoding the “dancing men” script

One man’s invention is another man’s discovery

Nature’s inventions ought to be Biologist’s discoveries!

DNA and protein alphabets

How are instructions for assembling amino acids into proteins encoded into DNA?

The alphabet of English: 26 letters
The alphabet of Hindi or Assamese or …: __ letters

The alphabet of DNA: 4 letters (A, C, G, T)
The alphabet of protein: 20 letters (names intentionally omitted here)

Decoding the genetic code

Sherlock Holmes in
The dancing men

How can one possibly use 4 dancing men to send messages in a script that contains 20 letters?

$$4^1 = 4$$
$$4^2 = 16$$
$$4^3 = 64$$

both images are from http://www.harsmedia.com/SoundBlog/Archief/00800.php

Genetic codon reference chart

UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys
UUC		UCC		UAC		UGC	
UUA	Leu	UCA		UAA	Stop	UGA	Stop
UUG		UCG		UAG		UG[illegible]	Trp
CUU		CCU	Pro	CAU	[illegible]	[illegible]	Arg
CUC		CCC		CA[illegible]		[illegible]	
CUA		CCA		[illegible]	Gln	CGA	
CUG		CC[illegible]		[illegible]AG		CGG	
AUU	Thr	[illegible]		AAU	Asn	AGU	Ser
AU[illegible]		[illegible]CC		AAC		AGC	
AUA		ACA		AAA	Lys	AGA	Arg
AUG	Met	ACG		AAG		AGG	
GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly
GUC		GCC		GAC		GGC	
GUA		GCA		GAA	Glu	GGA	
GUG		GCG		GAG		GGG	

DO NOT MEMORIZE

Har Gobind Khorana

1968 Nobel prize in Physiology or Medicine
For showing how the genetic components control the synthesis of proteins
Along with Robert W. Holley

Marshall W. Nirenberg

Universality of the genetic code

A firefly gene in a tobacco plant

A jellyfish gene in a pig

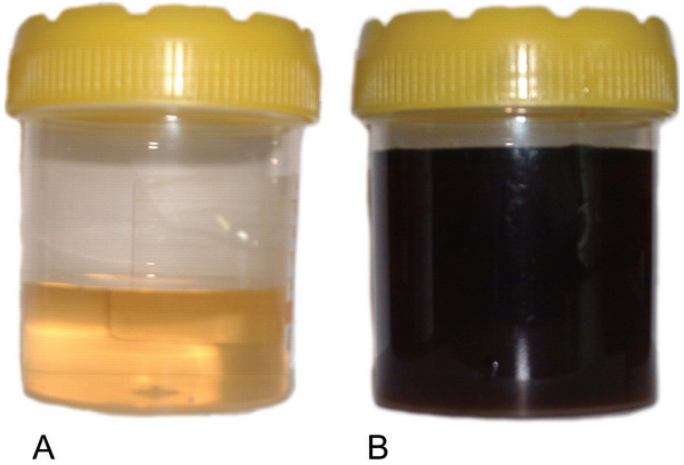
- Basis of biotechnology
  - GM food
  - Recombinant therapeutics
  - COVID vaccine

Figure 17.6 in Campbell Biology by Reece et al., (10th edition)

Today's topics

- DNA, RNA, and proteins
- DNA to protein – Central Dogma
- The genetic code and mutations
- Inherited DNA leads to specific traits
- Elucidating arginine biosynthesis pathway
- Stem cells

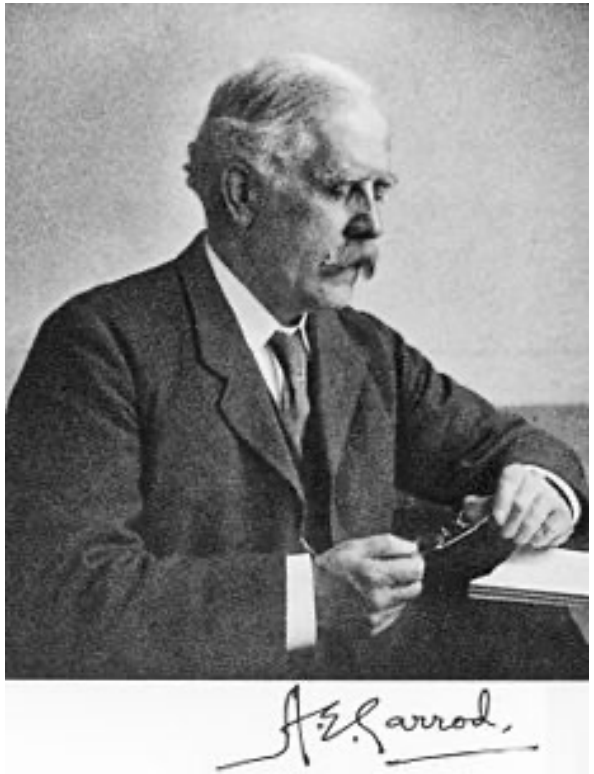
Black urine disease



- Urine of some people becomes black because it contains the chemical alkapton (homogentisic acid)
- Most people have an enzyme that converts (i.e., metabolizes) alkapton
- People who do not inherit this enzyme suffer from the disease alkaptonuria

Images of urine and pigmented hands taken from https://lrodgers93.wordpress.com/

Inborn error of metabolism



Archibald Garrod
(1857-1936)
English Physician

- Garrod proposed the usage “inborn error of metabolism”
- Neither the chemical reactions nor the enzymes that catalyze these reactions were known at that time

He was ahead of his time!

Image of Garrod taken from Wikipedia

https://www.iitb.ac.in 110%

English हिन्दी

भारतीय प्रौद्योगिकी संस्थान मुंबई

Indian Institute of Technology Bombay

Azadi Ka Amrit Mahotsav

G20 भारत 2023 INDIA वसुधैव कुटुम्बकम् ONE EARTH ONE FAMILY ONE FUTURE

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Web page –> what we see

Computer code –> determines what we see

Inspector | Console | Debugger | Style Editor | Performance | Memory | Network | Storage | Accessibility | Application | Adblock Plus

Search HTML

```
<script src="/sites/all/libraries/tablesc
<div class=" container region1wrap">…</div>
<!--End Region 1 Wrap-->
<!--Region 2 Wrap-->
<div class="container region2wrap">…</div>
<!--End Region 2 Wrap-->
<!--Region 4 Wrap-->
<div class="container region4wrap">…</div>
<!--End Bottom Content-->
<!--End Region 4 Wrap-->
<!--Region 9 Wrap drupal_is_front_page()-->
<div class="container region9wrap">…</div> overflow
<!--End Region 9 Wrap-->
<!--Region 10 Wrap-->
<div class="container region10wrap">…</div>
```

```
.region4wrap { common-style.css:458
  background: none repeat scroll 0 0 #FFF;
}
.container { common-style.css:415
}
body, div, dl, dt, dd, ul, ol, common-style.css:43
li, pre, form, fieldset, p,
blockquote, th, td {
  color: #333;
  font-size: 16px;
}
body, div, dl, dt, dd, ul, foundation.min.css:96
ol, li, h1, h2, h3, h4, h5,
h6, pre, form, p, blockquote, th, td {
  margin: 0;
```

Computed | Changes | Compatibility

Select a Flex container or item to continue.

Grid

CSS Grid is not in use on this page

Box Model

margin 0 | border 0 | padding 0 | 1296×1815.9

html..js.js.no-touch.svg.inlinesvg.svgcl... > body.html.front.not-logged-in.one-sideba... > div.container.region4wrap

Filter Output | Errors | Warnings | Logs | Info | Debug | CSS | XHR | Requests

⚠ Cookie "_ga" has been rejected for invalid domain. analytics.js:25:486

Phenotype and genotype

B

Characteristics that we (can) see

"Phenotype"

DNA of the individual

"Genotype"

Images taken from https://lrodgers93.wordpress.com/

Figure 16.1
Biology. A global approach

Wildtype and mutant

B

Affected individuals

"Mutant"

Can be wild type for some other characteristic

A

Most common appearance

"Wild type"

Can be a mutant for some other characteristic

Images taken from https://lrodgers93.wordpress.com/

https://www.wrvo.org/post/obesity-linked-osteoarthritis-hands

Mutations are changes in genotype

How does a change in genotype result in a change in phenotype?

Today's topics

- DNA, RNA, and proteins
- DNA to protein – Central Dogma
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- Stem cells

Growth media

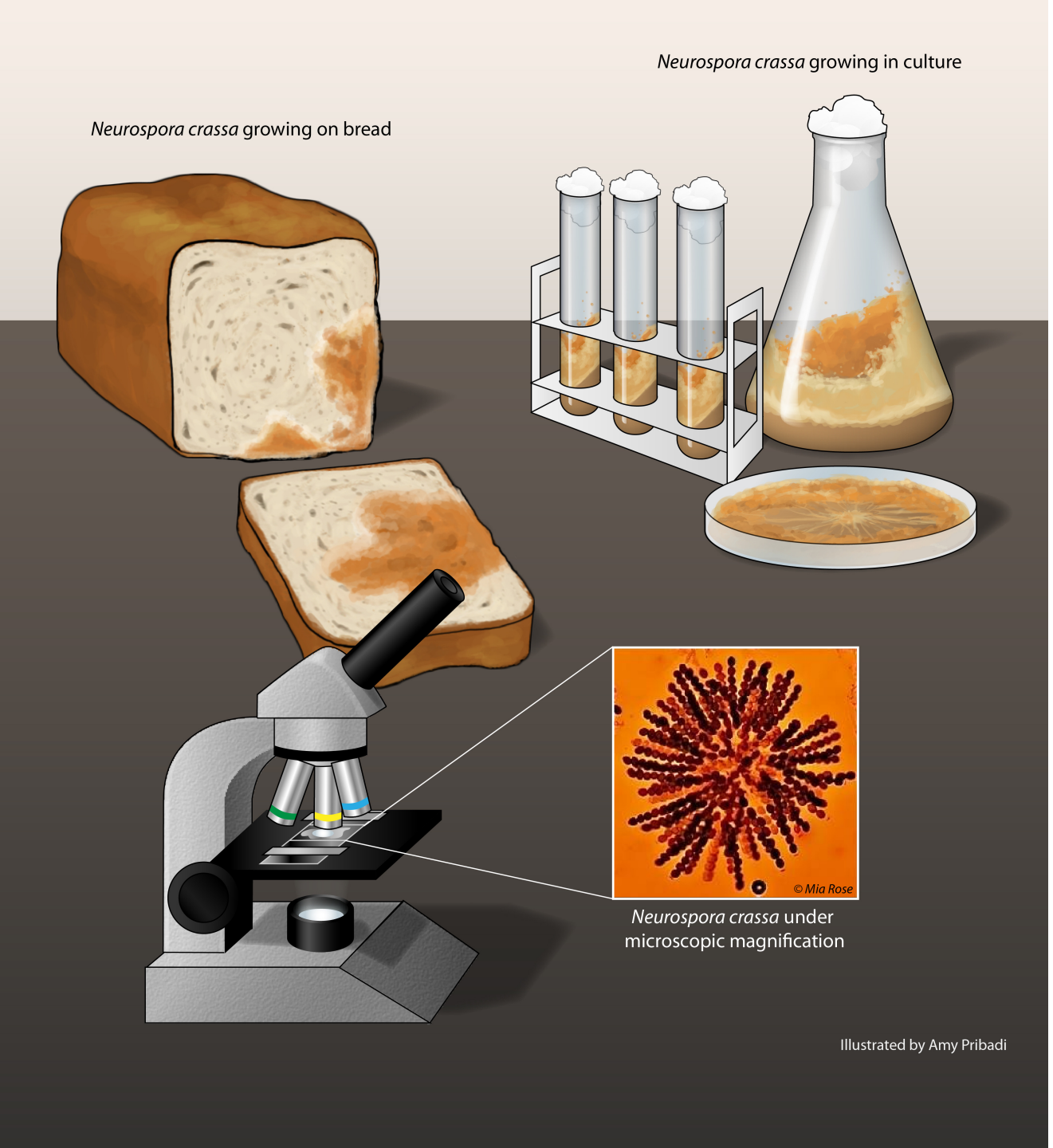
Minimal medium consists of
- inorganic salts,
- glucose and
- biotin (a vitamin)

in agar, a support medium

Complete medium consists of
- minimal media,
- all 20 amino acids and
- a few other nutrients

in agar, a support medium

Neurospora crassa



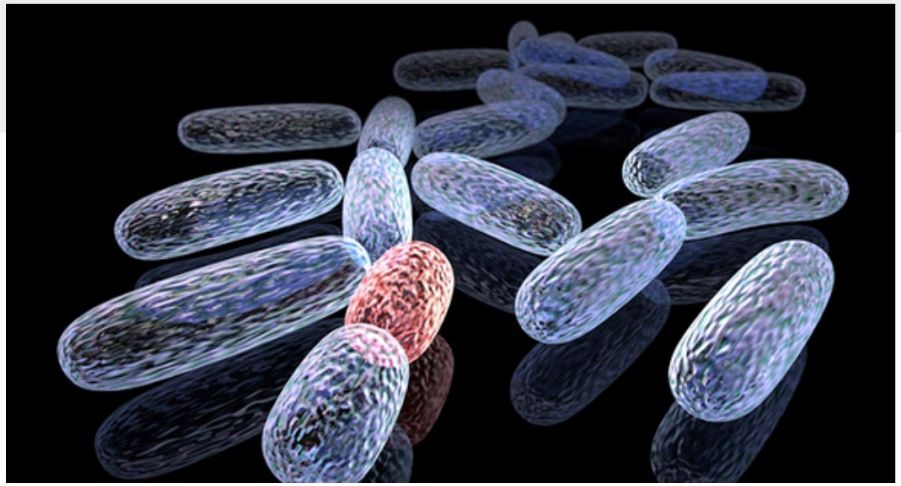
Commonly known as bread mould, a type of fungus

A model organism... relatively easier to reverse engineer

https://embryo.asu.edu/pages/neurospora-crassa

https://internationalsugarjournal.com/tag/neurospora-crassa/

NEUROSPORA CRASSA INTERNATIONAL SUGAR JOURNAL



BIOFUELS NEWS 10 MAR 2015

Cellulosic biofuels production enhanced by yeast bioengineered with Neurospora crassa metabolic pathway [Registered]

"We've discovered new chemicals generated by fungi and bacteria as metabolites in their strategy for consuming the plant cell wall that are a general part of the global carbon cycle," says the lead researcher Jamie Cate, a staff scientist in Berkeley Lab's Physical Biosciences Division. "We should now be able to engineer biofuel-producing yeast to do what these fungi and bacteria do, opening up many new possible scenarios for making biofuels and other important products."

https://internationalsugarjournal.com/tag/neurospora-crassa/

https://mopng.gov.in/en/refining/bio-diesal

REFINERY DIVISION
Oil Refinery
Bio Fuel
About Bio Fuel

Bio Diesel

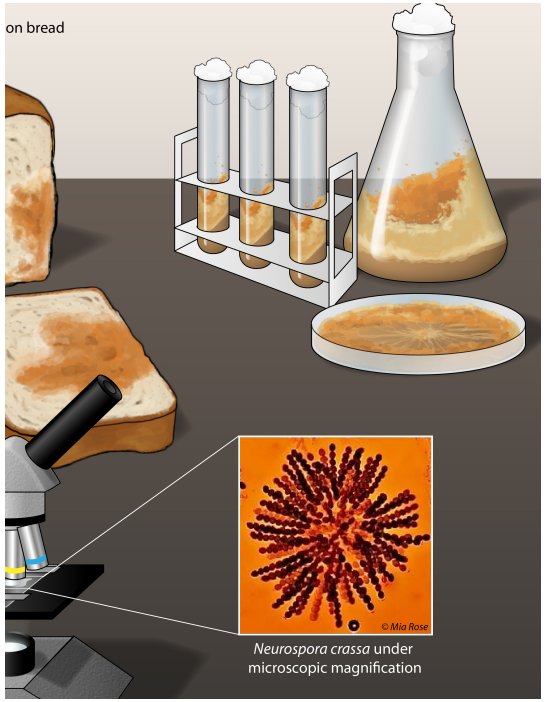
MoP&NG announced a Biodiesel Purchase Policy which became effective 1st January 2006. On 10.08.2015, Government allowed direct sale of Biodiesel (B100) for blending with diesel to Bulk Consumers such as Railways, State Road Transport Corporations. On 29.06.2017 Government allowed sale of biodiesel to all consumers for blending with diesel.

Government has notified Guidelines for sale of biodiesel for blending with High Speed Diesel for transportation purposes on 30.4.2019. Through this Notification Government has granted permission exclusively for sale of biodiesel (B-100) only and not for any mixture thereof of whatever percentage.

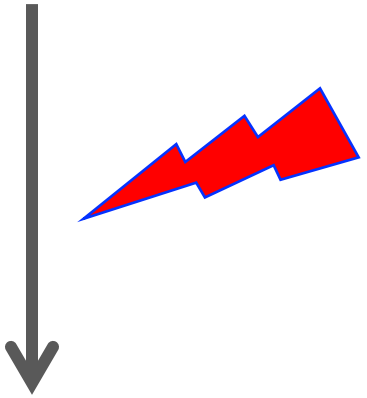
Neurospora can grow on minimal media

- Wild type Neurospora is what one can find growing in nature
  - *What is "wild type"?*
  - *Definition: native organism, before we start to alter its DNA*
- It can grow even in minimal medium
  - It can biosynthesize all other molecules (= components) required for growth and reproduction

Exposure to X-rays may cause mutation



Wild type



Expose to x-rays

Mutant

https://embryo.asu.edu/pages/neurospora-crassa

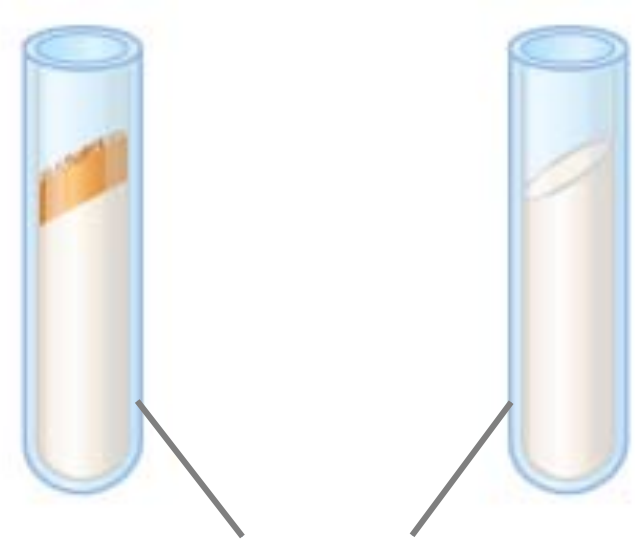
Growth of mutants in minimal / complete media

Growth in minimal medium	Growth in complete medium	What to do with the mutant?
Grows	Grows	Discard
Grows	Does not grow	Unlikely to find such mutants If found, identify inhibitory factors
Does not grow	**Grows**	**This is what we are interested**
Does not grow	Does not grow	Nothing to do

One cannot retain or discard what one does not have!

Wild type as a positive control

Growth:
Wild-type cells
growing and dividing



No growth:
Mutant cells cannot grow
/ reproduce (divide)

Control: Minimal
medium

INFERENCE
Mutant is not able to synthesize
one or more essential components

Figure 17.2b in Campbell Biology by Reece et al., (10th edition)

Screening for a "desired" mutant

Medium	Supplement	Phenotype
Complete	None	Grows
Minimal	None	No growth
Minimal	Component #1	No growth
Minimal	**Component #2 (say, arginine)**	**Grows**
Minimal	Component #3	No growth
Minimal	....	No growth
Minimal	....	No growth
Minimal	Component #N	No growth

Positive control

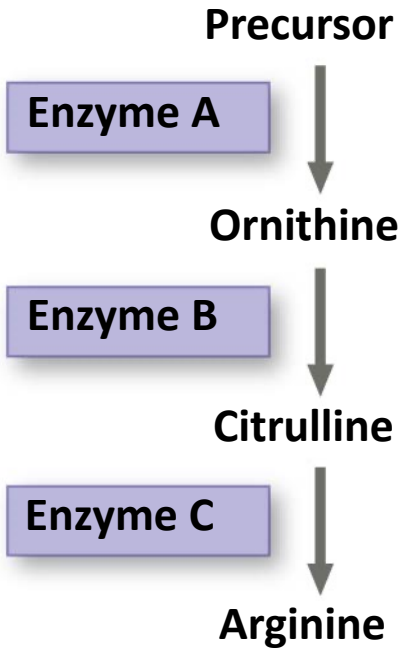
Negative control

Mutant is NOT able to biosynthesize component #2 (e.g., arginine)

A (part of a) metabolic pathway

Experiments of Adrian Srb and Norman Horowitz

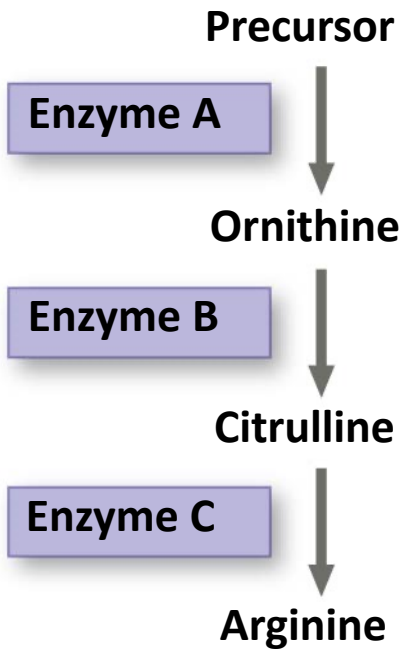
Pathway for arginine biosynthesis described in the mammalian liver



Arginine is one of the 20 amino acids that make up proteins in ALL organisms

Figure 17.2 in Campbell Biology by Reece et al., (10th edition)

Experimental set up



Results Table	Classes of *Neurospora crassa*			
Condition	Wild type	Class I mutants	Class II mutants	Class III mutants
Minimal medium (MM) (control)				
MM + ornithine				
MM + citrulline				
MM + arginine (control)				
Summary of results	Can grow with or without any supplements	Can grow on ornithine, citrulline, or arginine	Can grow only on citrulline or arginine	Require arginine to grow

Figure 17.2 in Campbell Biology by Reece et al., (10th edition)

Experimental set up

Precursor
Enzyme A
Ornithine
Enzyme B
Citrulline
Enzyme C
Arginine

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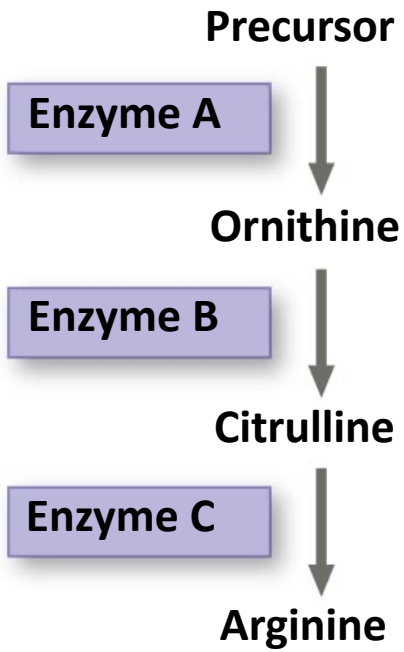
Gene (codes for enzyme)	Wild type
Gene *A*	Precursor → Enzyme A → Ornithine
Gene *B*	Ornithine → Enzyme B → Citrulline
Gene *C*	Citrulline → Enzyme C → Arginine

Figure 17.2 in Campbell Biology by Reece et al., (10th edition)

Experimental set up



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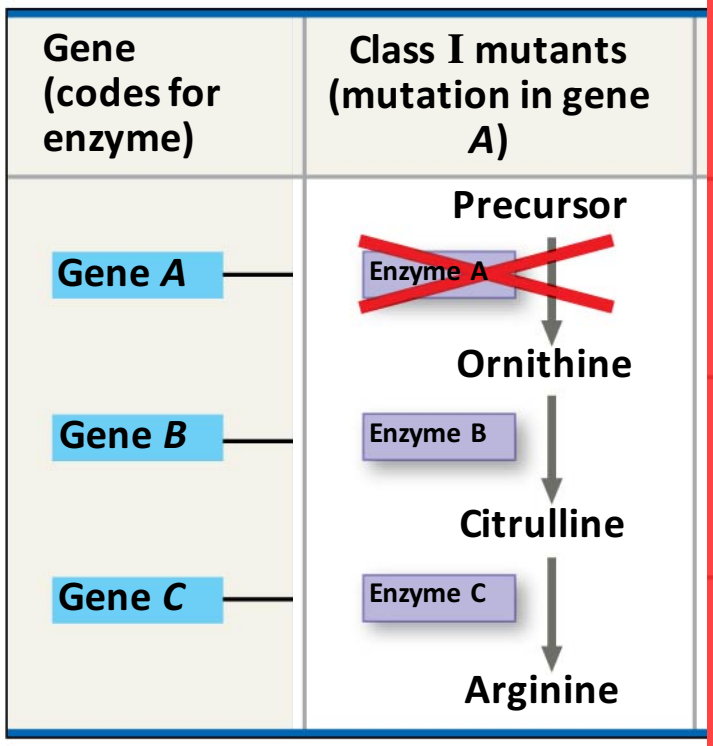

Figure 17.2 in Campbell Biology by Reece et al., (10th edition)

Experimental set up

Precursor
Enzyme A
Ornithine
Enzyme B
Citrulline
Enzyme C
Arginine

Results Table — Classes of *Neurospora crassa*

Condition	Wild type	Class I mutants	Class II mutants	Class III mutants
Minimal medium (MM) (control)	Gene (codes for enzyme): Gene *A*, Gene *B*, Gene *C*	Class II mutants (mutation in gene *B*): Precursor → Enzyme A → Ornithine → Enzyme B (crossed out) → Citrulline → Enzyme C → Arginine		
MM + ornithine				
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Figure 17.2 in Campbell Biology by Reece et al., (10th edition)

Experimental set up

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Enzyme B
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Gene (codes for enzyme)	Class III mutants (mutation in gene *C*)
Gene *A*	Precursor → Enzyme A → Ornithine
Gene *B*	Enzyme B → Citrulline
Gene *C*	Enzyme C (crossed out) → Arginine

Figure 17.2 in Campbell Biology by Reece et al., (10th edition)

Interpretation of data

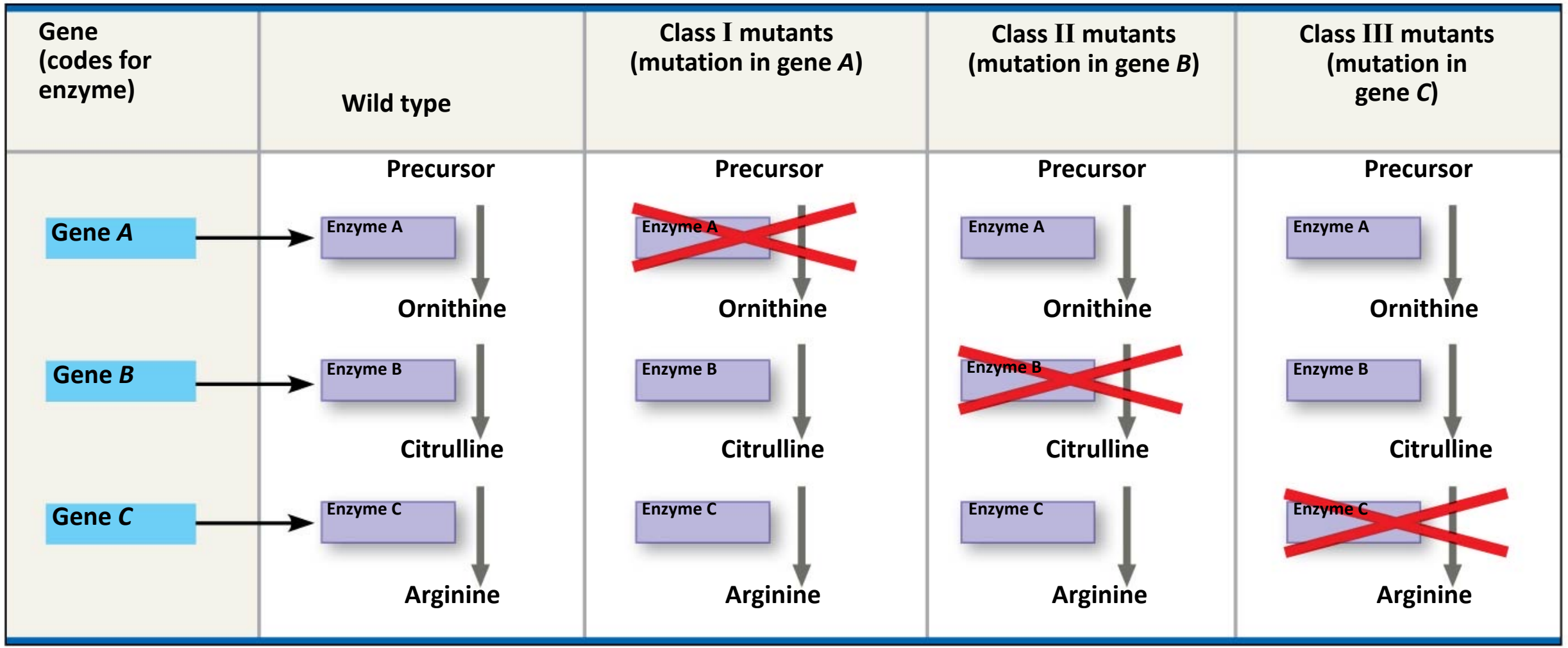


Figure 17.2 in Campbell Biology by Reece et al., (10th edition)

Inference from the experiments

Mutation can cause a change in the phenotype

How?

Change in codon leads to a change in the amino acid sequence

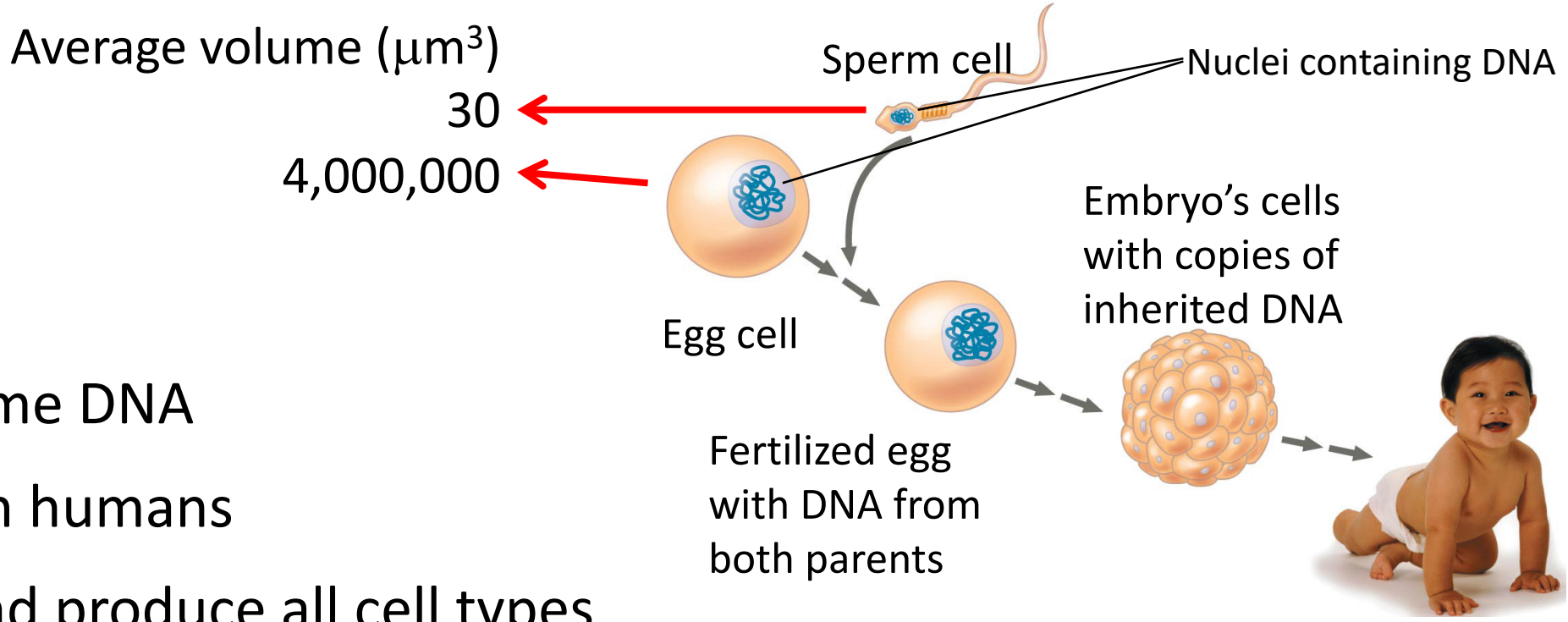
Today's topics

- DNA, RNA, and proteins
- DNA to protein – Central Dogma
- The genetic code and mutations
- Inherited DNA leads to specific traits
- Elucidating arginine biosynthesis pathway
- Stem cells

Differentiation

General English	The process of becoming different from others of same type Examples: quality of service, display boards, food (look, feel, taste), web sites, personal qualities and so on…
Mathematics	The process of finding the derivative or the rate of change
Biology (in case of multi-cellular organisms)	The process by which a cell acquires specialized function or feature Starting point: “zygote” – this is what is formed by the fusion of an egg and a sperm

Development by differentiation



All cells have the same DNA

200-220 cell types in humans

Zygote can divide and produce all cell types

As development advances, cells undergo differentiation and become more restricted cell types

Figure 1.10 in Campbell Biology by Reece et al., (10th edition)

Differentiation of cells in embryos

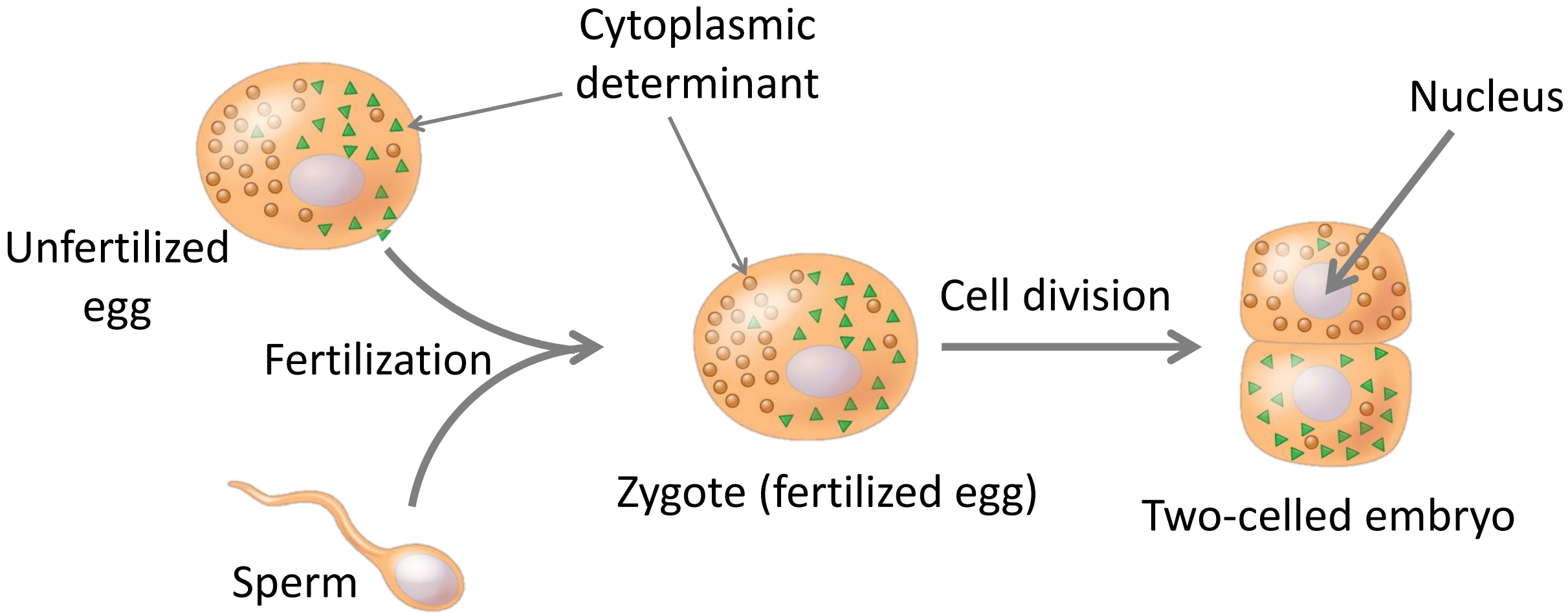


Figure 18.17a in Campbell Biology by Reece et al., (10th edition)

Stem cells

In normal individuals, stem cells are required for repair and regeneration