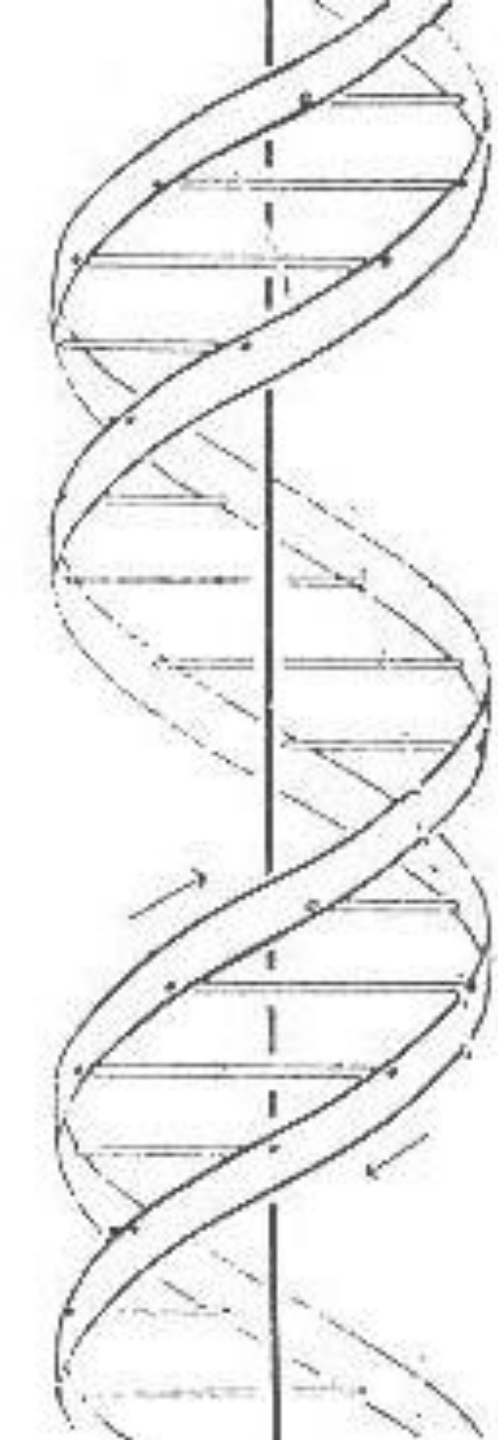


MBB 331
Molecular Biology
Summer 2026

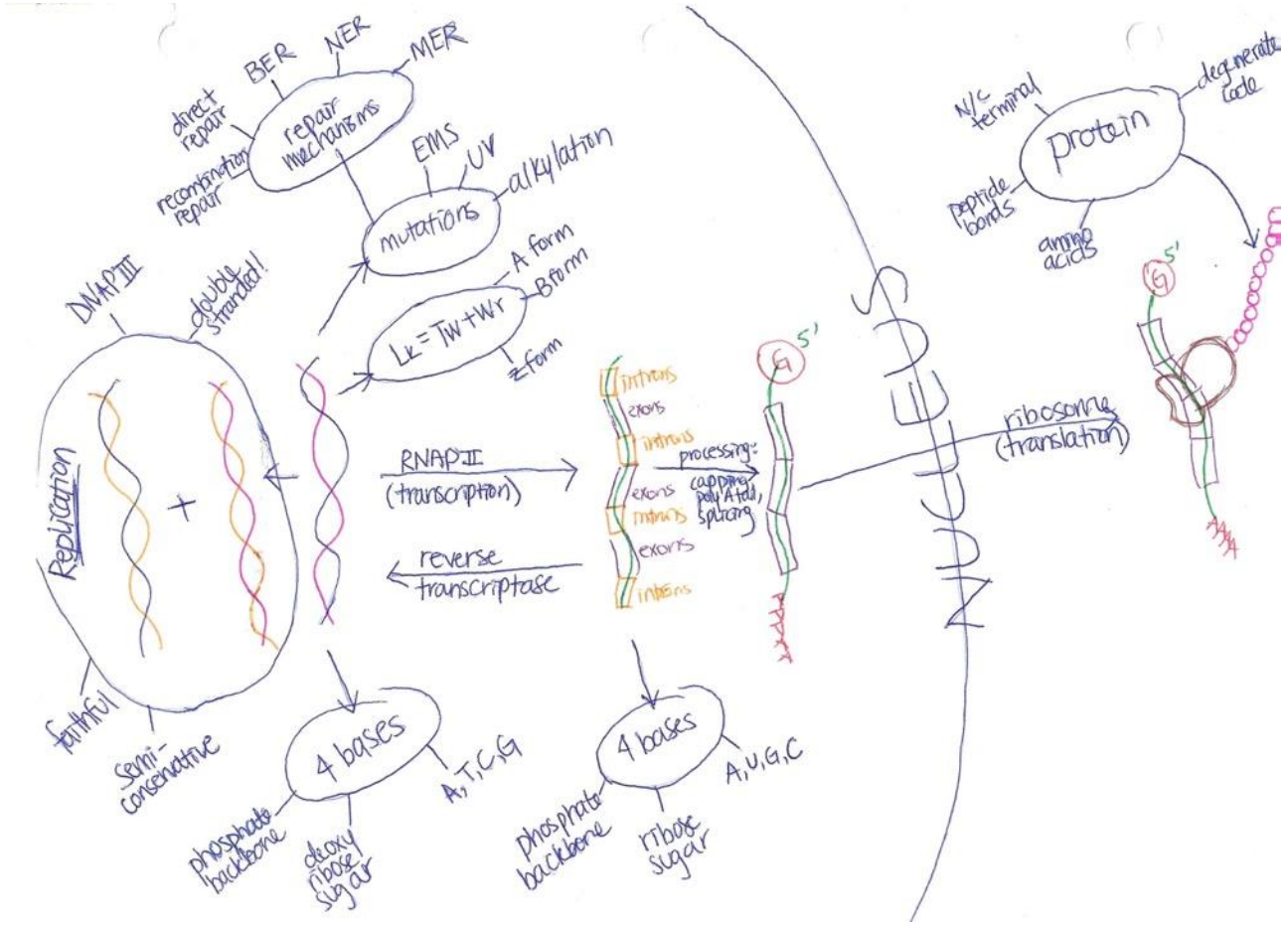
Tue & Thu 10:30 am – 12:20 pm, WMC 3520

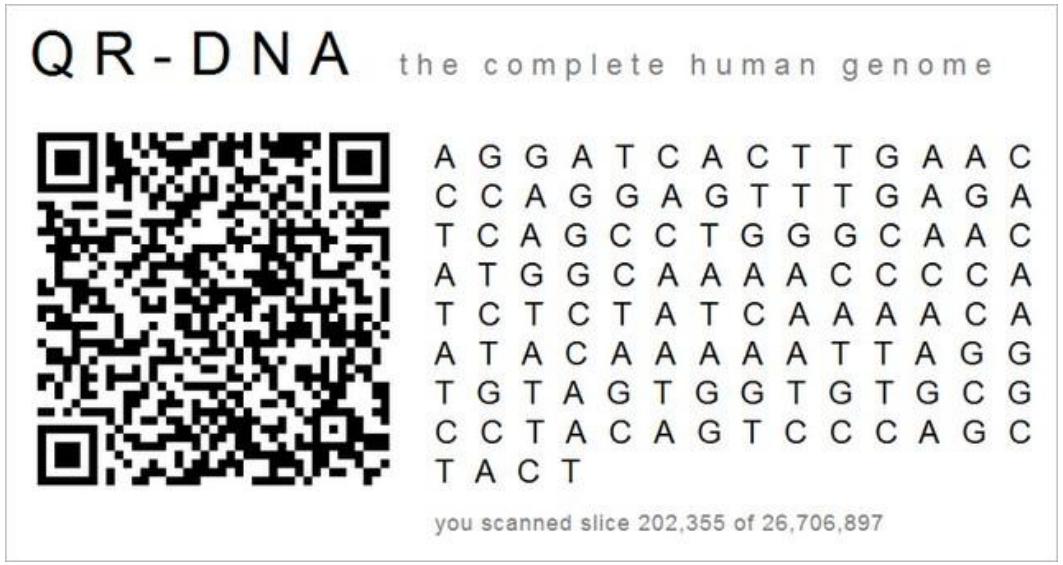
1 hour of tutorial per week (as scheduled)

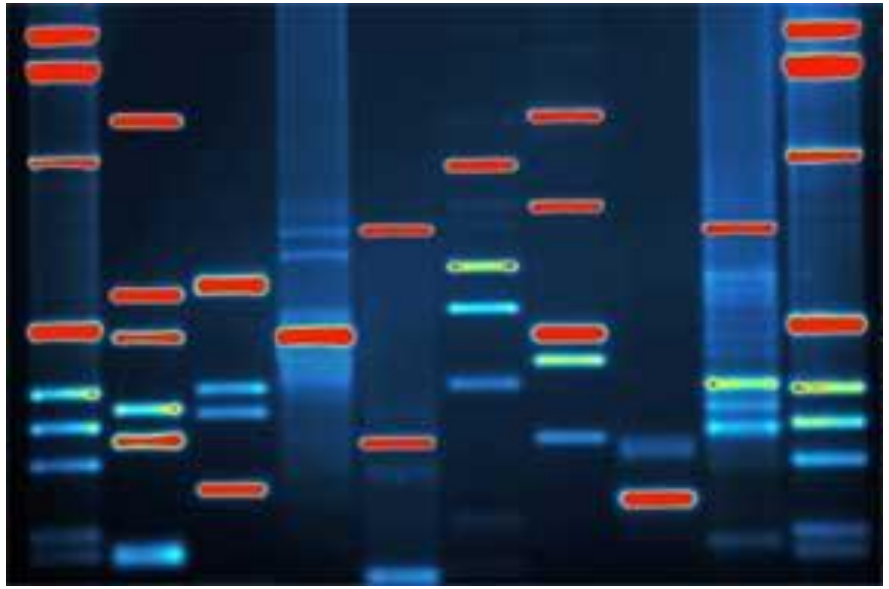
Instructor: Dr. Sophie Sneddon
Email: sophie_sneddon@sfu.ca

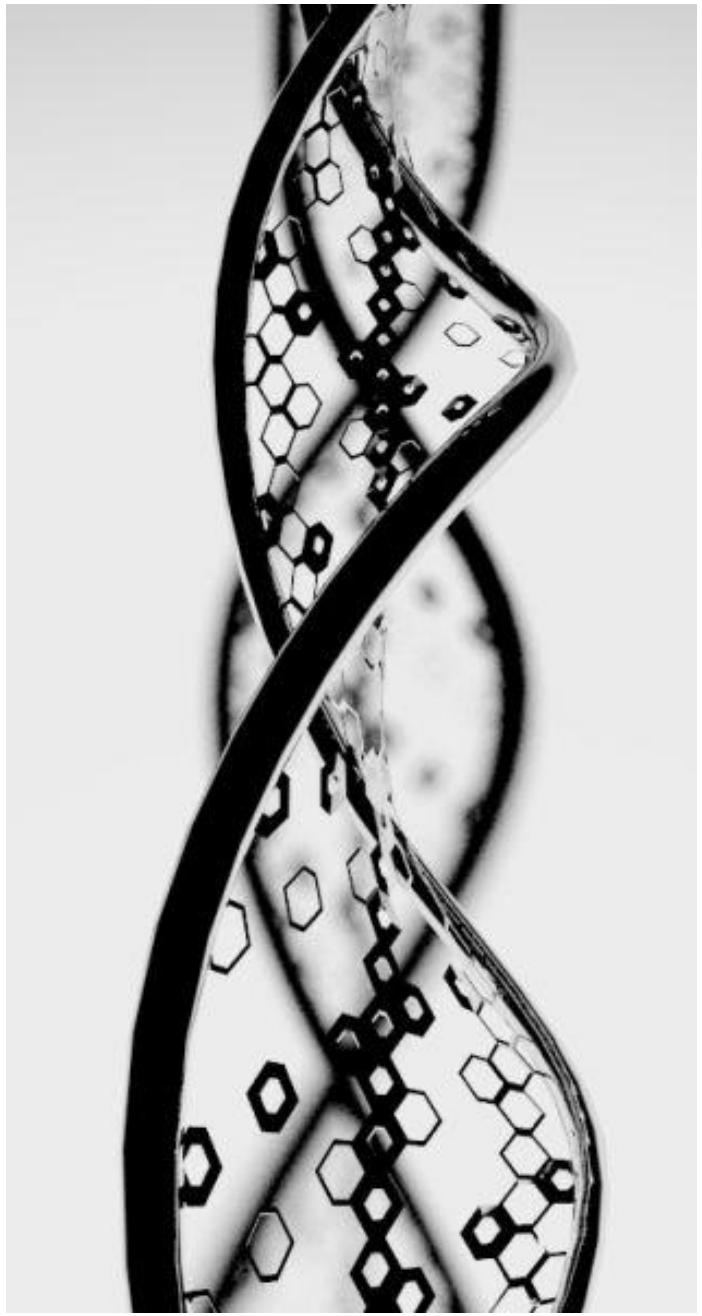
Teaching Assistant: Carmita Lemus Valdes
Email: carmita_lemus_valdes@sfu.ca

What is this course about?









This course has a CANVAS site

Log into http://canvas.sfu.ca using your SFU email account ID and password.

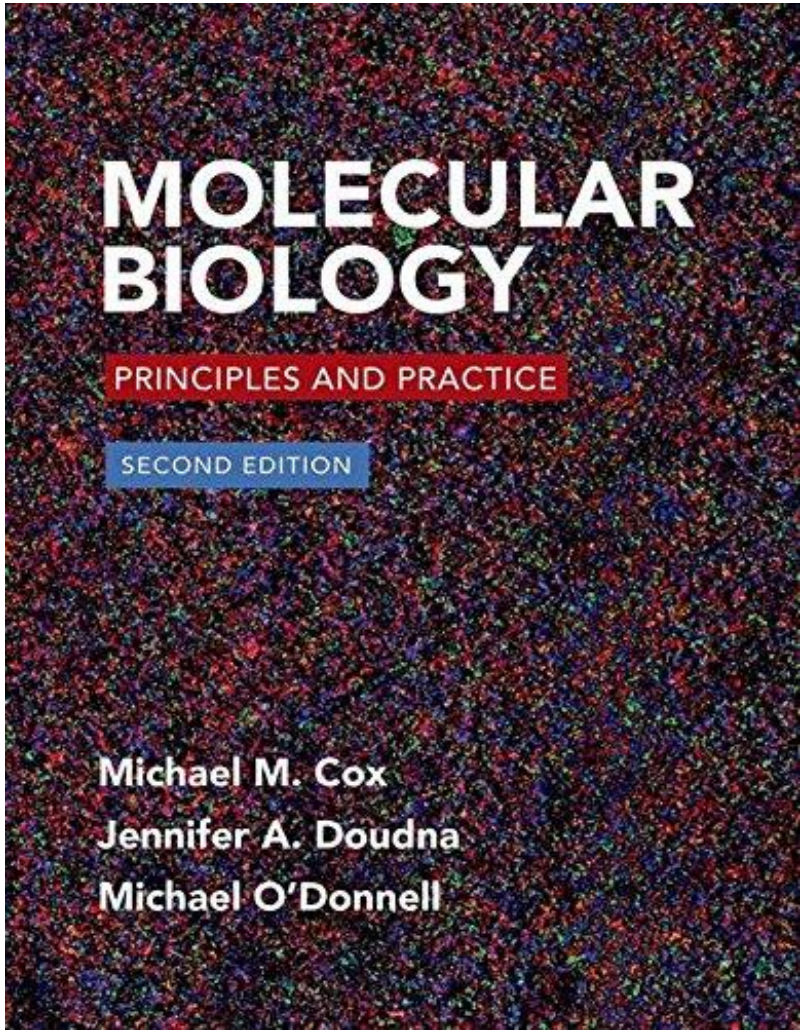
You will find there:

- course policies, syllabus, lecture notes, tutorials info (instructions for presentations, evaluation sheet, problem sets and answers), required readings, practice exams, discussion threads, online quizzes, important announcements, research papers discussed in lectures, your grades, etc.

Required **textbook:**

Molecular Biology: Principles and Practice, 2nd edition, by Michael M. Cox, Jennifer A. Doudna, Michael O'Donnell, W.H. Freeman & Company, 2015. eText also available. ISBN: 9781464126147

MBB331 is a content-heavy course and your instructor expects you to complete all assigned readings. Your exams and quizzes may feature material in your textbook we do not cover in class



LECTURES

- All lectures will be recorded and posted on Canvas (technology issues notwithstanding)
- In lectures your instructor will introduce new material and relate it to the previously covered material and go over select problems and questions
- This is your time to ask questions and clarify details

TUTORIALS

- Go over problem set questions
- Go over midterm exams and online quizzes (as necessary)
- Work on critical analysis project

- D101 Tuesday 2.30-3.20 BLU10655
- D102 Thursday 9.30-10.20 BLU10655
- D103 Thursday 12.30-1.20 BLU10655
- D104 Friday 11.30-12.20 RBC6125




TUTORIALS

- Tutorials are MANDATORY and attendance will be taken
- Your tutorial attendance accounts for 5% of your final grade
- You have 3 unexcused absences no questions asked
- The fourth absence onwards will result in a loss of 1% from your tutorial attendance grade until it reaches 0

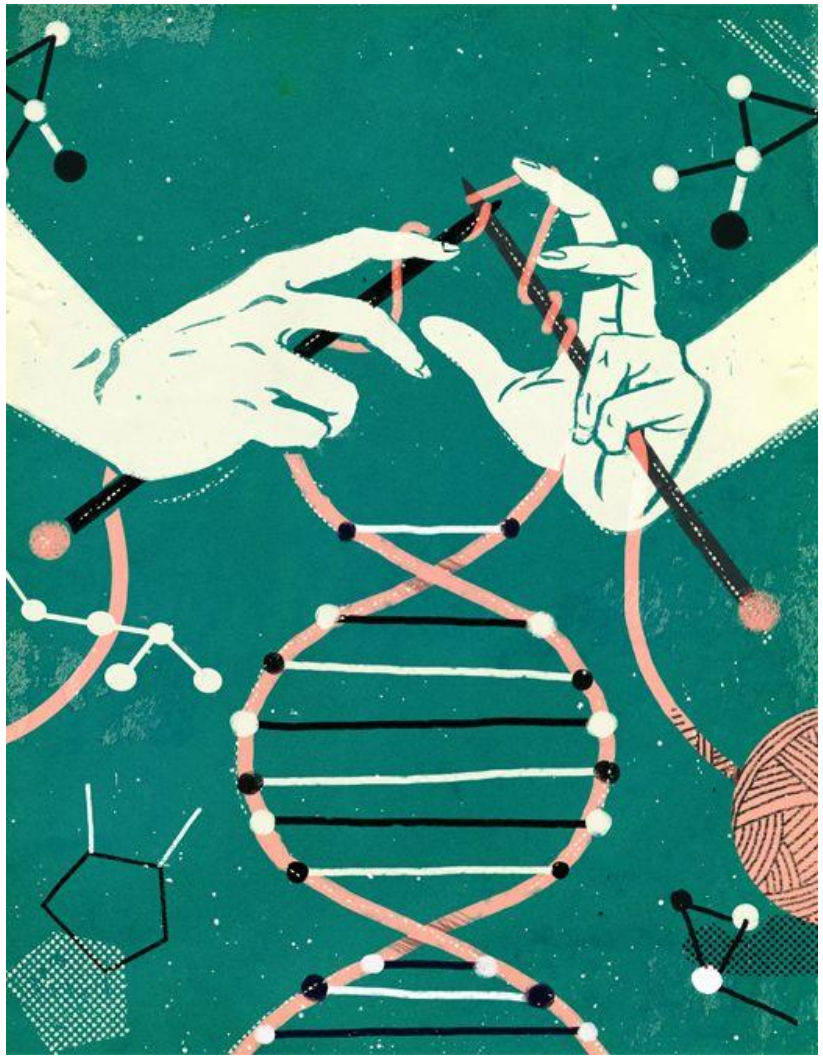



On CANVAS

- Find lecture notes and links to lecture recordings, tutorials and office hours
- Find and complete online quizzes
- Find, complete and submit tutorial problem sets
- Find and go over practice exams
- Read announcements
- Check your grades
- Etc…

https://www.the-scientist.com/cover-story/making-dna-data-storage-a-reality-30218

Critical analysis of literature assignment



- Will take place in the second half of the semester
- Select a research paper **from the list provided**
- Find an alternative/conflicting argument yourself by searching literature databases (i.e. PubMed, SFU Library Website, etc)
- You will be given instructions on how to write up your analysis later in the semester

Image: https://www.pinterest.com/pin/272327727240188823/

Problem sets

- Problem sets are designed to expose you to the types of questions you will see on exams.
- Each problem set is due before your scheduled tutorial the next week.
- Submit online.
- Grading is for completion not correctness. Full marks are assigned answering all questions in good faith. If at least one question is skipped, half marks awarded. Zero marks for not attempted.

Online quizzes on Canvas

- Generous time limit imposed, no locking answers, no showing one question at a time
- The idea behind these quizzes is to HELP you review the course material (there will be a lot of it!): it is important to keep up with the material if you want to do well!
- Due dates: Should be completed each week as we work through the material, BUT the hard deadline for each set of quizzes is before the following midterm
- You have 3 attempts at each quiz and the highest grade will be recorded

GRADING

- Midterm exam 1 (Jun 4) 10%
- Midterm exam 2 (Jun 30) 15%
- Midterm exam 3 (Jul 23) 15%
- Online weekly quizzes 10%
- Tutorial problem sets 5%
- Critical analysis 15%
- Tutorial attendance 5%
- FINAL EXAM (cumulative) 25%

100%

Image: *Selected, collected, health-inspected: Cartoons by Roz Chast*, 1978-2006. Bloomsbury, USA (2006).

Course policies in brief
(read the complete document posted on CANVAS)

- Students are expected to attend all lectures and tutorials and complete all course requirements to receive credit in this course
- Students must have a valid, verifiable excuse to miss an exam or a tutorial
- If you anticipate a conflict with any of the scheduled exams, email or see me ASAP (contact your TA for any conflicts related to tutorials)

Email and communication with your professor and TA:

We would like to remind everyone of their position as undergraduate students and the Student Conduct Policy at SFU
http://www.sfu.ca/policies/gazette/student/s10-05.html

Email policy

- Send me messages only from your SFU account
- Write “MBB331” in the subject line
- Write in full sentences (no texting language)
- I will reply within 48 hours if the above conditions are met
- For detailed responses ask questions in class or come to my office hours

- Your TA will inform you of her office hours in your first tutorial (next week)

A note on the use of LLMs in this course

LLMs have become commonplace within the academic setting, but the onus is on the student to not use LLMs to create work for submission for this course. There are several ways in which you can responsibly use LLMs to augment your existing study habits:

- Creating study guides from course content
- Brainstorming ideas
- Testing you on course material

Understand that LLMs are largely fancy predictive text machines and don't have any actual knowledge on the material they produce. I have worked extensively in understanding the capabilities of LLMs, and note the high rate of error in their answers, as well as completely made up "facts."

If a student submits work that indicates possible LLM usage, they will be subject to an oral examination on the submitted work in order to receive a grade. Failure to pass the oral examination will lead to a zero for that assignment on the first offence and any subsequent event will lead to the filing of an academic dishonesty report and potentially failure of the course.

NOTE

- **In tutorials:** **NO TUTORIALS** this week (week 1). Tutorials begin next week (week 2). Optional: solve problems at the end of Chapter 2 in your textbook. Submit your completed problem sets **BEFORE** your tutorial.

- **Online quiz 1:** No quiz this week.

Every lecture will begin with an overview which will look like this

Lecture 1

- 1st 50 min: Introduction to the course, central dogma of molecular biology, Mendel's peas, Beadle and Tatum experiment
- 10 min break
- 2nd 50 min: Discovery of DNA structure, aka the double helix: Griffith/Avery, Chargaff, Hershey/Chase, Franklin/Wilkins/Watson/Crick, DNA nomenclature

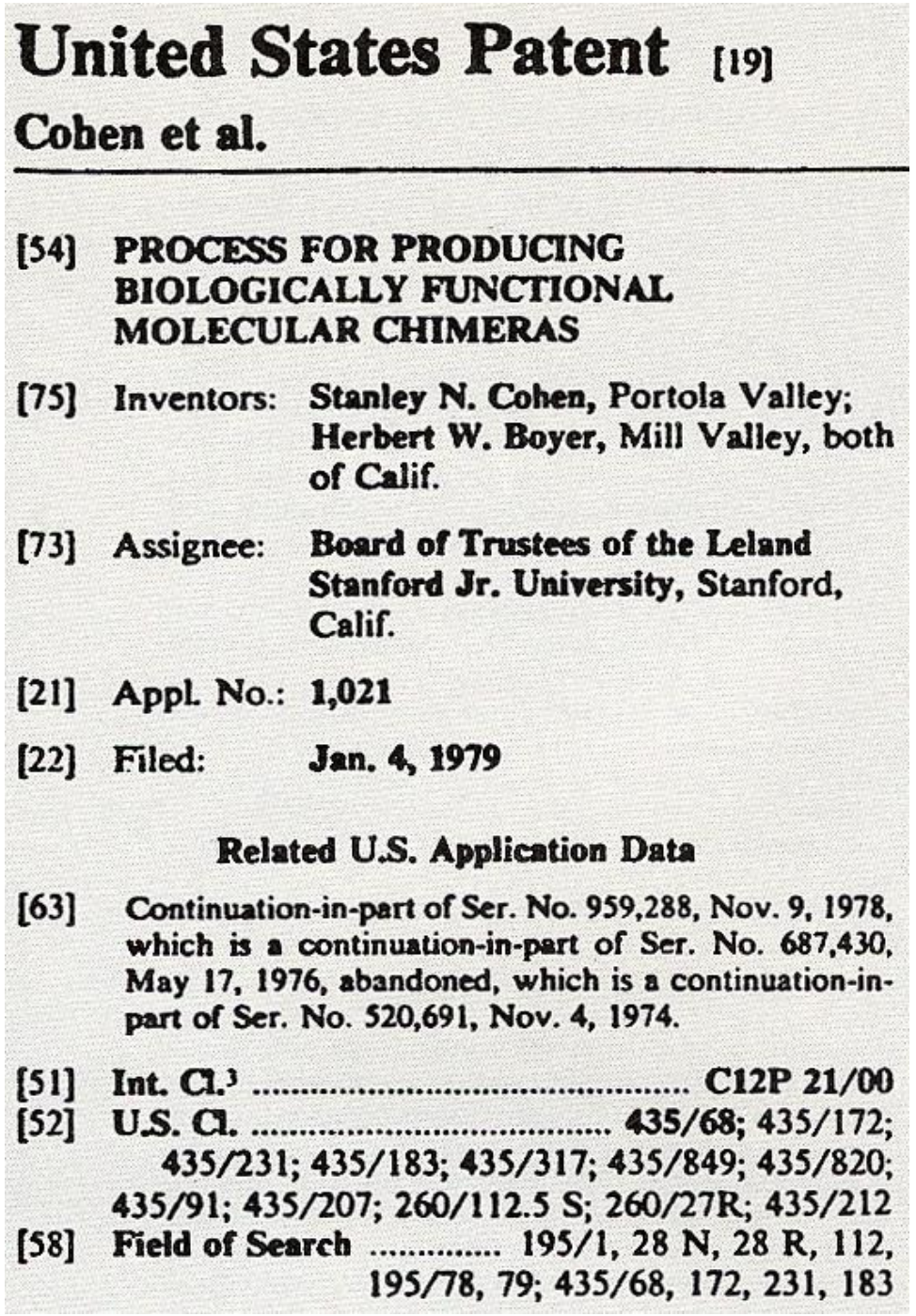
What is molecular biology?

What are some things that come to mind?

What is molecular biology?

"the study of gene structure and function at the molecular level"

- genetics
- biochemistry
- biotechnology



United States Patent [19]

Cohen et al.

[54] PROCESS FOR PRODUCING BIOLOGICALLY FUNCTIONAL MOLECULAR CHIMERAS

[75] Inventors: Stanley N. Cohen, Portola Valley; Herbert W. Boyer, Mill Valley, both of Calif.

[73] Assignee: Board of Trustees of the Leland Stanford Jr. University, Stanford, Calif.

[21] Appl. No.: 1,021

[22] Filed: Jan. 4, 1979

Related U.S. Application Data

[63] Continuation-in-part of Ser. No. 959,288, Nov. 9, 1978, which is a continuation-in-part of Ser. No. 687,430, May 17, 1976, abandoned, which is a continuation-in-part of Ser. No. 520,691, Nov. 4, 1974.

[51] Int. Cl.³ C12P 21/00

[52] U.S. Cl. ..... 435/68; 435/172; 435/231; 435/183; 435/317; 435/849; 435/820; 435/91; 435/207; 260/112.5 S; 260/27R; 435/212

[58] Field of Search ..... 195/1, 28 N, 28 R, 112, 195/78, 79; 435/68, 172, 231, 183

Reminder: pathways of biological information flow

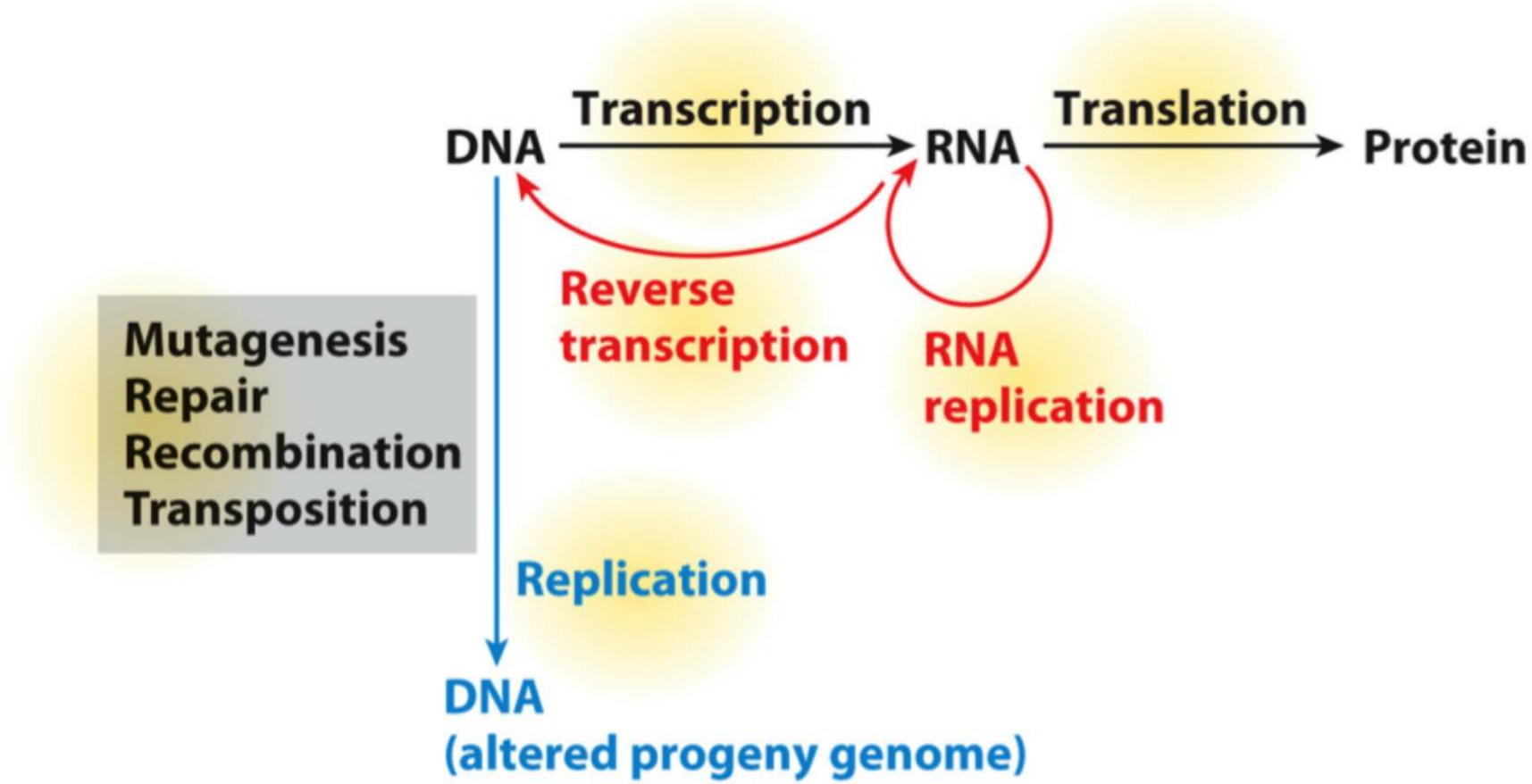


Figure 1-4
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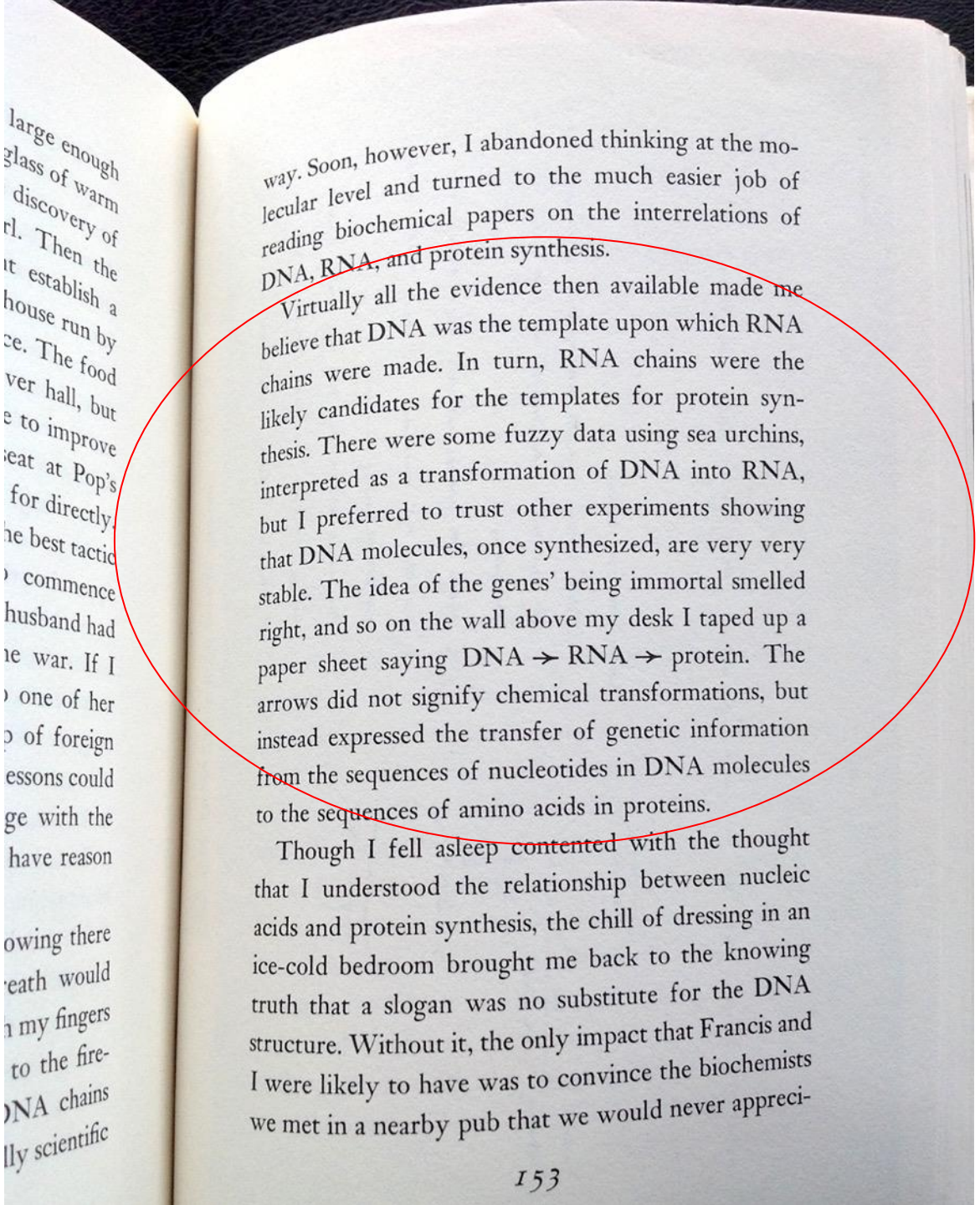


way. Soon, however, I abandoned thinking at the molecular level and turned to the much easier job of reading biochemical papers on the interrelations of DNA, RNA, and protein synthesis.

Virtually all the evidence then available made me believe that DNA was the template upon which RNA chains were made. In turn, RNA chains were the likely candidates for the templates for protein synthesis. There were some fuzzy data using sea urchins, interpreted as a transformation of DNA into RNA, but I preferred to trust other experiments showing that DNA molecules, once synthesized, are very very stable. The idea of the genes' being immortal smelled right, and so on the wall above my desk I taped up a paper sheet saying DNA → RNA → protein. The arrows did not signify chemical transformations, but instead expressed the transfer of genetic information from the sequences of nucleotides in DNA molecules to the sequences of amino acids in proteins.

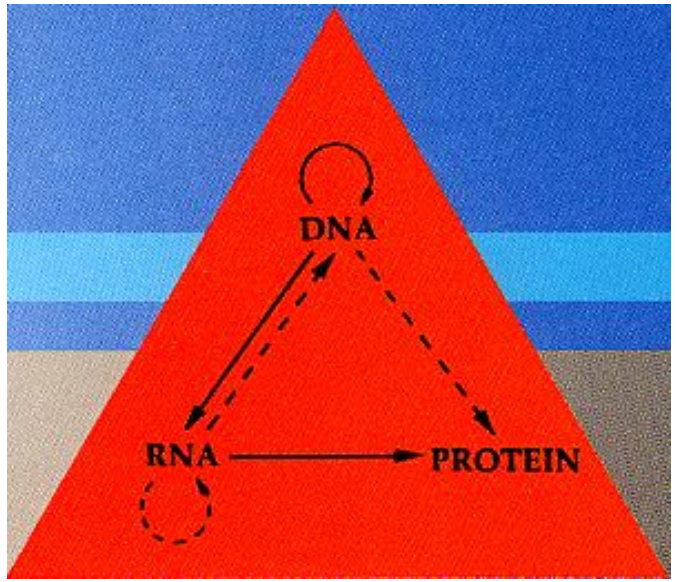
Though I fell asleep contented with the thought that I understood the relationship between nucleic acids and protein synthesis, the chill of dressing in an ice-cold bedroom brought me back to the knowing truth that a slogan was no substitute for the DNA structure. Without it, the only impact that Francis and I were likely to have was to convince the biochemists we met in a nearby pub that we would never appreci-

153

From: James D. Watson,
The Double Helix,
A Personal Account
of the Discovery of the
Structure of DNA.
Scribner: 1968.

DNA to RNA to protein

- REPLICATION
  DNA duplication
- TRANSCRIPTION
  synthesis of RNA
- TRANSLATION
  synthesis of protein



Crick, 1970

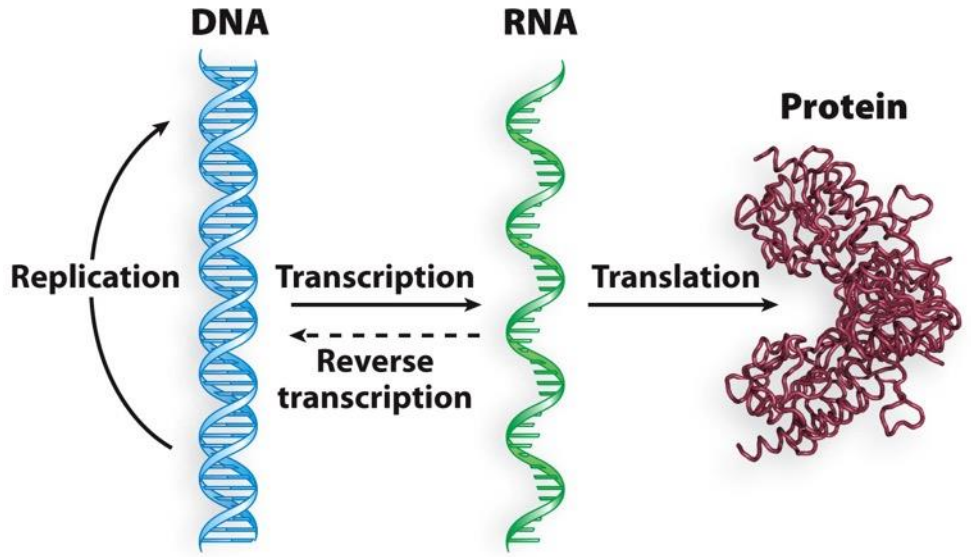


Figure 2-24
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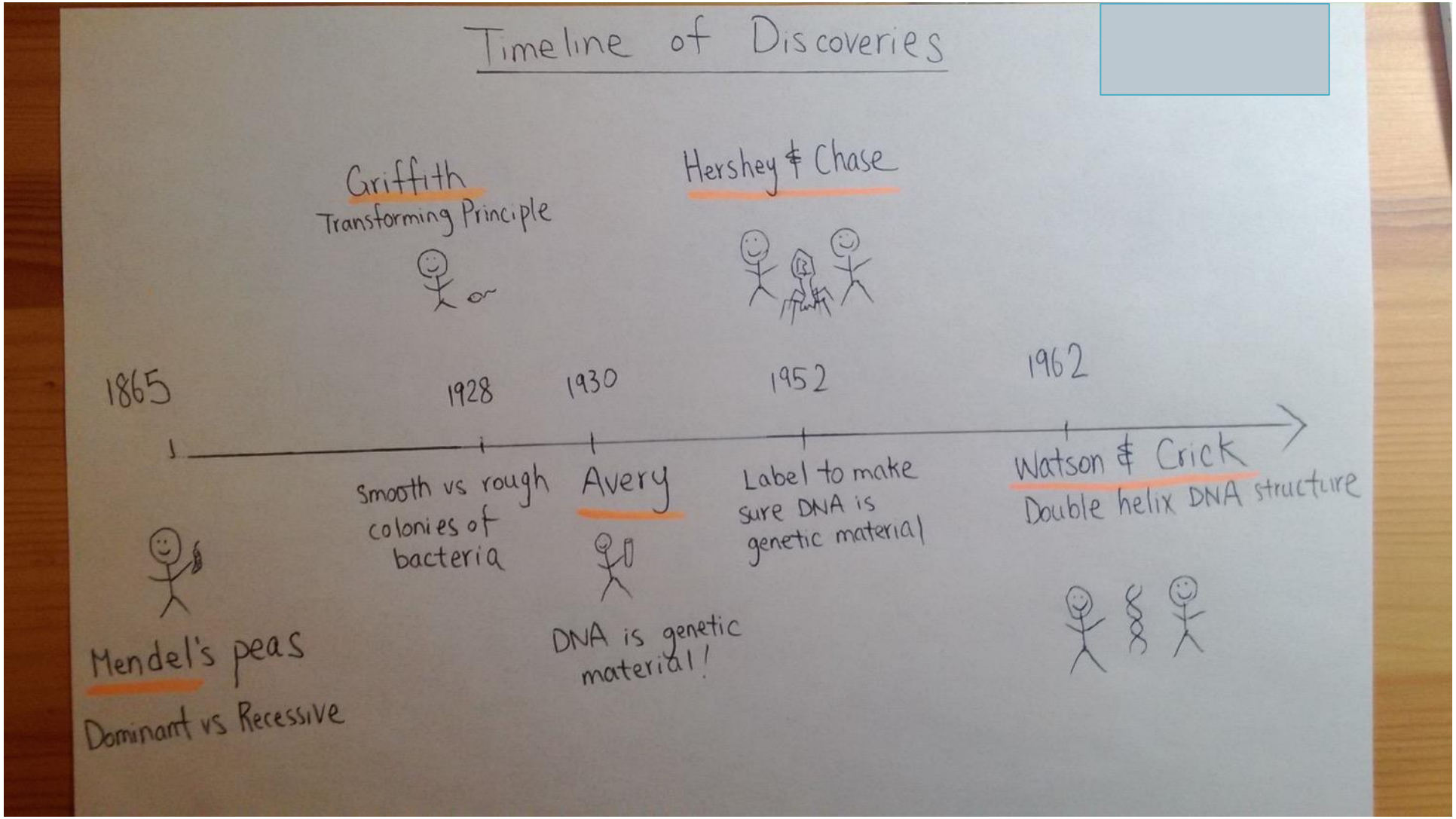
Historical overview of molecular biology



Historical overview of molecular biology

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Molecular Biology: Principles and Practice, Second Edition
Pictorial Press Ltd/Alamy

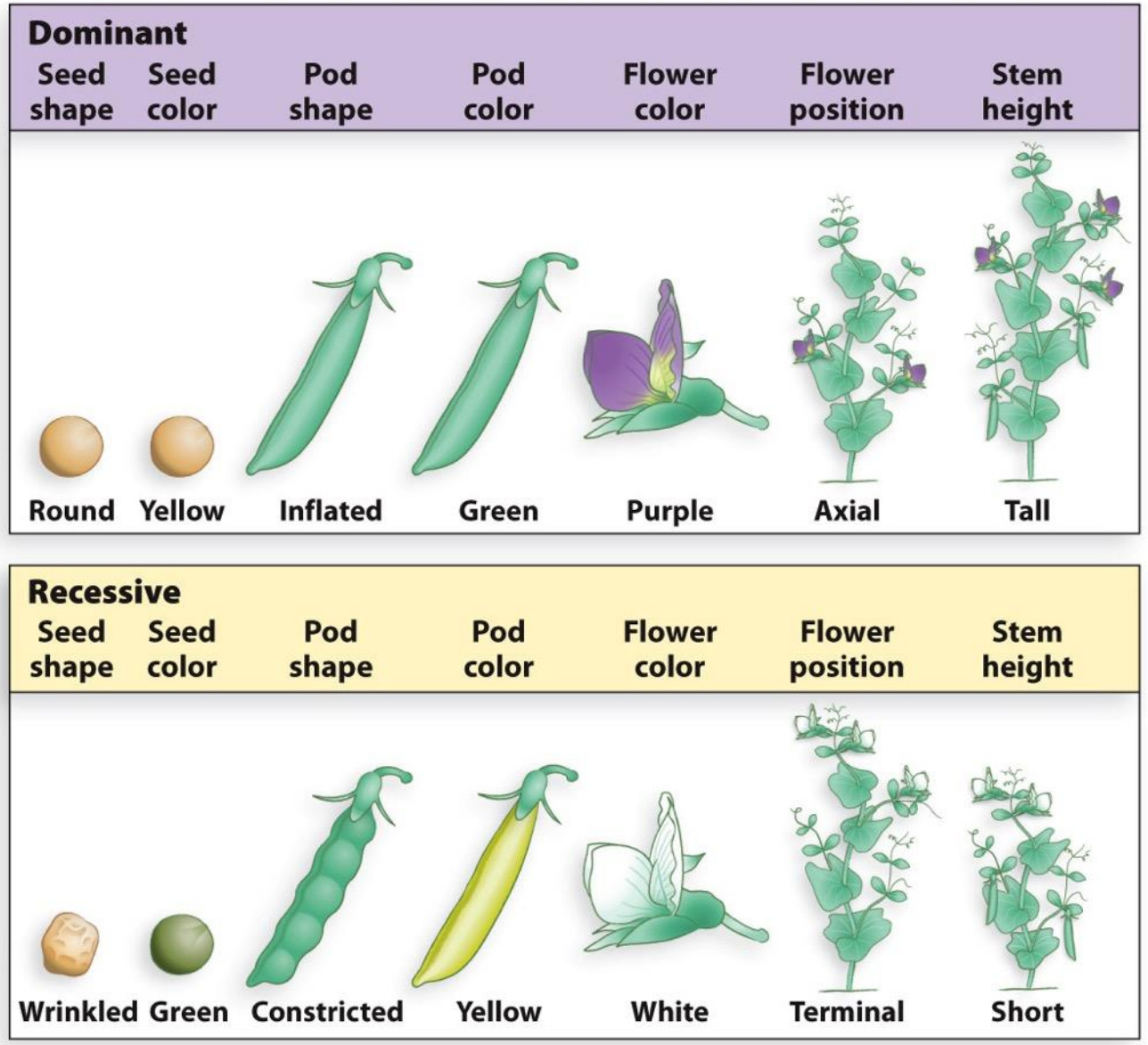

Figure 2-1
Molecular Biology: Principles and Practice, Second Edition

Mendel's peas

In 1865, Mendel published *Experiments on Plant Hybrids* in which he described particulate inheritance in the garden peas

More then a century later the molecular nature of four genes responsible for the traits observed by Mendel were identified

"A major conclusion from Mendel's work was that the factors determining individual traits segregated independently of one another"

Review

Cell Press

Mendel, 150 years on

T.H. Noel Ellis[1], Julie M.I. Hofer[1], Gail M. Timmerman-Vaughan[2], Clarice J. Coyne[3] and Roger P. Hellens[4]

[1] Institute of Biological, Environmental & Rural Sciences, Aberystwyth University, Gogerddan Campus, Aberystwyth, Ceredigion, SY23 3EB, UK
[2] The New Zealand Institute for Plant & Food Research Ltd, Christchurch 8140, New Zealand
[3] USDA-ARS Western Regional Plant Introduction Station, Washington State University, Pullman, Washington, USA
[4] The New Zealand Institute for Plant & Food Research Ltd, Auckland, New Zealand

Mendel's paper 'Versuche über Pflanzen-Hybriden' is the best known in a series of studies published in the late 18th and 19th centuries that built our understanding of the mechanism of inheritance. Mendel investigated the segregation of seven gene characters of pea (*Pisum sativum*), of which four have been identified. Here, we review what is known about the molecular nature of these genes, which encode enzymes (*R* and *Le*), a biochemical regulator (*I*) and a transcription factor (*A*). The mutations are: a transposon insertion (*r*), an amino acid insertion (*i*), a splice variant (*a*) and a missense mutation (*le-1*). The nature of the three remaining uncharacterized characters (green versus yellow pods, inflated versus constricted pods, and axial versus terminal flowers) is discussed.

Mendel's studies: species, traits and genes

Mendel's paper 'Versuche über Pflanzen-Hybriden' [1] is the best known in a series of studies published in the late 18th and 19th centuries [2–4] that built our understanding of the mechanism of inheritance [5]. The title of Mendel's paper is usually mistranslated in English as 'Experiments in Plant Hybridisation' rather than 'Experiments on Plant Hybrids', reflecting the impact of his work on the science of genetics rather than Mendel's own concern with the nature of hybrids and their implications for the 'Umwandlung einer Art in eine andere' - transformation of one species into another. There is also a misconception, as a result of R.A. Fisher's attack on Mendelism [6], that Mendel's results and experimentation were in some way suspect. These defamatory criticisms include imputations on the scope of his experimental work, his understanding of what he wrote and statistical interpretations of his results; although they have been roundly debunked [7,8], they remain embedded in common opinion.

In his paper, Mendel described eight single gene characters of pea, of which he investigated the segregation of seven. The eighth is the 'purple podded' character determined by the gene *Pur* on linkage group I. He also discussed the segregation of three traits (tall versus short, green versus yellow pods and inflated versus constricted pods) in common bean (*Phaseolus vulgaris*) that are likely orthologues of the corresponding characters he studied in pea. For both species Mendel used additional species names (such as *Phaseolus nanus* or *Pisum saccharatum*). These names are no longer used and we would consider these types as variants – Mendel commented that there is no 'sharp line between the hybrids of species and varieties as between species and varieties themselves'.

From a biological perspective Mendel's genes appear to be an unrelated set of genes that are uninformative about a single process; but they did elucidate the process of genetic inheritance itself. They are therefore important from an historical perspective and they illustrate a diversity of gene functions and types of mutation. Uncovering the molecular basis of these mutations solves a longstanding mystery in genetics.

This review focuses on the identification of four of Mendel's genes (*R/r*, round versus wrinkled seed; *I/i*, yellow versus green cotyledons; *A/a*, coloured versus unpigmented seed coats and flowers; and *Le/le*, long versus short internode length). In addition, the possible natures of three other characters studied by Mendel (*Gp/gp*, green versus yellow pods; *P/p* or *V/v*, inflated versus constricted pods; and *Fa/fa* or *Fas/fas*, axial versus terminal flowers) are discussed.

Linkage

A major conclusion from Mendel's work was that the factors determining individual traits segregated independently of one another. We now know that this is not always the case. The associated segregation of parental allelic combinations, known as genetic linkage, is well established. Fortunately Mendel studied segregation at multiple unlinked loci. This meant his results were not confounded by linkage, which would have been much more difficult to interpret. The issue of linkage is sometimes egregiously combined with the criticism of the quality of Mendel's data to imply falsely that he somehow suppressed inconvenient data [7]. Unfortunately these discussions suffered from confusion in the literature regarding chromosome numbers, linkage data and their combination [9]. Our current view of the position of the genetic loci Mendel studied is presented in Figure 1. As discussed below, there is some uncertainty about the identity of the genes for the fasciated (terminal) flowers (*Fa* or *Fas*) or the constricted pod phenotypes (*P* or *V*); therefore, the map locations of all are indicated. From this distribution of genetic loci it is clear that there are two possible cases where linkage could have confounded Mendel's results: these are *R–Gp* and *Le–V*.

The wrinkled seed character that Mendel studied was *R* versus *r* on linkage group V [10]. The character 'green versus

Corresponding author: Hellens, R.P. (roger.hellens@plantandfood.co.nz).

1360-1385/$ – see front matter © 2011 Elsevier Ltd. All rights reserved. doi:10.1016/j.tplants.2011.05.008 Trends in Plant Science, November 2011, Vol. 16, No. 11

The molecular nature of these genes was learned MANY YEARS later

Review

Trends in Plant Science November 2011, Vol. 16, No. 11

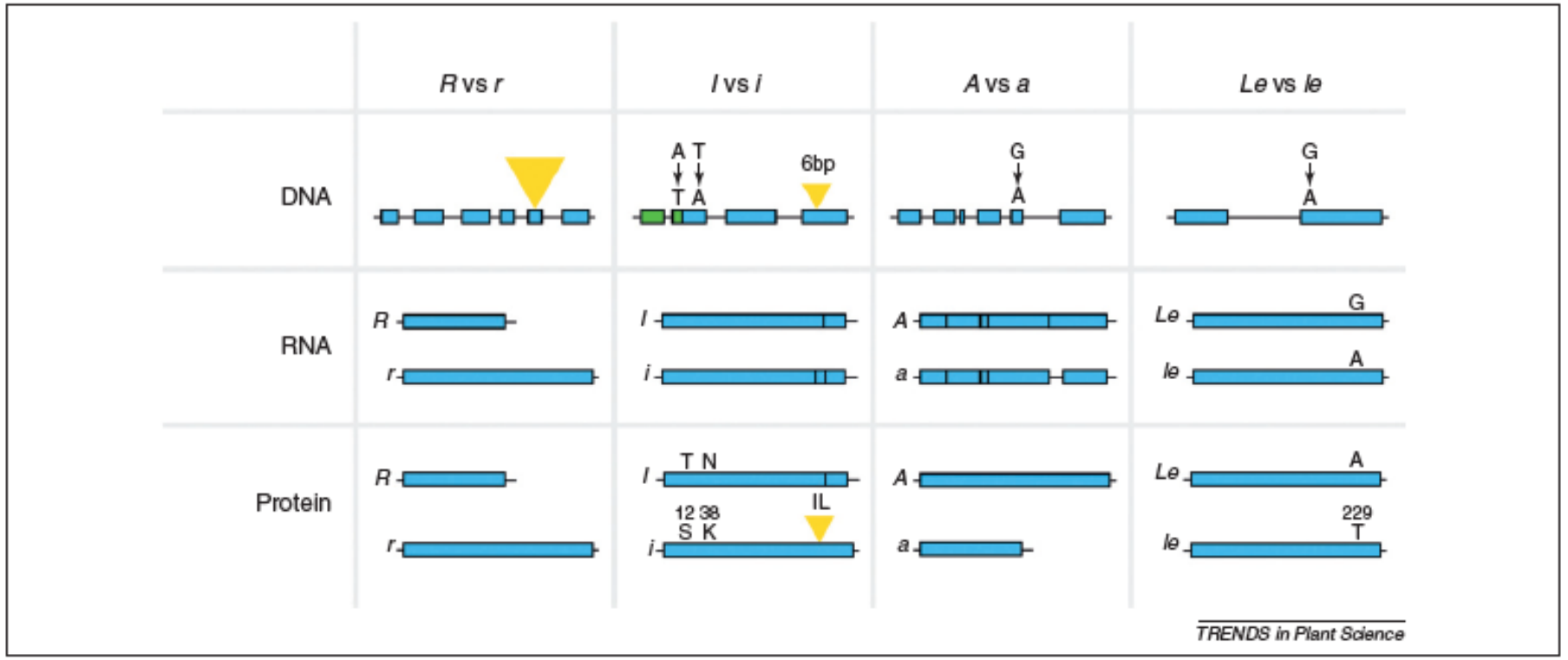

Figure 2. Mutations in Mendel's genes. Round versus wrinkled (*R* vs *r*): encoding starch branching enzyme I (SBEI). In the mutant allele, a transposon is inserted into the open reading frame (large triangle), disrupting both transcription (larger transcript) and translation in mutant lines. Yellow versus green cotyledons (*I* vs *i*): encoding a stay-green protein (SGR). In the mutant allele, a six nucleotide insertion in the coding sequence leads to a two amino acid insertion in the translated protein, disrupting gene function. Other amino acid changes in the signal peptide are not thought to disrupt function. Seed coat (and flower) colour (*A* vs *a*): encoding a basic helix–loop–helix transcription factor (bHLH). In the most common mutant allele, a single nucleotide change at an intron junction disrupts RNA processing leading to a transcript with an additional eight nucleotides and a truncated protein. Tall versus dwarf plants (*Le* vs *le*): encoding gibberellic acid 3-oxidase. A single nucleotide substitution in the coding sequence leads to an alanine (A) to threonine (T) substitution at position 229 that reduces the activity of the enzyme.

Mendel's laws have extensions and exceptions: i.e. difference in inheritance and penetrance

THE TRANSFORMING PRINCIPLE (Griffith, 1928)

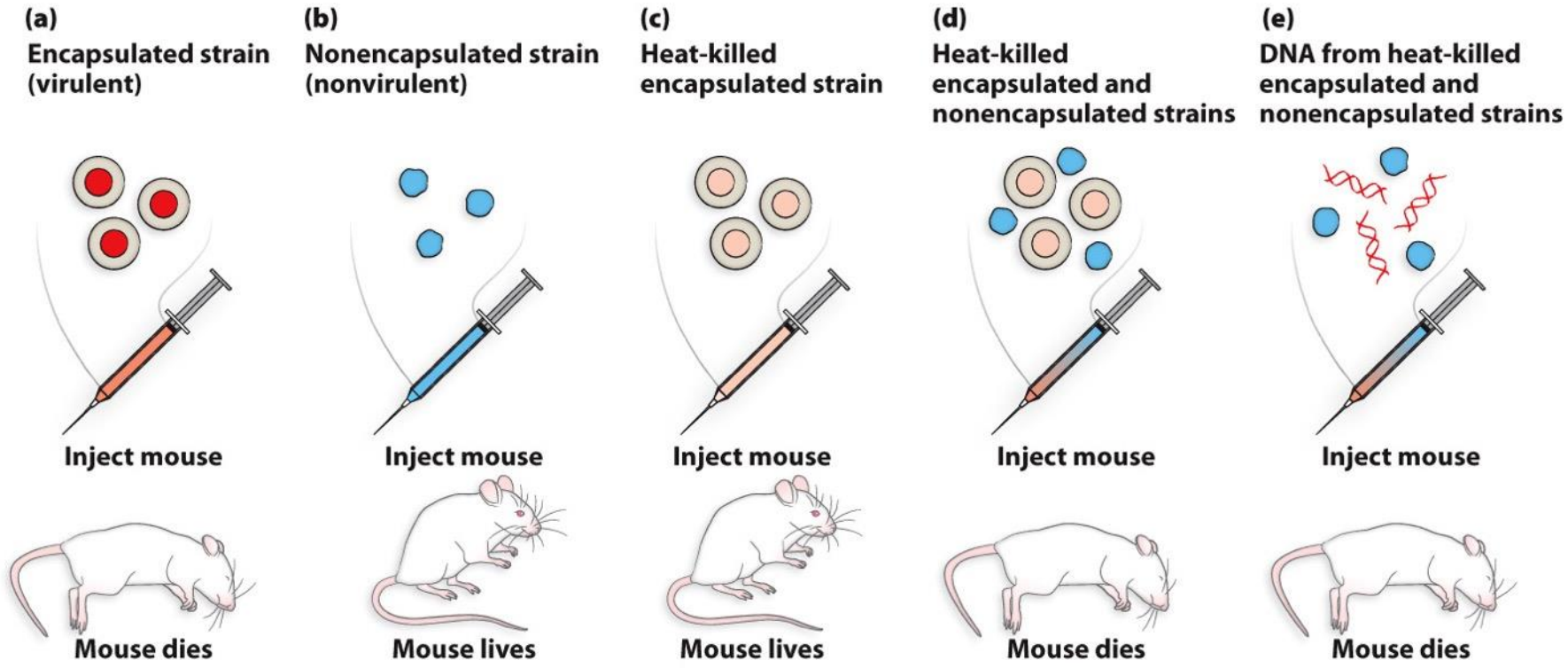

Figure 2-22
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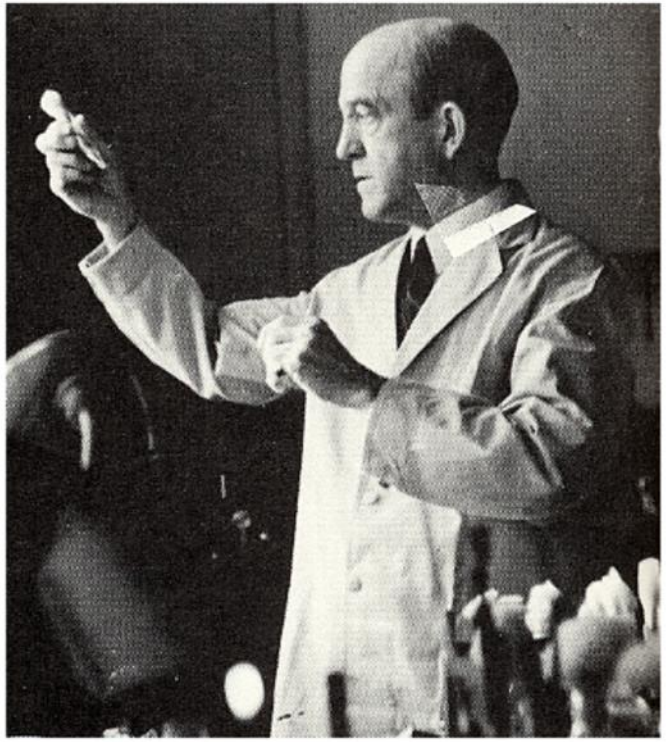
A mixture of strain R and head-killed strain S bacteria kills the mouse.

HOW COULD THIS HAPPEN?

The killed virulent (S) bacteria have transformed the avirulent (R) bacteria into virulent (S).

Clue #2: Avery and co-workers

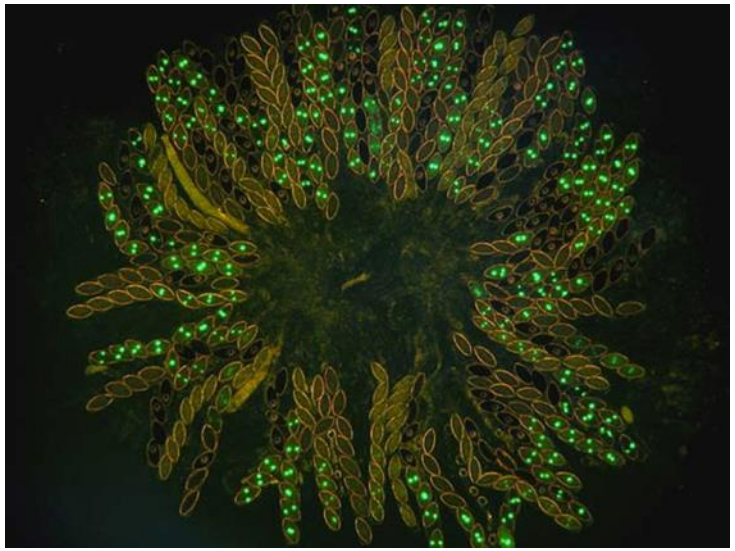


Avery ~1930: DNA is the genetic material

- Determined the chemical nature of the transforming substance from virulent *S. pneumoniae* cells
- Used a variety of analysis tools (such as chemical fractionation) to identify and confirm the chemical nature of the transforming material **(DNA)**
- Removed protein→ no effect on transformation
- Destroyed protein with enzymes → no effect on transformation
- Used ribonuclease to destroy RNA → no effect on transformation
- Used DNAse→ **no transformation occurred!**

How do genes work?
THE ONE GENE–ONE ENZYME HYPOTHESIS

Beadle and Tatum, 1941 (used bread mold *Neurospora*)

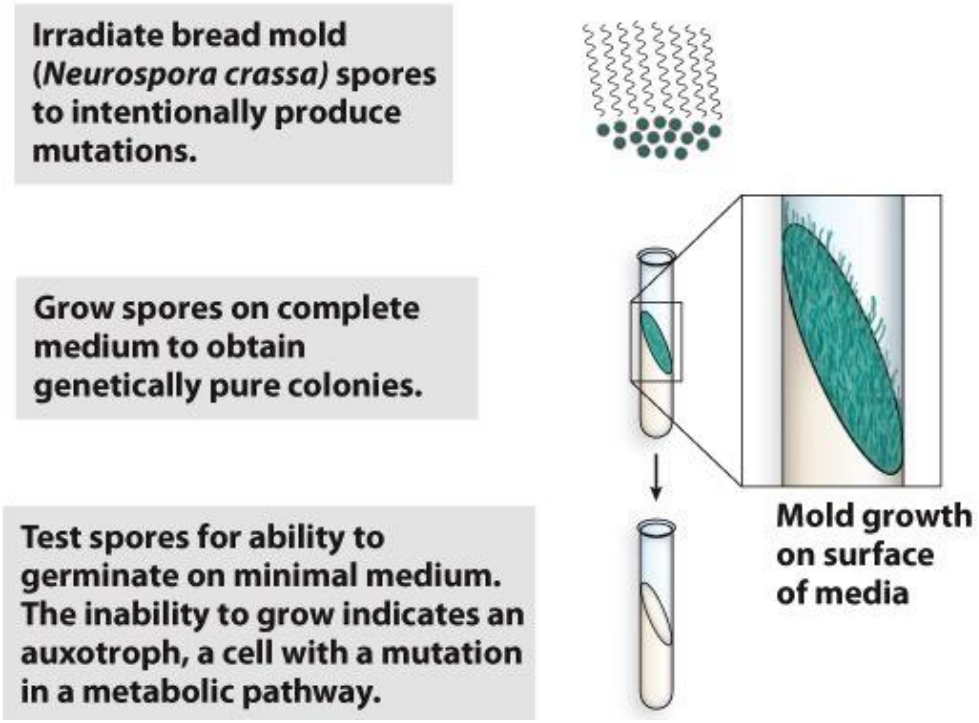


The Beadle and Tatum experiment starts with creating mutant colonies of *Neurospora crassa*.

There are several important reasons for using this fungus. The main one is that each hyphae of *Neurospora* has several nuclei, but each is in a haploid state.

Thus, if there is a mutation on one of the seven chromosomes it will be seen straight away in the new generation. What is the difference between haploid and diploid organisms? Why might diploid organisms be difficult to use in mutational analysis?

How do genes work?
THE ONE GENE–ONE ENZYME HYPOTHESIS



X-rays are the easiest mutating agents to use.

After exposure to X-rays, a lot of the nuclei will have a mutation in them. Some of the nuclei will give rise to ascospores (asci). The asci are dissected and individual spores are inoculated onto a rich medium which will cause all spores to grow.

This would have been repeated using MANY tubes!

If the fungus develops on minimum medium, the colony is discarded because it means it has not mutated. If it doesn't, further tests are performed.

Beadle and Tatum (1940s)
THE ONE GENE–ONE ENZYME HYPOTHESIS

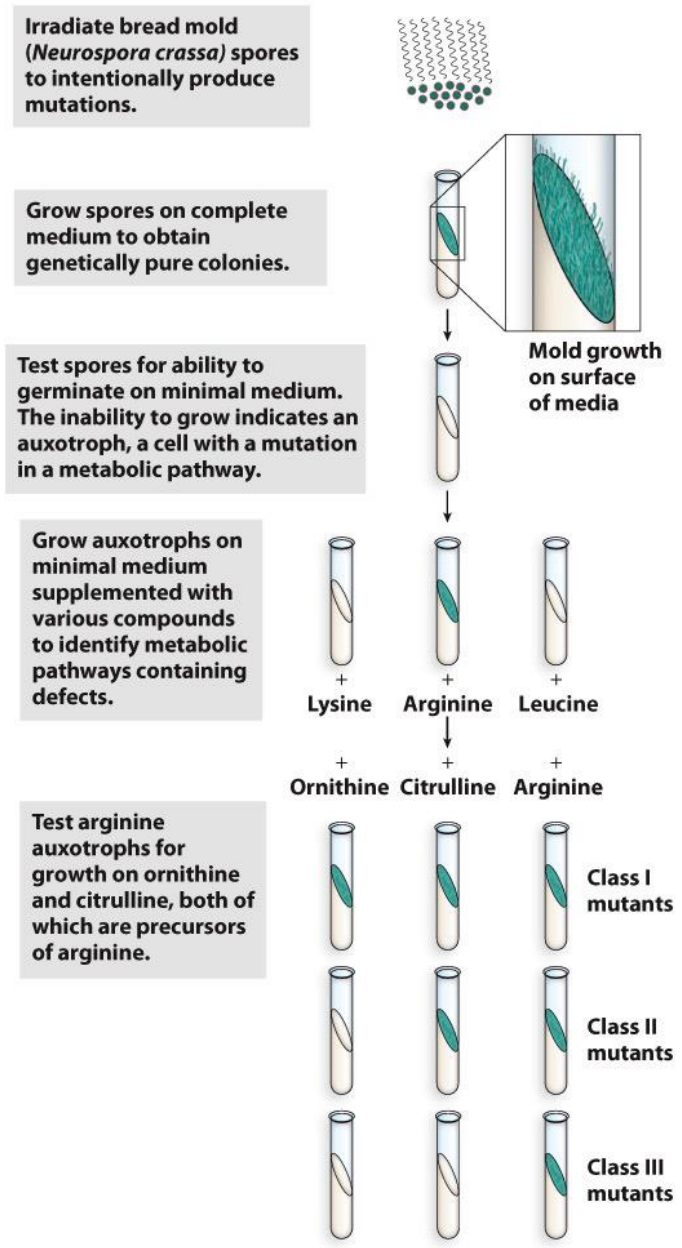


Figure 2-23 part 1
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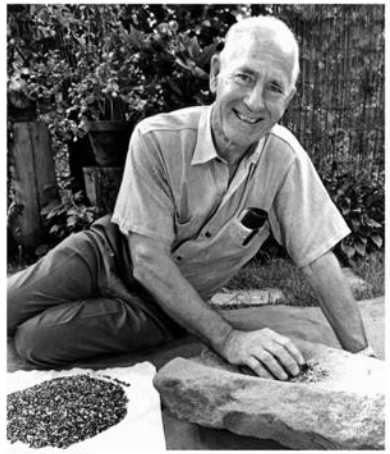

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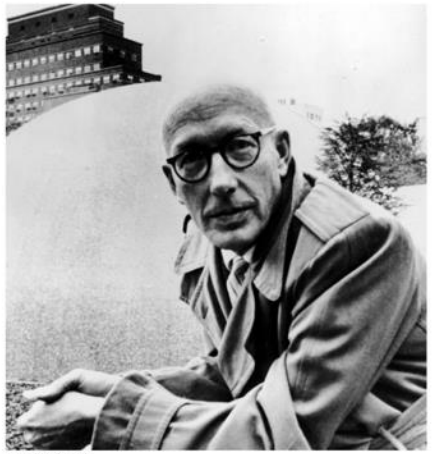
Molecular Biology: Principles and Practice, Second Edition
Courtesy of the Archives, California Institute of Technology



Unnumbered 2 p45b
Molecular Biology: Principles and Practice, Second Edition
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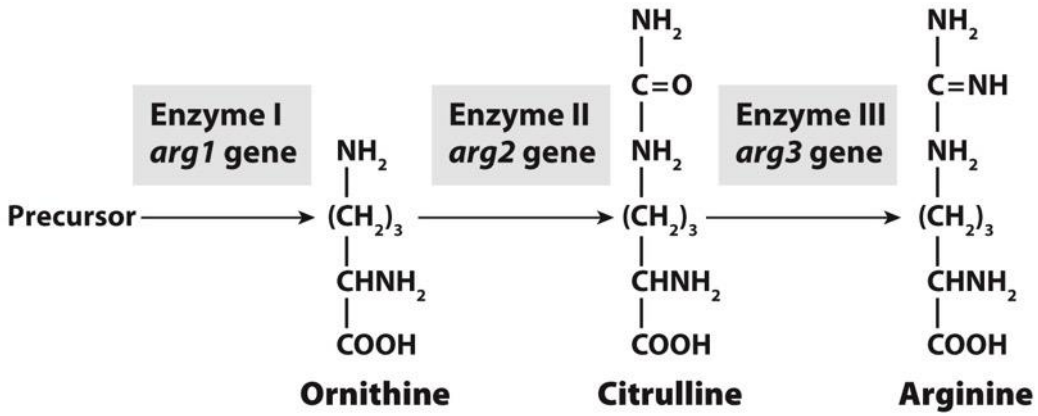

Figure 2-23 part 2
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Beadle and Tatum isolated a huge collection of mutants deficient in one aspect of their metabolism. They were shown not to be able to make one particular enzyme.

ONE GENE = ONE ENZYME?

The one gene-one enzyme hypothesis does not always hold because:

1. an enzyme can be composed of more than one polypeptide produced by more than one gene (*e.g.*, microtubules are composed of alpha- and beta-tubulin)

1. many genes make polypeptides that are not enzymes (*e.g.*, collagen)

2. the end products of some genes are RNAs, not polypeptides (e.g., RNAs in the ribosome)

This work was revised to the "one gene, one polypeptide" hypothesis

Nevertheless, this earned Beadle & Tatum the Nobel prize in Physiology and Medicine (1958)

The discovery of DNA

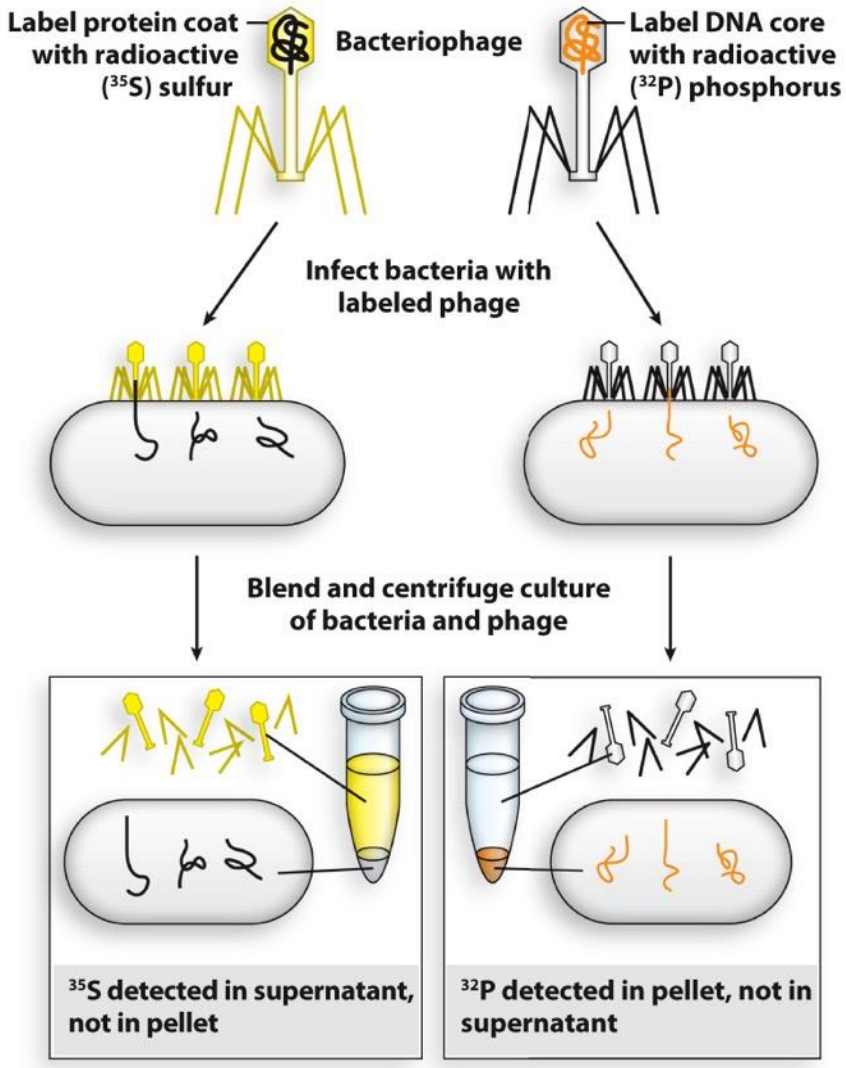
How do genes work? What do they do?

- Chargaff, Watson and Crick, Franklin & Wilkins

CLUE #3: TRANSFORMATION BY PHAGE DNA

How did did we know, pg. 57

- T2 phage (E. coli phage)
- Composed of DNA and protein only (no RNA), so a good model
- Labeled phage DNA with ^{32}P & phage protein with ^{35}S
- Since the phage DNA enters the host cell during infection, the type of label found in the infected host cells would indicate the nature of genes
- Following treatment with a blender, most of the labeled protein (^{35}S) remained on the outside and the labeled DNA (^{32}P) was found inside bacteria and in progeny phage
- **CONCLUSION**: DNA is T2 genetic material (it directed the formation of new proteins within the bacterial host)



How We Know 2-1 Figure 3
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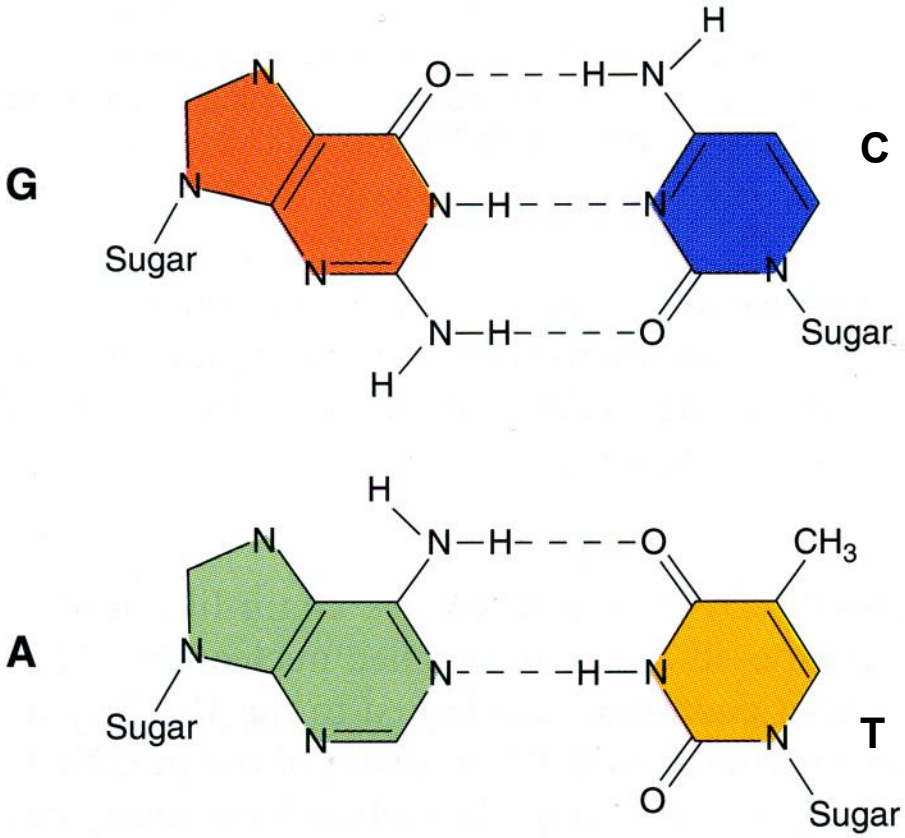
CLUE #4



Chargaff's ratios:

- dGTP = dCTP
- dATP = dTTP
- purines = pyrimidines

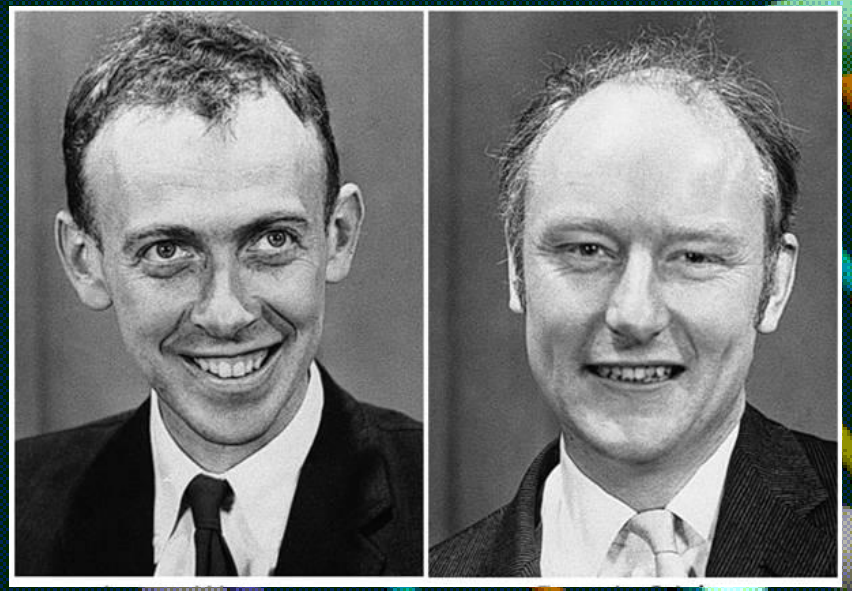
Erwin Chargaff's studies of the base compositions of DNAs from various sources revealed that the content of purines was always roughly equal to the content of pyrimidines. Furthermore, the amounts of adenine and thymine were always roughly equal, as were the amounts of guanine and cytosine. These findings, known as Chargaff's rules, provided a valuable foundation for Watson and Crick's model.

This table presents Chargaff's data. Some deviation from the rules are due to incomplete recovery of some of the bases, **but the overall pattern is clear: C=G, A=T**

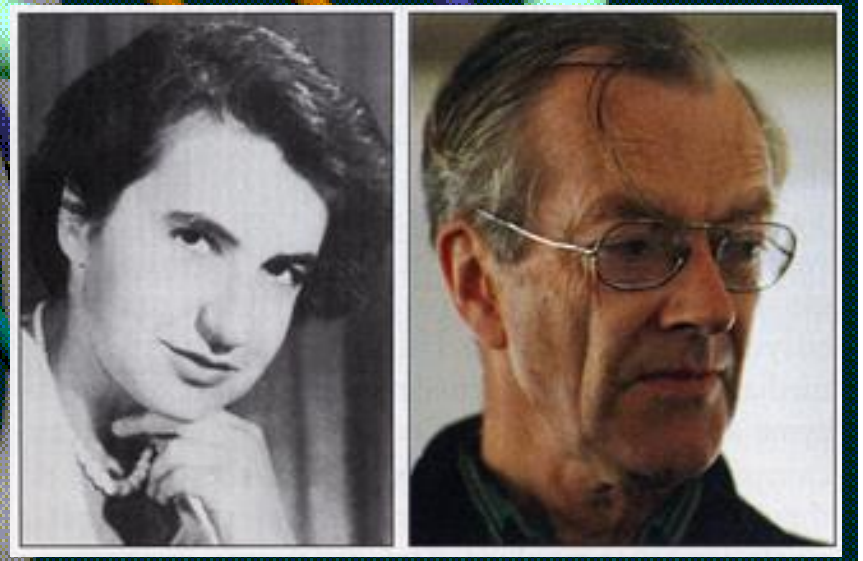
	Human						Avian Tubercle Bacilli	Bovine				
	Sperm		Thymus	Liver Carcinoma	Yeast			Thymus			Spleen	
	#1	#2			#1	#2		#1	#2	#3	#1	#2
A:	0.29	0.27	0.28	0.27	0.24	0.30	0.12	0.26	0.28	0.30	0.25	0.26
T:	0.31	0.30	0.28	0.27	0.25	0.29	0.11	0.25	0.24	0.25	0.24	0.24
G:	0.18	0.17	0.19	0.18	0.14	0.18	0.28	0.21	0.24	0.22	0.20	0.21
C:	0.18	0.18	0.16	0.15	0.13	0.15	0.26	0.16	0.18	0.17	0.15	0.17
Recovery:	0.96	0.92	0.91	0.87	0.76	0.92	0.77	0.88	0.94	0.94	0.84	0.88

Source: E. Chargaff "Chemical Specificity of Nucleic Acids and Mechanism of Their Enzymatic Degradation," *Experientia* 6:206, 1950.

THE DNA HELIX: THE DISCOVERY

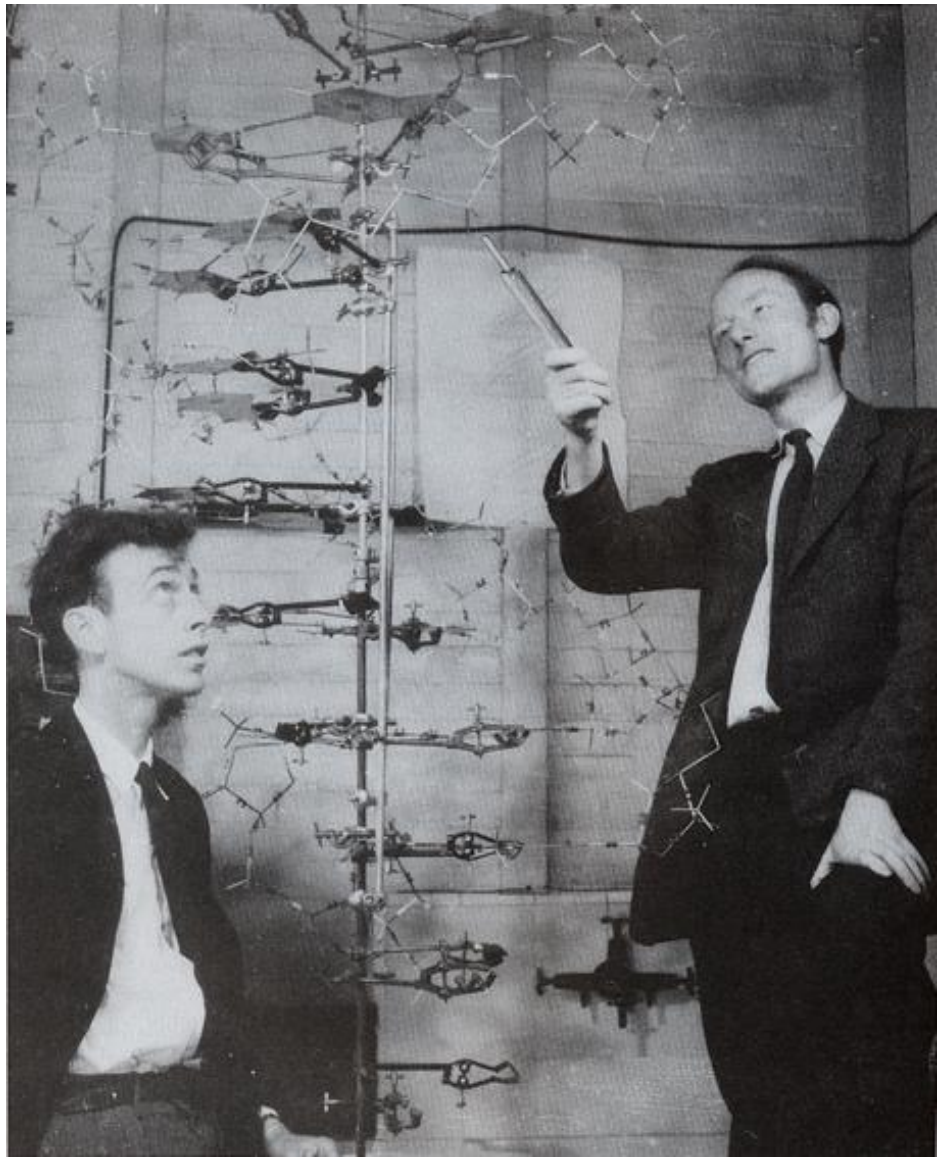


WATSON CRICK



FRANKLIN WILKINS

The Discovery of DNA Structure



- History's most important scientific discovery?
- Watson & Crick & Wilkins & Franklin

WHAT WERE THE CLUES?

X-ray diffraction pattern of DNA fiber (May 1952)

How did did we know, pg. 204

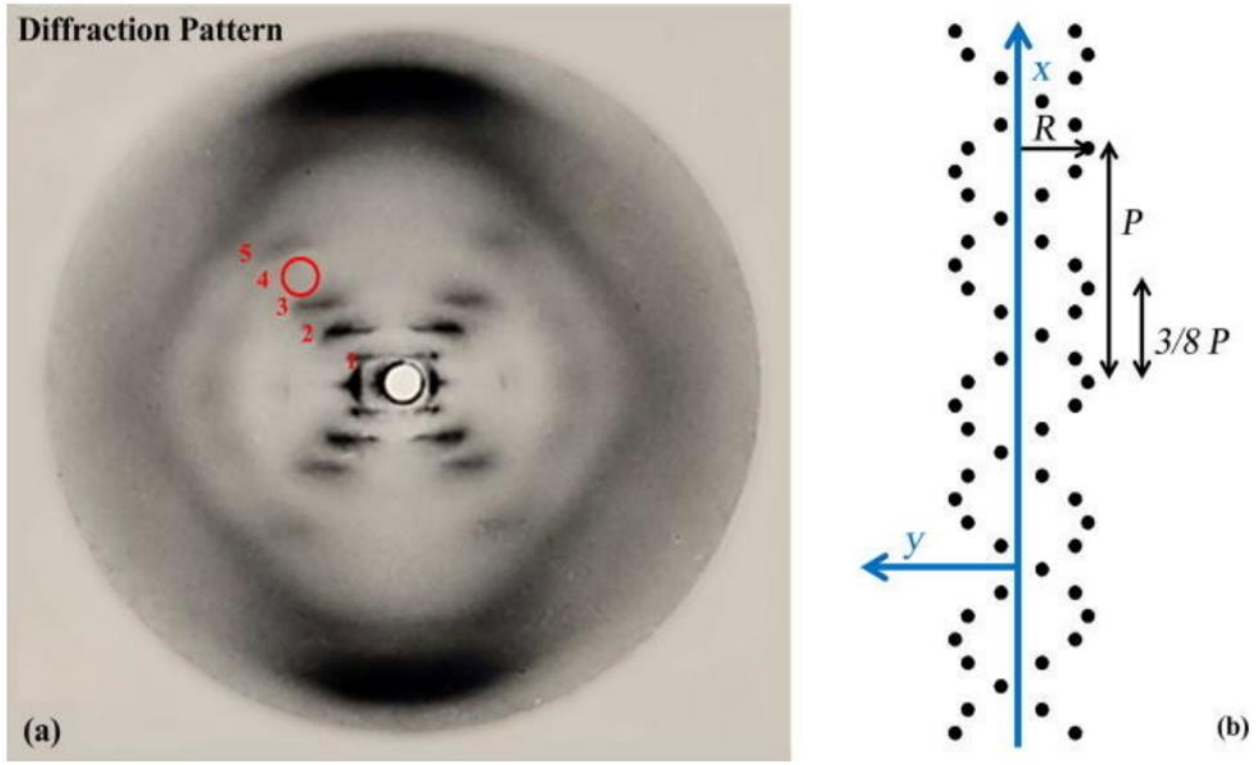


Fig. 1. (a) The well-known Photo 51, the diffraction pattern from DNA in its so-called B configuration. The dimensions of DNA are: pitch P = 3.4 nm, radius R = 1 nm, and a phase difference between the two helices (sine waves) of ΔP = 3P/8. Several important features include the characteristic X-shape or distorted rhombus, the ten diffracted orders per X, and the missing fourth order. (b) A two-dimensional projection of the phosphate molecules in the DNA backbone. The projection outlines two sine waves. We justify this flat model theoretically in Sec. II.

Rosalind Franklin and Raymond Gosling's DNA X-ray diffraction pattern (aka Photo 51):

X = helix

- Distance between bases
- Repeated, ordered pattern

NUCLEOTIDES: BASES - SUGARS - PHOSPHATES

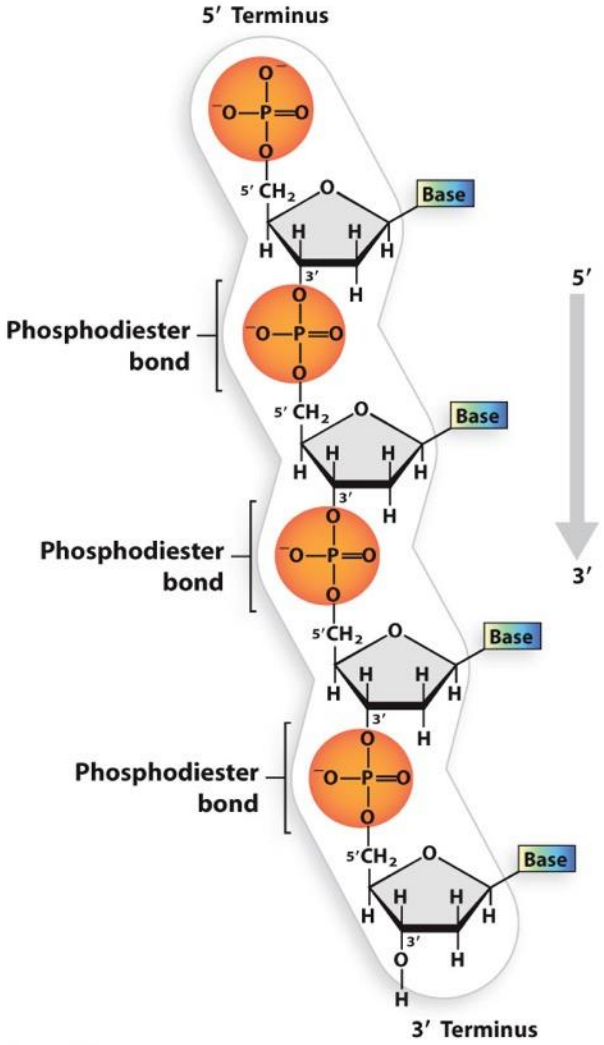


Figure 6-6
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- BASES: N-contain rings
- SUGARS: 5C sugar

  Bases & sugars joined by N-glycosidic bond
- PHOSPHATES: Mono-, di-, tri-phosphates

  Phosphate joined at C5 hydroxyl of ribose, deoxyribose

Watson & Crick's DOUBLE HELIX DNA STRUCTURE

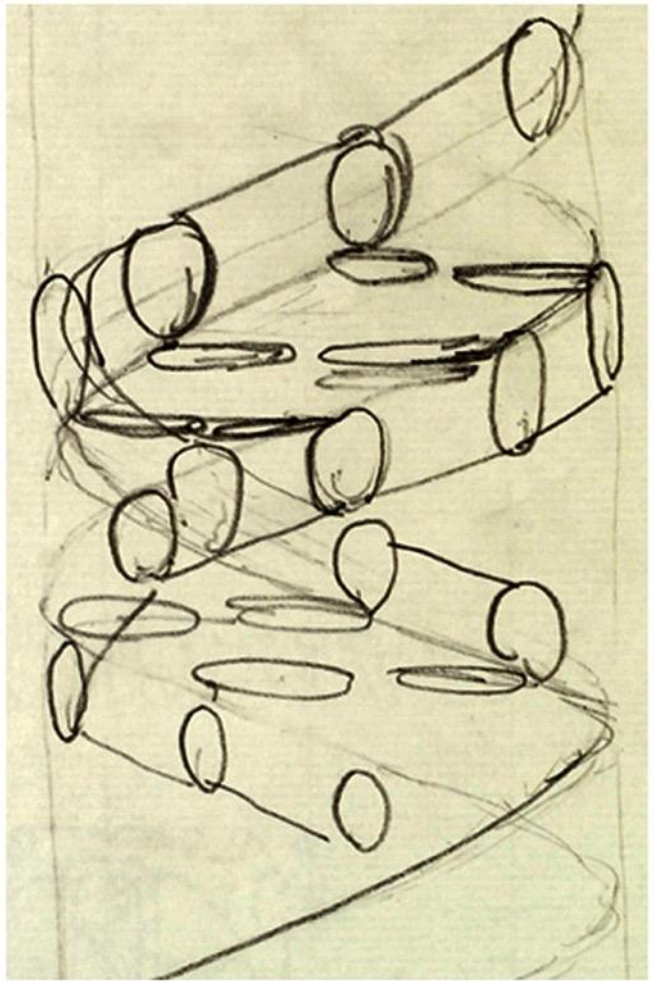

Figure 6-1
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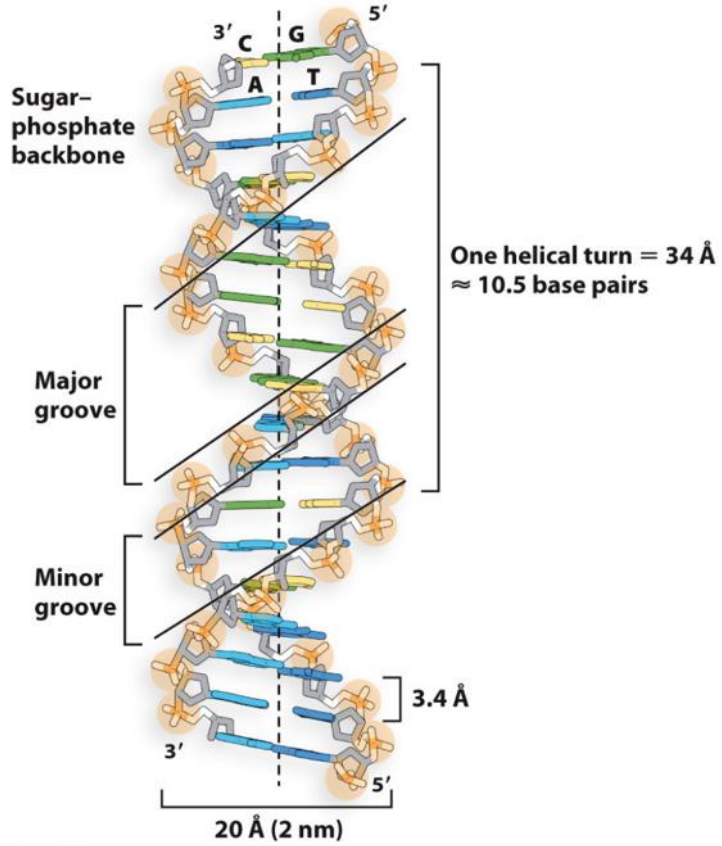

Figure 6-14
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Nature, Vol. 171, No. 4356, April 25, 1953
pp. 737–738.

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.

This figure is purely diagrammatic. The two ribbons symbolize the two phosphate–sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining β-D-deoxyribofuranose residues with 3′,5′ linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's[2] model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There is a residue on each chain every 3·4 A. in the z-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 A. The distance of a phosphorus atom from the fibre axis is 10 A. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical z-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally[3,4] that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data[5,6] on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at

CLUE #6: NUCLEIC ACID PROPERTIES

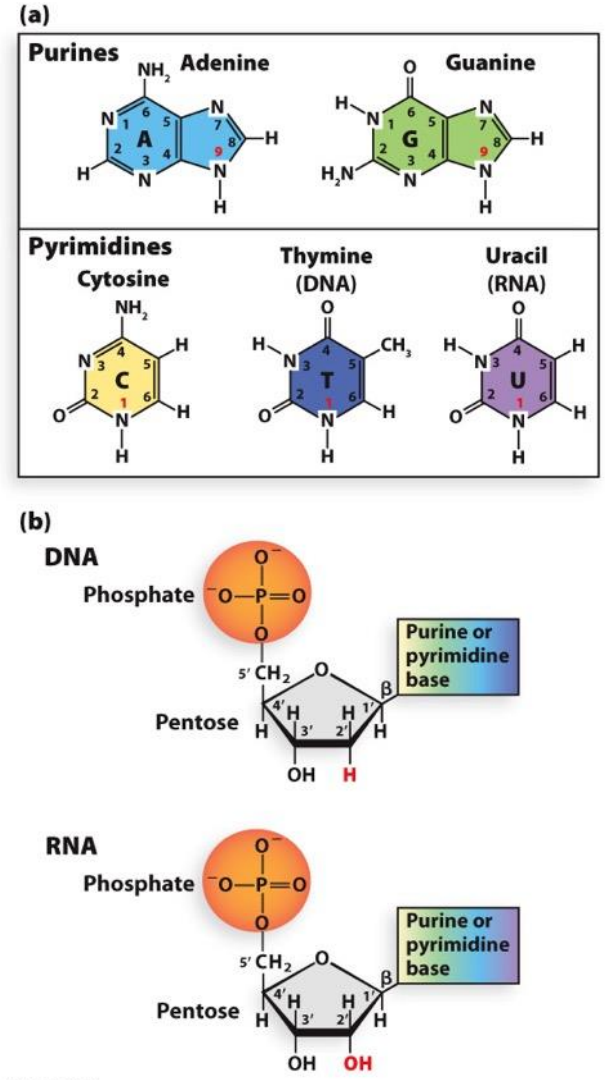

Figure 6-2
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- PURINES: dATP, dGTP
- PYRMIDINES: dCTP, dTTP (UTP in RNA)
- Nucleotide: base, pentose + phosphate
- Nucleoside: base, pentose

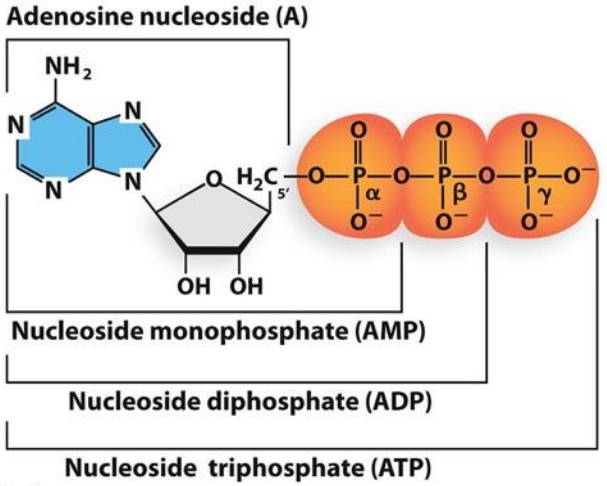

Figure 6-12
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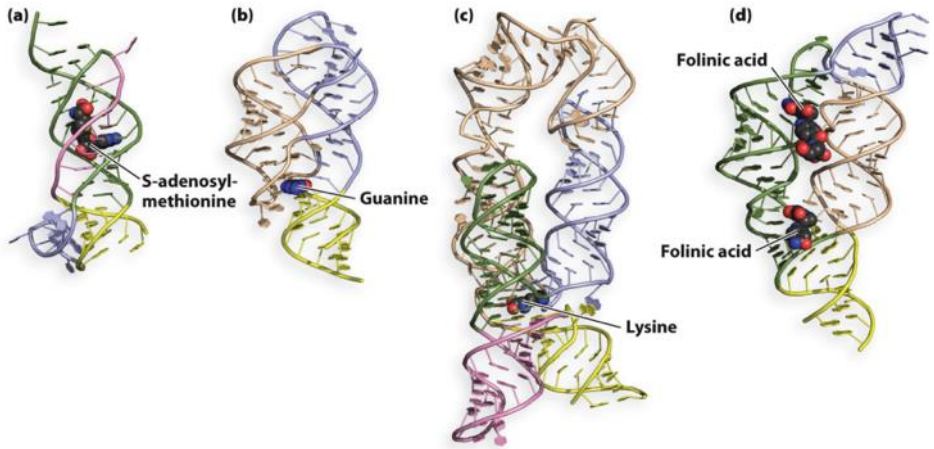
Examples of the diversity nucleic acid structures

- RNA riboswitches and ribozymes



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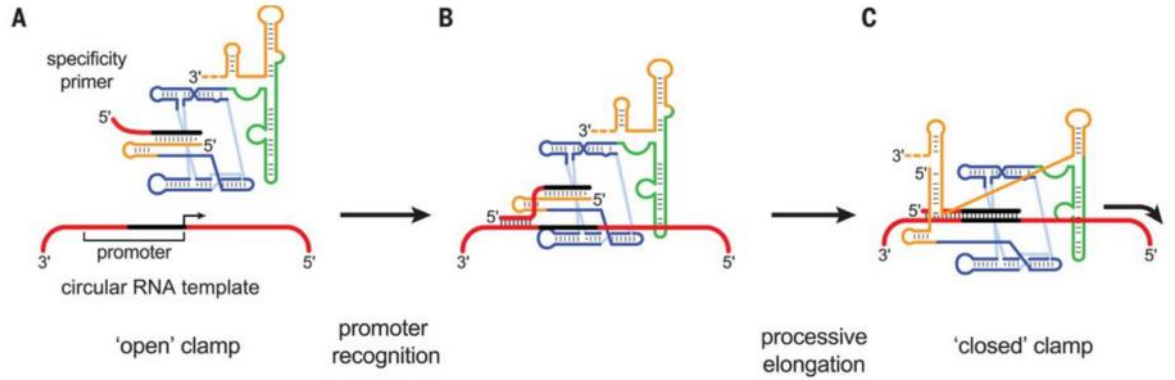

Cojucaru, R & Unrau, P *Science* 2021

- DNA G-quadruplexes

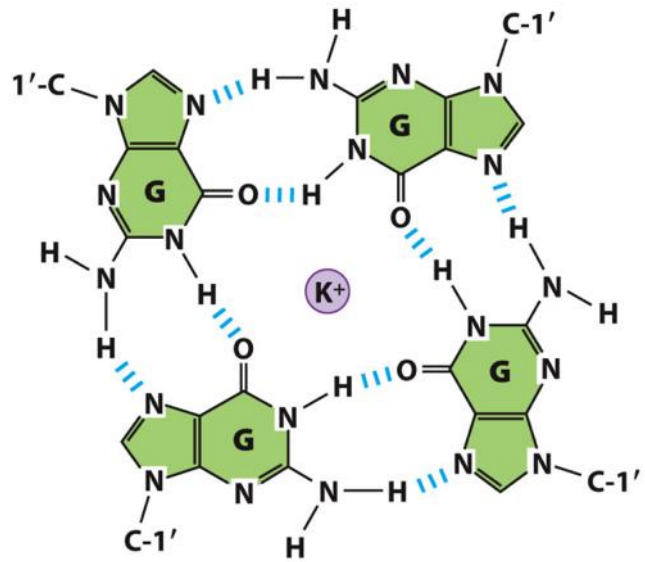

Figure 6-21c
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Reminder: pathways of biological information flow

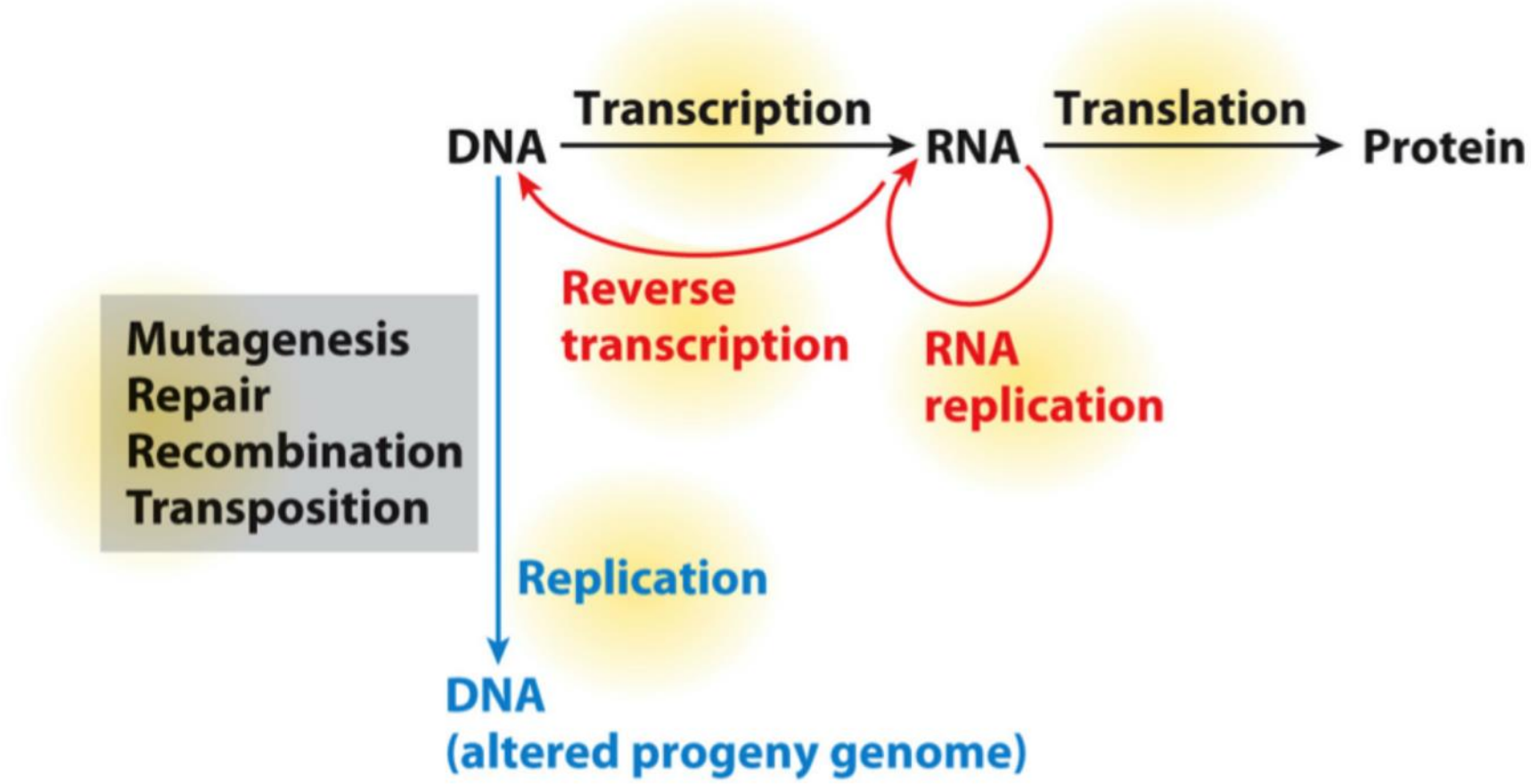

Figure 1-4
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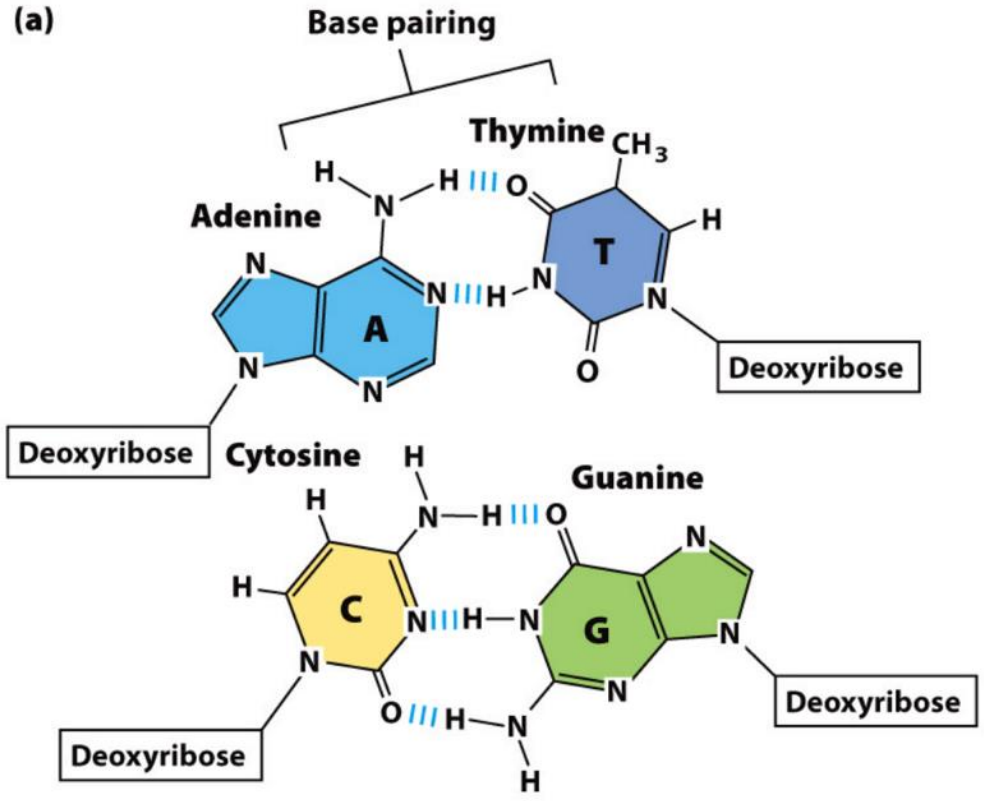
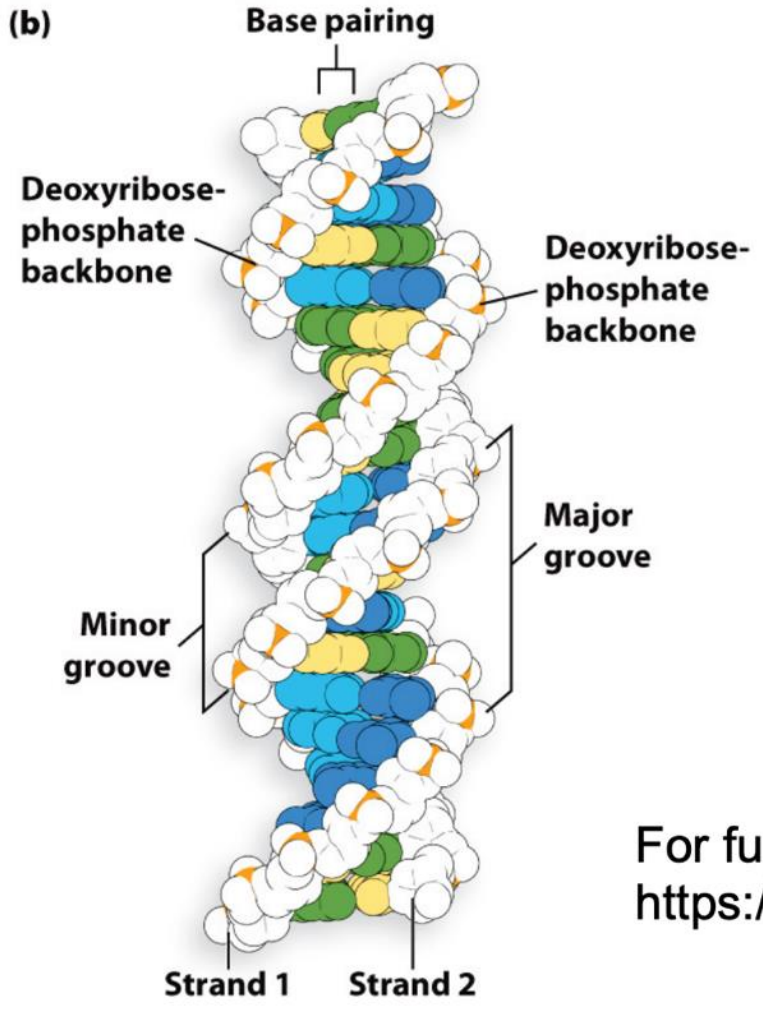
DNA is the standard macromolecule for the **long-term storage and transmission of biological information.** It is exquisitely adapted for that function Why?





For fun, watch:
https://vimeo.com/65811205

Figure 1-3
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