Methods and Manners in Science

The Responsible Conduct of Research

Francis L. Macrina
Vice President for Research
Virginia Commonwealth University

VCU

The Scientific Method

What are the steps of the scientific method as typically described in textbooks? Do you think scientific research usually progresses according to the scientific method?

The Textbook Scientific Method

1. Create a hypothesis
2. Test the hypothesis
3. Hypothesis not supported: modify it
   or return to step 1
4. Hypothesis supported: devise new tests
   to prove it wrong
5. Hypothesis not proven wrong: accept, publish,
   and build on it
6. Well tested hypotheses that withstand experimental
   scrutiny become part of the body of scientific
   knowledge

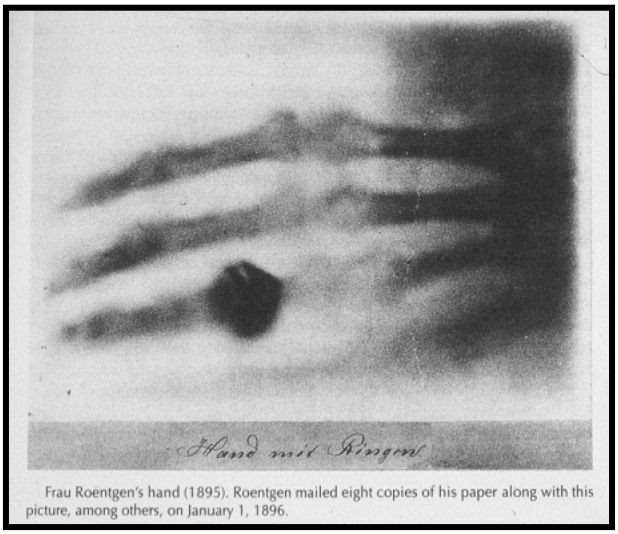
Some Stories About Scientific Discovery (three "Nobel" examples)

Accident

Luck

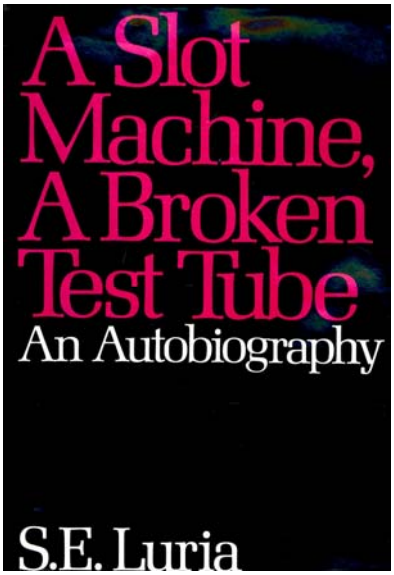
Intutition

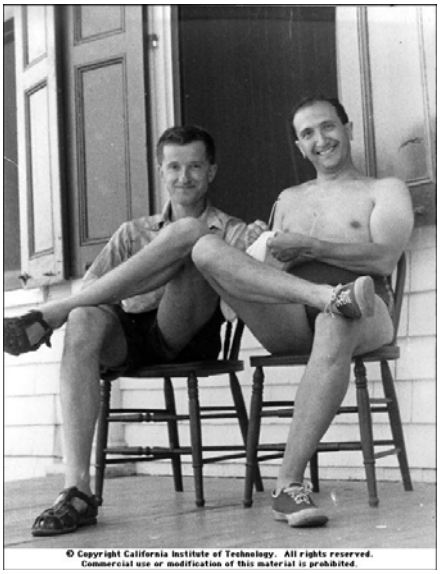
Roentgen and his laboratory



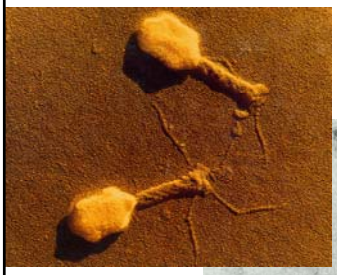
Frau Roentgen's hand (1895). Roentgen mailed eight copies of his paper along with this picture, among others, on January 1, 1896.

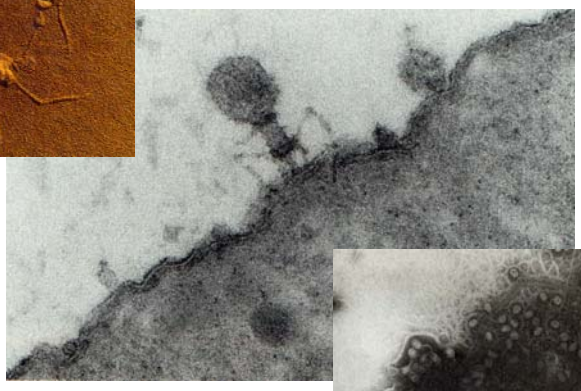
Nobel Prize 1901

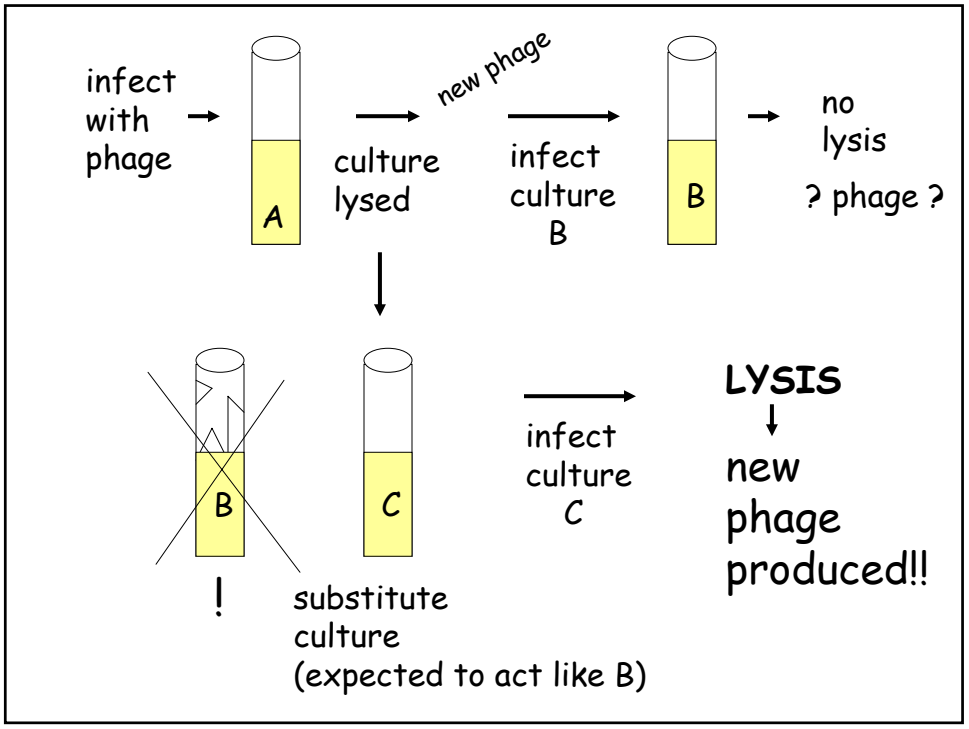




Bacteriophage (a.k.a. bacterial viruses "phage" for short)







Bacterial Restriction-Modification

1. Luria's discovery: a primitive system of "recognition of self" in bacteria.

2. "A"- propagated phage were recognized by "B" bacteria and destroyed with enzymes that chop up DNA (specifically).

3. Bacteria A and C were similar (recognized each as "self")

4. Ultimately DNA degrading enzymes of bacteria "B" purified and used to "cut and splice" DNA, enabling recombinant DNA technology to be developed.

Nobel Prize 1969

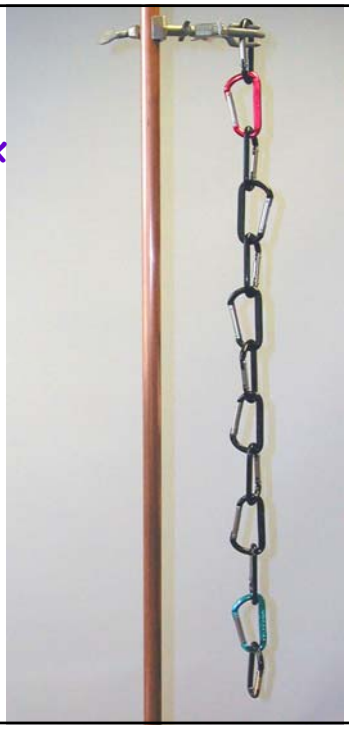
Barbara McClintock

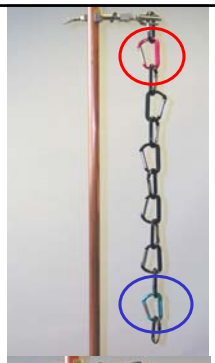
1902-1992

Carnegie Institution-Cold Spring Harbor Laboratory

DNA: the double helix

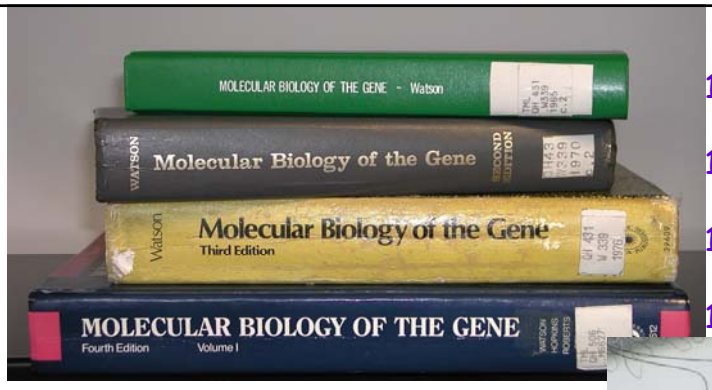
A molecule of stability, fidelity, integrity





Pigment
Gene "off"

Pigment
Gene "on"



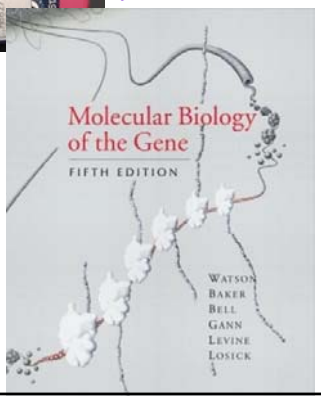
1965

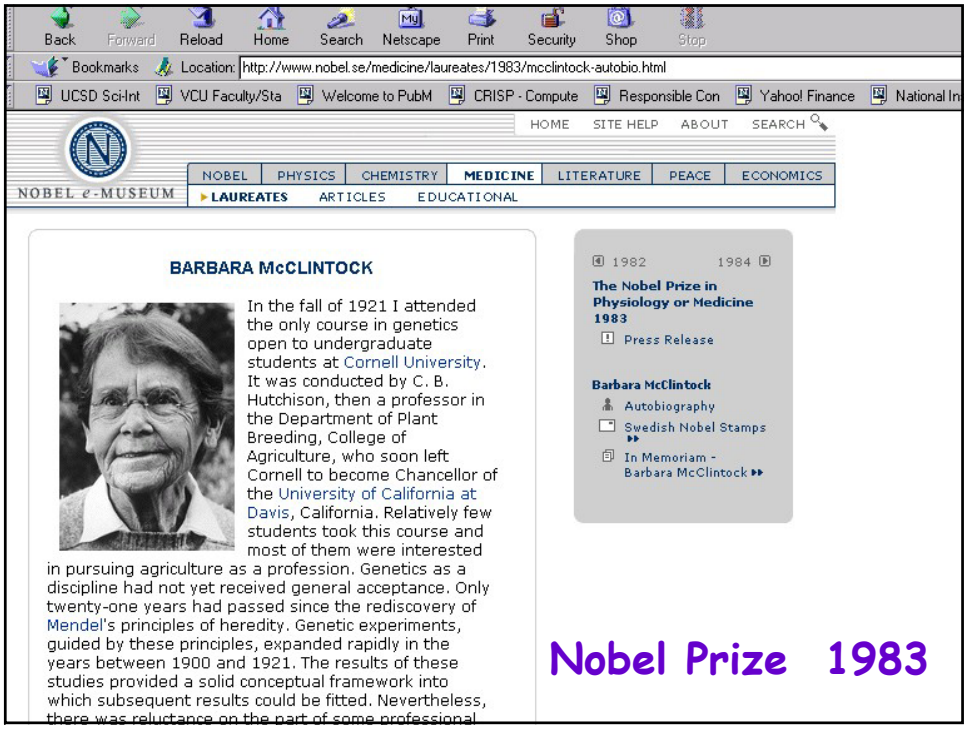
1970

1976

1987

2003





Science in the public eye

Understanding and Accountability

Lessons from Reading the Headlines….

1986 "Oat Bran may be the Next Miracle Food"

1988 "But not by Oats Alone"

1989 "Hot on the Heels of Oat Bran"

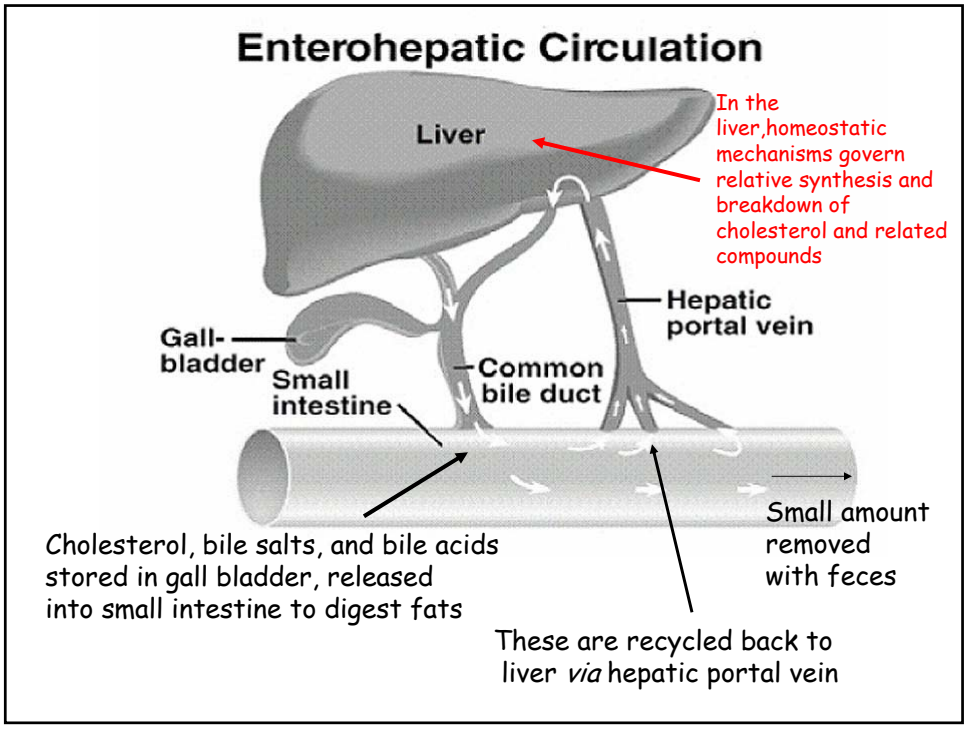
1990 "Oat Bran's Claims Weakened"

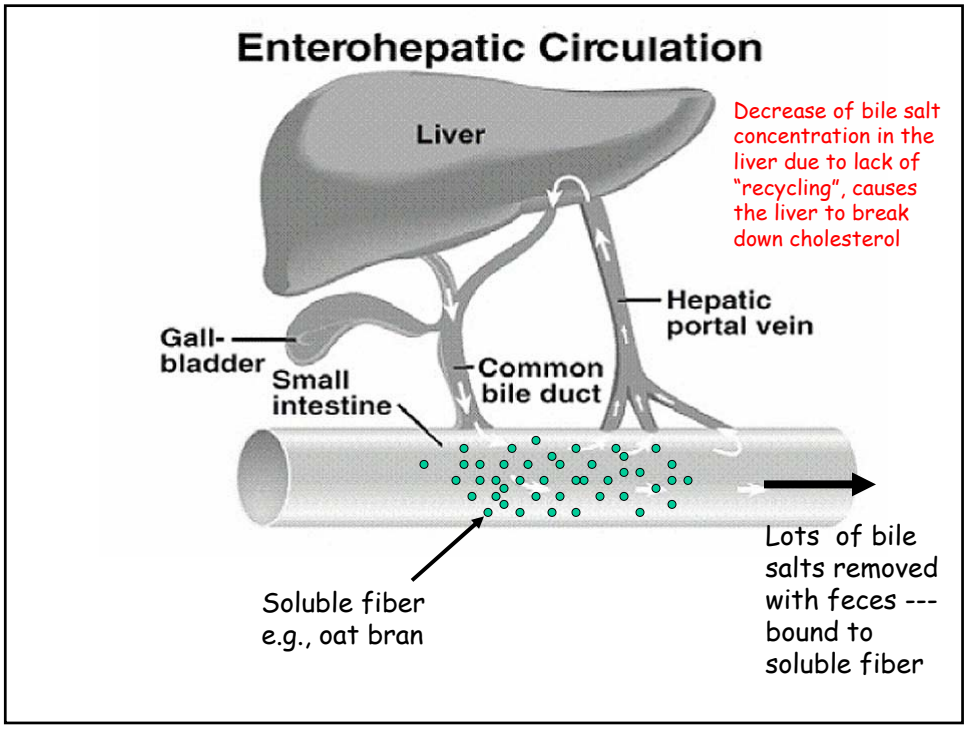
1990 "Oat Bran Bites the Dust"

1991 "New Oat Bran Study Says Cholesterol is Lowered"

1992 "Oat Bran Really Does Cut Cholesterol"

1992 "Lots of Oat Bran Found to Cut Cholesterol"


Enterohepatic Circulation
Liver
In the liver,homeostatic mechanisms govern relative synthesis and breakdown of cholesterol and related compounds
Hepatic portal vein
Gall-bladder
Small intestine
Common bile duct
Cholesterol, bile salts, and bile acids stored in gall bladder, released into small intestine to digest fats
Small amount removed with feces
These are recycled back to liver *via* hepatic portal vein


Enterohepatic Circulation
Liver
Decrease of bile salt concentration in the liver due to lack of "recycling", causes the liver to break down cholesterol
Hepatic portal vein
Gall-bladder
Small intestine
Common bile duct
Soluble fiber e.g., oat bran
Lots of bile salts removed with feces --- bound to soluble fiber

USA TODAY

NO. 1 IN THE USA

Monday, June 16, 2003

Health guidelines: It's tough keeping up

Exercise, blood pressure, obesity: The standards keep changing. One weight warrior's lament: 'I don't pay attention anymore.' Such resignation concerns doctors.

By Nanci Hellmich and Rita Rubin
USA TODAY

Milwaukee mother Linda Blake-DeLeo'n, 33, has struggled for years to do what the federal government advised: exercise for at least 30 minutes a day. But when a new set of standards last fall raised the bar to an hour a day, she felt like hanging up her walking shoes and cracking open a gallon of ice cream.

She's also battling unsuccessfully to control her high blood pressure. So what happens? Medical experts set the country's blood pressure goals lower than ever.

She resents that these guidelines keep changing and that the bar for what constitutes good health keeps going up. "It's very discouraging," says Blake-DeLeo'n, who figures she's about 40 pounds overweight.

After a hard day selling classified ads and running four children around, all she wants to do in the evening is sit. "Some days I can't even find time to do 15 minutes of exercise, let alone an hour," she says. "I walk into my bedroom and see that treadmill and think, 'I can't do it today.'"

Like Blake-DeLeo'n, many Americans feel they're losing the numbers game when it comes to their bodies. They say it's too hard to make the lifestyle changes necessary to conform to the ever-stricter definition of healthy. Consider:

Tipping the scales
Adults 20 to 74 who are overweight or obese:

1960-1962	45%
1971-1974	47%
1976-1980	47%
1988-1994	56%
1999-2000	64.5%

Source: National Health and Nutrition Examination Survey
By Julie Snider, USA TODAY

Cover story

Please see COVER STORY next page ▸

Responsible Conduct of Research

Most, if not all senior scientists (those trained in the 1970s and early 80s) never received instruction or training in responsible conduct of research (also called scientific integrity, research ethics, etc.) Today, programs like the one you are in require that you receive instruction in this area. Why?

RCR Generation Timeline

Mid 1970-1980s	Highly publicized cases of alleged scientific misconduct grow in number
Early 1980s	Congressional hearings on fraud in biomedical research
Late 1980s-1990s	Infrastructure: definitions and policies; mandated education
1999-2001	Incidents and investigations: human subject experimentation; more mandated education
2001→	Revised definitions and broad based emerging educational policies
2005	Revised Federal Regulations on Research Misconduct
2006	High profile cases continue in the media

Major Elements of Responsible Conduct of Research

Subject protection
- -appropriate use of humans and animals in research

Research integrity
- -data management, sharing and ownership
- -authorship and publication practices
- -peer review
- -mentoring
- -collaborative research

Fiscal Accountability
- -proper use of research funds
- -conflict of interest

Environmental Health and Safety Issues
- -training and compliance

Sec. 93.103 Research misconduct. Research misconduct means fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results. (a) Fabrication is making up data or results and recording or reporting them. (b) Falsification is manipulating research materials, equipment, or processes, or changing or omitting data or results such that the research is not accurately represented in the research record. (c) Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit. (d) Research misconduct does not include honest error or differences of opinion.

Sec. 93.104 Requirements for findings of research misconduct. A finding of research misconduct made under this part requires that-- (a) There be a significant departure from accepted practices of the relevant research community; and (b) The misconduct be committed intentionally, knowingly, or recklessly; and (c) The allegation be proven by a preponderance of the evidence.

Responsible Conduct of Research

What's your definition of scientific misconduct? Some assert that scientific misconduct includes practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research. Others rebut this, saying that such thinking interferes with scientific creativity. What do you think?

Fabrication
Falsification
Plagiariarm

and

The Risk of Confusing Conduct with Misconduct in Science

Prime Time Live

The reporting of science in the media.

Handling of allegations of misconduct by:
- the government
- the scientific infrastructure

The behavior of scientists.

Insights on how science works.

Lessons learned?

April 8, 1992
ABC's Prime Time Live

Shown with permission

DEPARTMENT OF HEALTH & HUMAN SERVICES

National Institutes of Health
National Cancer Institute

Memorandum

Date August 19, 1985

From Chief, Laboratory of Tumor Cell Biology, DTP, DCT, NCI

Subject Science Article May 1983

To Associate Director, NCI

"Over the course of this work we were responding to a public health crisis and the need to develop useful assays such as the ELISA screening assay. We did not intend to keep records of legal standing and they are often incomplete. In contrast to this rather normal behavior is the meticulous and apparently premeditated documentation of others interested , it seems, more in patents and notoriety."

"When I came here nobody gave me whatsoever any instructions how we should write our notes or anything else. And when the litigation started, suddenly I was asked for notes"

http://www.sciencefictions.net

…major failing was his "refusal, flatly on several occasions, to look at the notebooks or peruse the primary data of people working for him. The buck's gotta stop somewhere"

"the poor quality and scant extent of his laboratory records was striking"

"…those notes which did exist were overwhelmingly cryptic and obscure, lacking even minimal detail necessary to understand what was done, what methods were used, and what results were obtained."

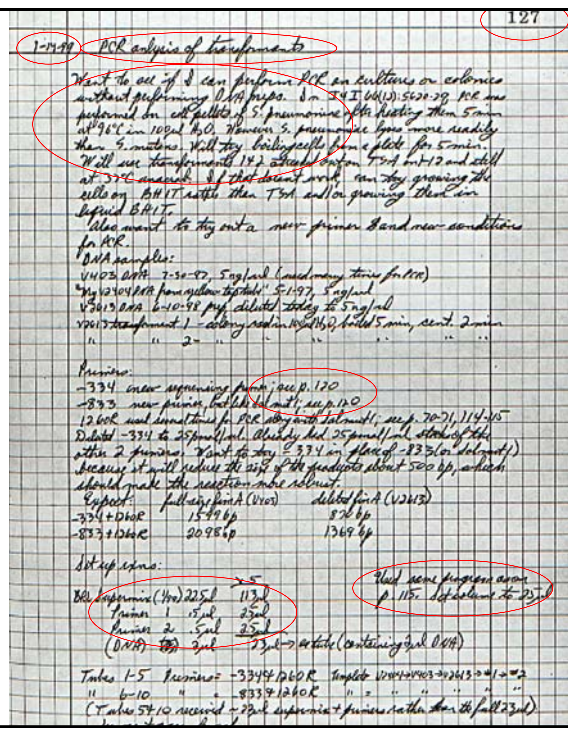
OSI Investigation
Crewdson, p. 417

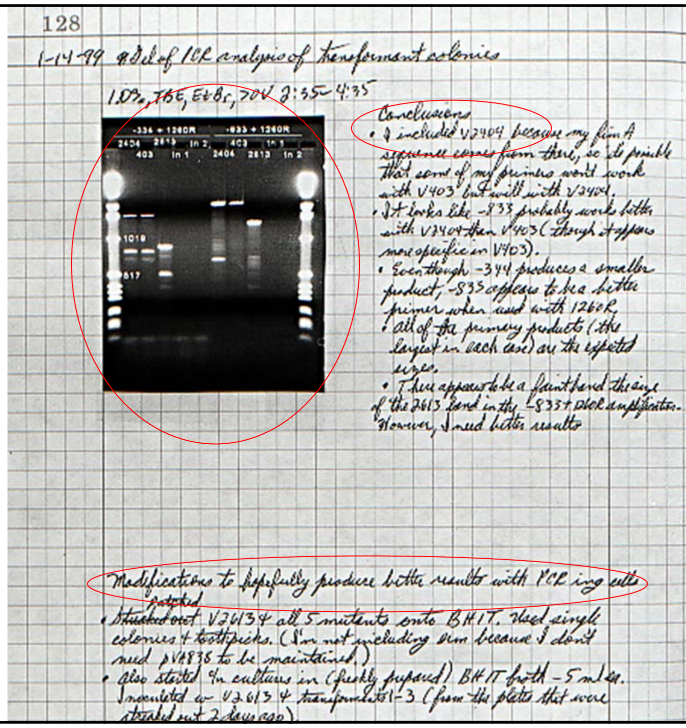
When I came there was no such thing as how you kept your notebook. In fact, nobody ever asked me if I kept a notebook. Later you could get investigated for not having the right notebook.

"Is there life after NIH?"
Gallo speech in Baltimore, MD
(Crewdson, p. 539)

Many lessons can be drawn from this early intense period and most suggest that science requires greater modesty.

N.Eng. J. Med. 12/11/03





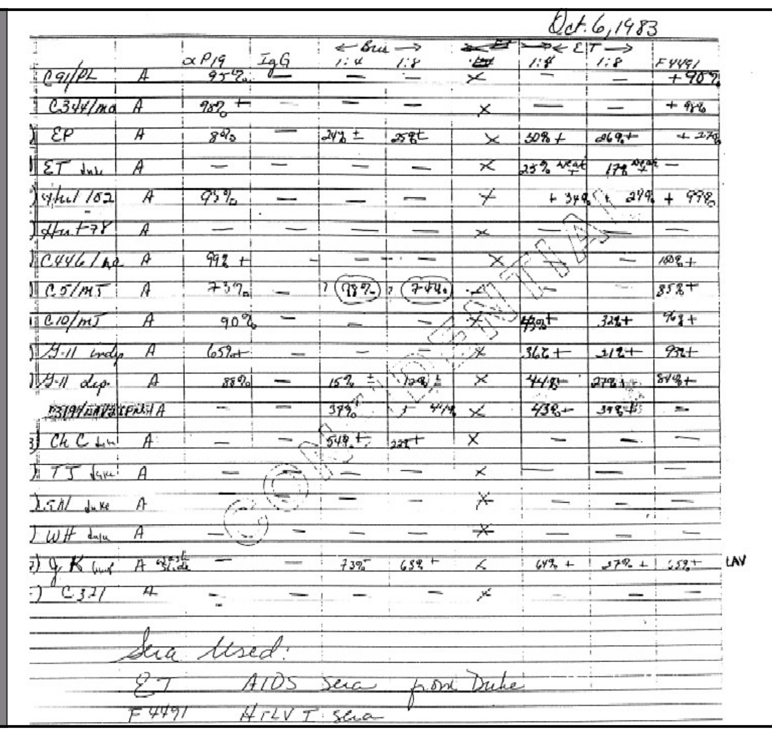
128

1-14-99 Gel of PCR analysis of transformant colonies

1.0%, TBE, EtBr, 70V 2:35–4:35

Conclusions
- I included V2404 because my fim A sequence comes from there, so it's possible that some of my primers won't work with V403 but will with V2404.
- It looks like -833 probably works better with V2404 than V403 (though it appears more specific in V403).
- Even though -344 produces a smaller product, -833 appears to be a better primer when used with 1260R.
- All of the primary products (the largest in each case) are the expected sizes.
- There appears to be a faint band the size of the 2813 band in the -833 + 1260R amplification. However, I need better results

Modifications to hopefully produce better results with PCR ing cells patched
- Streaked out V2613 + all 5 mutants onto BHIT. Used single colonies + toothpicks. (I'm not including sim because I don't need pVA838 to be maintained.)
- Also started O/n cultures in (freshly prepared) BHIT broth – 5 ml ea. Inoculated w V2613 + transformants 1-3 (from the plates that were streaked out 2 days ago).



Oct. 6, 1983

		αP19	IgG	← Bru 1:4	Bru → 1:8		← ET 1:4	ET → 1:8	F4491
C91/PL	A	95%	—	—	—	X	—	—	+ 90%
C344/ma	A	98% +	—	—	—	X	—	—	+ 98%
EP	A	89%	—	24% ±	25% ±	X	30% +	26% +	+ 27%
ET duke	A	—	—	—	—	X	25% weak +	17% weak +	—
4/hcl/102	A	93%	—	—	—	X	+ 34%	+ 29%	+ 99%
Hu F78	A	—	—	—	—	X	—	—	—
C446/	A	99% +	—	—	—	X		—	100% +
C5/MT	A	73%	—	? (98%)	? (74%)		—	—	85% +
C10/MT	A	90%	—	—	—	X	43% +	32% +	96% +
G-11 indep	A	65%	—	—	—	X	36% +	31% +	93% +
G-11 dep	A	88%	—	15% ±	12% ±	X	44%	27%	84% +
B3/94/	A	—	—	39%	? 41%	X	43% +	39%	—
Ch C duke	A	—	—	54% +	22% +	X	—	—	—
TJ duke	A	—	—	—	—	X	—	—	—
EN duke	A	—	—	—	—	X	—	—	—
WH duke	A	—	—	—	—	X	—	—	—
G K	A wash slide	—	—	73%	63% +	X	64% +	27% +	65% +
C321	A	—	—	—	—	X	—	—	—

LAV

Sera Used:

ET AIDS Sera from Duke

F4491 HTLV I Sera

University of Florida
http://rgp.ufl.edu/otl/goodrecords.html

Fox Chase Cancer Center
http://www.fccc.edu/ethics/RecordKeeping.html

DATA MANAGEMENT: RESEARCH RECORDS in NEW INVESTIGATORS: A QUICK GUIDE TO STARTING YOUR RESEARCH AT UCSF
http://www.research.ucsf.edu/QG/orQgDm.asp

Making the Right Moves: A Practical Guide to Scientific Management for Post Docs and New Faculty, Chapter 8: Data Management and Laboratory Notebooks, Burroughs Wellcome Fund and the Howard Hughes Medical Institutes.
http://www.medschool.vcu.edu/gp/HHMIMakingtheRightMoves2ndEd.html

NCSU Policy on Lab Notebook Maintenance
http://www.ncsu.edu/sparcs/compliance/integrity/lab_notebooks_supplement.doc

Record keeping advice from legal firms that specialize in intellectual property law

Fish and Richardson, P.C.

http://www.fr.com/practice/pdf/LABBOOK2.pdf

BTG

http://www.btgplc.com/btguploads/BTG_LabNotebook_Mar06.pdf

Pillsbury Winthrop Shaw Pittman

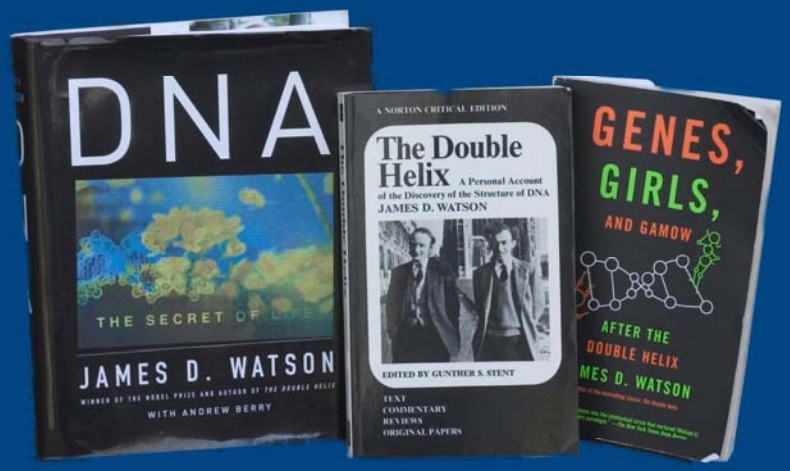
http://www.pillsburylaw.com/bv/bvisapi.dll/portal/ep/paPubDetail.do/pub/000052A2/channelId/-8595/pagetypeId/9203/tabId/0

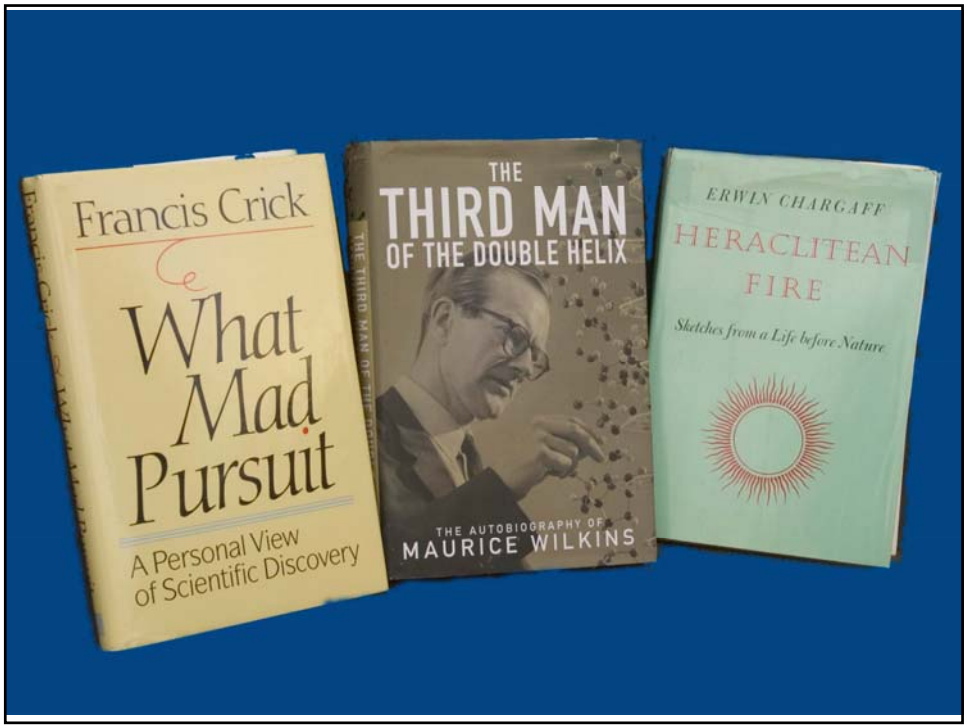
Fabrication
Falsification
Plagiariarm

and

The Risk of Confusing Conduct with Misconduct in Science

The Discovery of the Structure of DNA





No. 4356 April 25, 1953 NATURE 737

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1 Young, F. B., Gerard, H., and Jevons, W., *Phil. Mag.*, **40**, 149 (1920).
2 Longuet-Higgins, M. S., *Mon. Not. Roy. Astro. Soc., Geophys. Supp.*, **5**, 285 (1949).
3 Van Atta, W. S., Woods Hole Papers in Phys. Oceanog. Meteor., **11** (3) (1950).
4 Ekman, V. W., *Arkiv. Mat. Astron. Fysik. (Stockholm)*, **2** (11) (1905).

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 inter-twined 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 di-ester groups joining 5-D-deoxy-ribofuranose 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 form (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 inter-atomic 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 King's College, London. One of us (J. D. W.) has been aided by a fellowship from the National Foundation for Infantile Paralysis.

J. D. Watson
F. H. C. Crick
Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems,
Cavendish Laboratory, Cambridge.
April 2.

1 Pauling, L., and Corey, R. B., *Nature*, **171**, 346 (1953); *Proc. U.S. Nat. Acad. Sci.*, **39**, 84 (1953).
2 Furberg, S., *Acta Chem. Scand.*, **6**, 634 (1952).
3 Chargaff, E., for references see Zamenhof, S., Erwerman, G., and Chargaff, E., *Biochim. et Biophys. Acta*, **9**, 402 (1952).
4 Wyatt, G. R., *J. Gen. Physiol.*, **36**, 201 (1952).
5 Astbury, W. T., Symp. Soc. Exp. Biol. 1, Nucleic Acid, 66 (Camb. Univ. Press, 1947).
6 Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, **10**, 192 (1953).

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[1] Young, F. B., Gerard, H., and Jevons, W., *Phil. Mag.*, **40**, 149 (1925).

[2] Longuet-Higgins, M. S., *Mem. Nat. Roy. Astro. Soc., Geophys. Supp.*, **5**, 285 (1949).

[3] Von Arx, W. S., Woods Hole Papers in Phys. Oceanog. Meteor., **11** (3) (1950).

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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 form (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.

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J. D. Watson
F. H. C. Crick

Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems,
Cavendish Laboratory, Cambridge.
April 2.

[1] Pauling, L., and Corey, R. B., *Nature*, **171**, 346 (1953); *Proc. U.S. Nat. Acad. Sci.*, **39**, 84 (1953).

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[5] Astbury, W. T., Symp. Soc. Exp. Biol. 1, Nucleic Acid, 66 (Camb. Univ. Press, 1947).

[6] Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, **10**, 192 (1953).

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Giving Credit

[3]Chargaff, E., for references see Zamenhof, S., Brawerman, G, and Chargaff, E. *Biochim et Biophys. Acta* 9:402 (1952)

No. 4356 April 25, 1953 NATURE 737

equipment, and to Dr. G. E. R. Deacon and the captain and officers of R.R.S. *Discovery II* for their part in making the observations.

[1] Young, F. B., Gerard, H., and Jevons, W., *Phil. Mag.*, **40**, 149 (1925).
[2] Longuet-Higgins, M. S., *Mon. Not. Roy. Astro. Soc., Geophys. Supp.*, **5**, 285 (1949).
[3] Van Arx, W. S., Woods Hole Papers in Phys. Oceanog. Meteor., **11**, 59 (1950).
[4] Ekman, V. W., *Arkiv. Mat. Astron. Fysik.* (Stockholm), **2** (11) (1905).

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 inter-twined 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.

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738 NATURE

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Properly acknowledging

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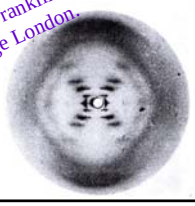
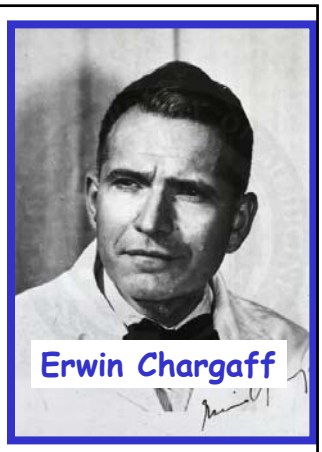


Case 1:

Nitrogenous Base Pairs
and
the Structure of
DNA

Columbia Univ. (Erwin Chargaff)
Kings College (Maurice Wilkins, Rosalind Franklin)
Cambridge Univ. (James Watson Francis Crick)
Cal Tech (Linus Pauling)

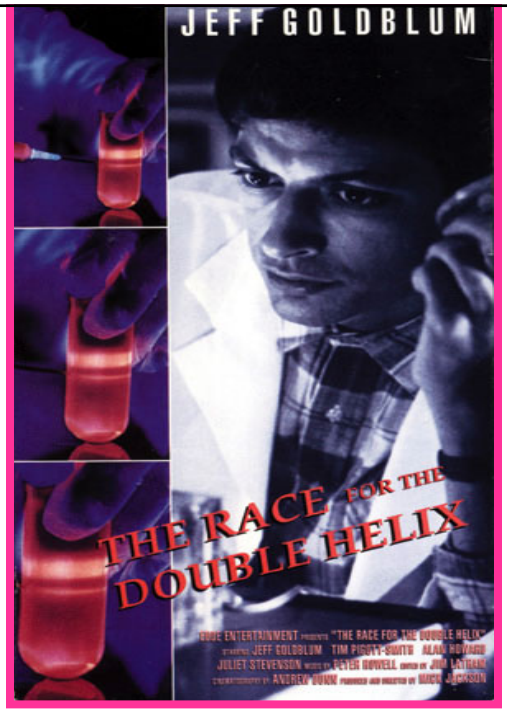
James D. Watson Francis Crick



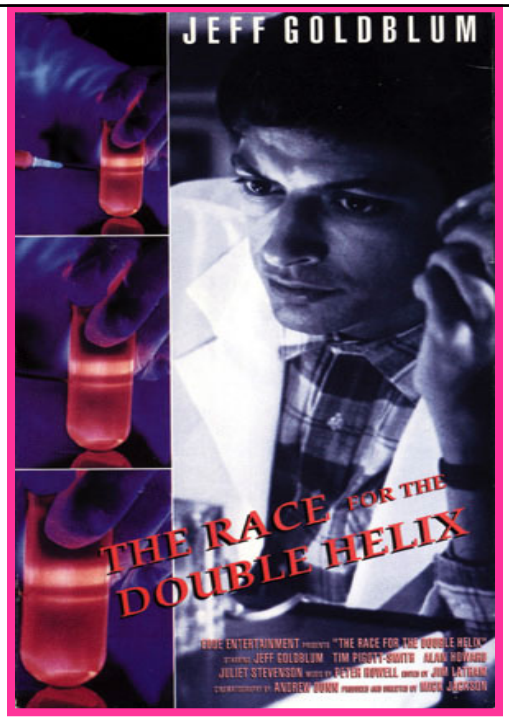
Erwin Chargaff

Erwin Chargaff's analysis of DNA (1950):

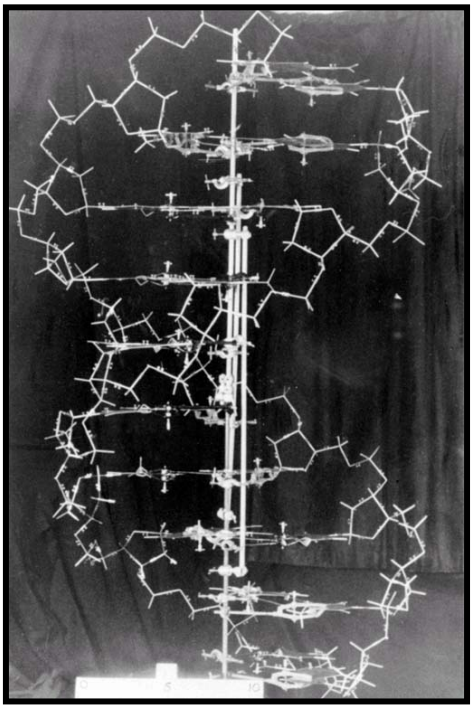
	Relative amounts of N-bases in: Ox Thymus		Ox spleen	
Expt #:	1	2	1	2
Adenine	.26	.28	.25	.26
Guanine	.21	.24	.20	.21
Cytosine	.16	.18	.15	.17
Thymine	.25	.24	.24	.24

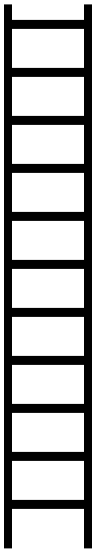


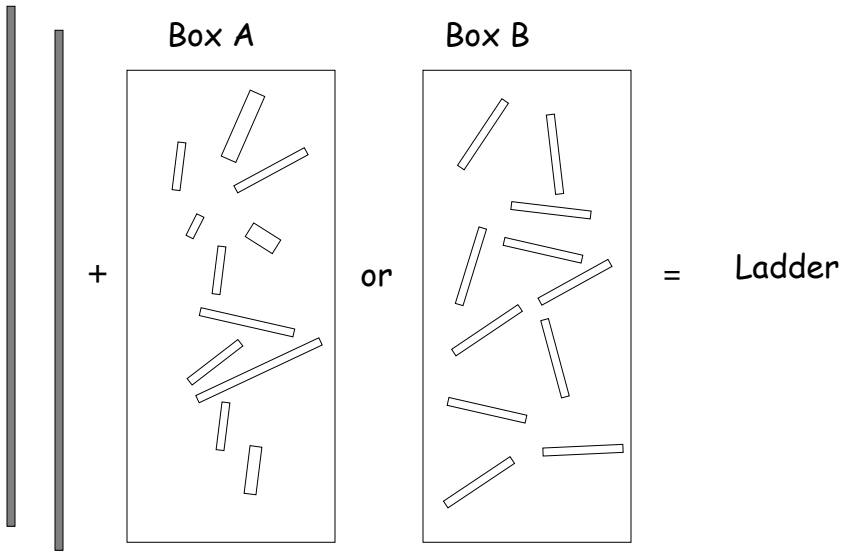
A conversation with Dr. Chargaff



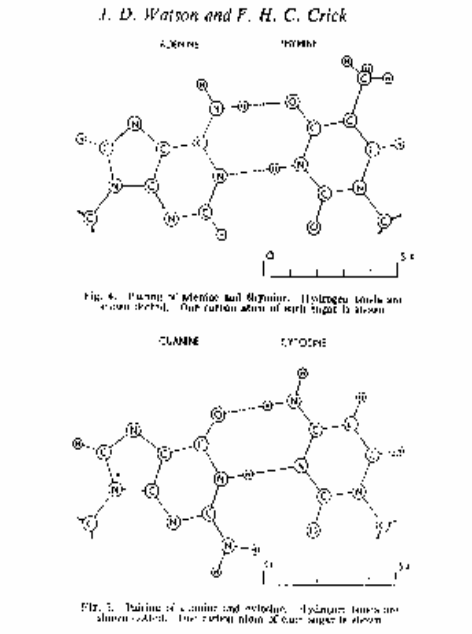
Base pairing

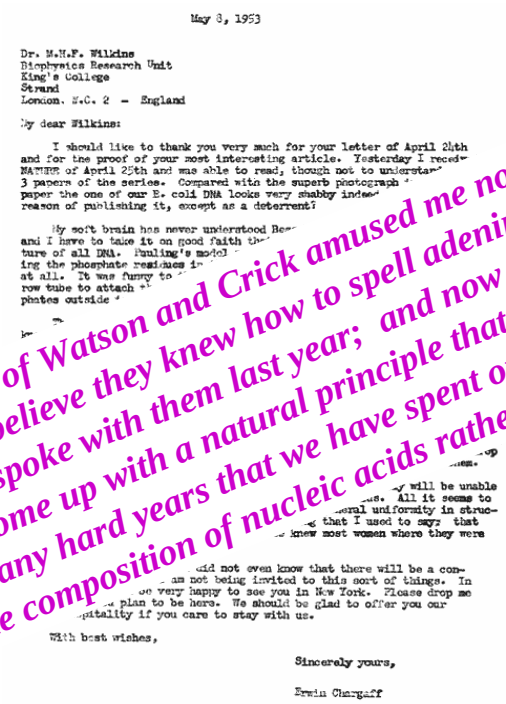






Which box of rungs will you select to build your ladder?





May 3, 1953

Dr. M.H.F. Wilkins
Biophysics Research Unit
King's College
Strand
London. W.C. 2 - England

My dear Wilkins:

I should like to thank you very much for your letter of April 24th and for the proof of your most interesting article. Yesterday I recei- NATURE of April 25th and was able to read, though not to understan- 3 papers of the series. Compared with the superb photograph paper the one of our E. coli DNA looks very shabby indee- reason of publishing it, except as a deterrent?

My soft brain has never understood Bea- and I have to take it on good faith th- ture of all DNA. Pauling's model - ing the phosphate residues i- at all. It was funny to - row tube to attach +- phates outside -

k- -s

-up
-em.

-y will be unable
-s. All it seems to
-eral uniformity in struc-
-t that I used to say: that
- knew most women where they were

-did not even know that there will be a con- - am not being invited to this sort of things. In -e very happy to see you in New York. Please drop me - plan to be here. We should be glad to offer you our -pitality if you care to stay with us.

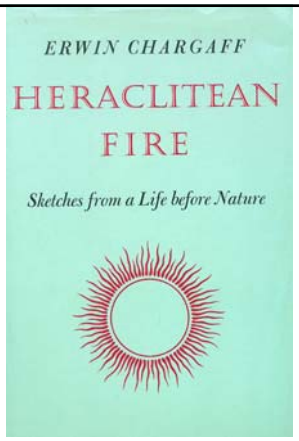
With best wishes,

Sincerely yours,

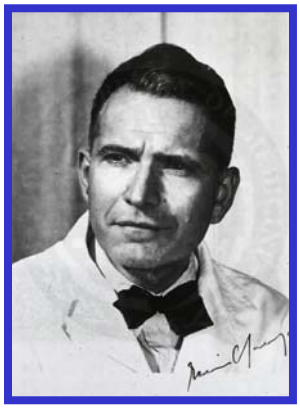
Erwin Chargaff

"The note of Watson and Crick amused me no end. I do not believe they knew how to spell adenine when I spoke with them last year; and now they have come up with a natural principle that makes the many hard years that we have spent on getting at the composition of nucleic acids rather wasted."

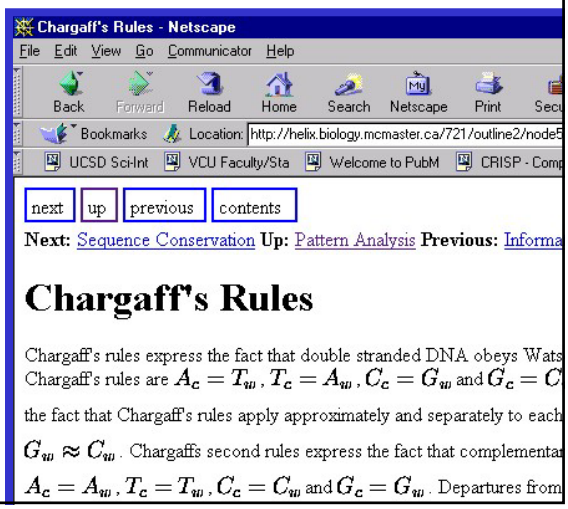
1978



So far as I could make out, they wanted, unencumbered by any knowledge of the chemistry involved, to fit DNA into a helix…I told them all I knew. If they had heard about the pairing rules, they concealed it. But as they did not seem to know much about anything, I was not unduly surprised.



Erwin Chargaff



The New York Times
nytimes.com

June 30, 2002

Erwin Chargaff, 96, Pioneer In DNA Chemical Research

By NICHOLAS WADE

But in a fateful and testy lunch in May 1952, he discussed his results with Dr. Watson and Mr. Crick (who did not yet have his doctorate).

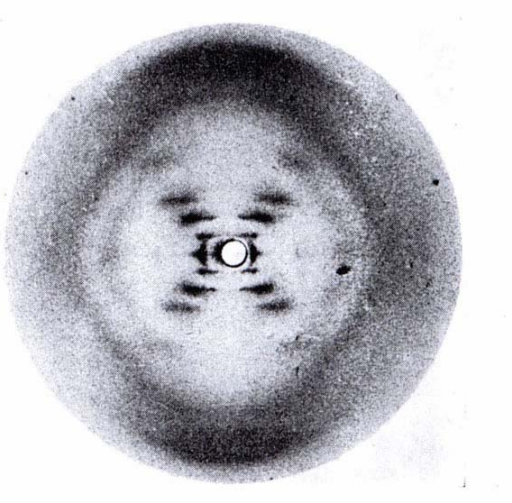
"They impressed me by their extreme ignorance," he later told Horace Judson, the historian of the discovery of DNA. "They told me they wanted to construct a helix, a polynucleotide to rival Pauling's alpha helix. They talked so much about 'pitch' that I remember I wrote down afterwards, 'Two pitchmen in search of a helix.' "

Though Dr. Chargaff tended toward the sardonic, it was hard for observers to understand the depth of his bitterness in his attitude to his fellow scientists. The reason, besides his disappointment at having missed discovering the structure of DNA, was that he was pushed to the sidelines by Dr. Crick in the worldwide effort to interpret the structure

Was Dr. Chargaff robbed
of the credit he deserved?

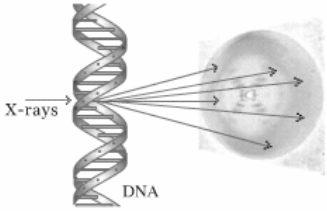
Case 2:

X-ray Crystallography
and
the Structure of
DNA



Rosalind Franklin and the Secret of Photograph 51

ANATOMY OF PHOTO 51 NOVA



Franklin aimed X-rays at a vertically suspended fiber the thickness of a single hair that contained millions of strands of the "B" or wet form of DNA from the thymus of a calf. First discovered by Franklin, the B form of DNA is the form found within a living cell.

close

Using X-rays

Franklin used a technique called X-ray diffraction to capture DNA, a molecule too small to image using regular photography. X-rays can create pictures of minuscule structures like DNA because their wavelengths are so short that X-rays actually bounce off atoms. As if inside a microscopic pinball machine, X-rays passing through the DNA molecule ricochet off molecular structures in their path and scatter, or diffract, in different directions. As the X-rays exit the DNA they leave behind a pattern on a piece of photographic film.

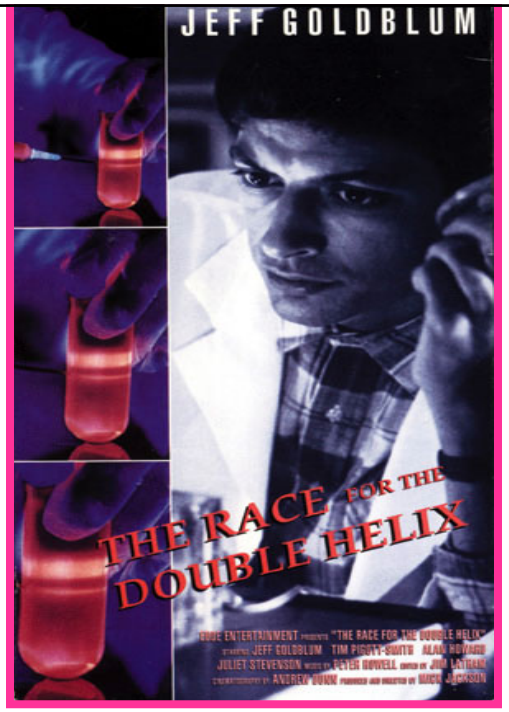
Watson, who was shown the image by Franklin's boss Maurice Wilkins without Franklin's knowledge, instantly saw the solution to problems he and Francis Crick had in determining the structure of DNA.

View X-ray diffraction diagram

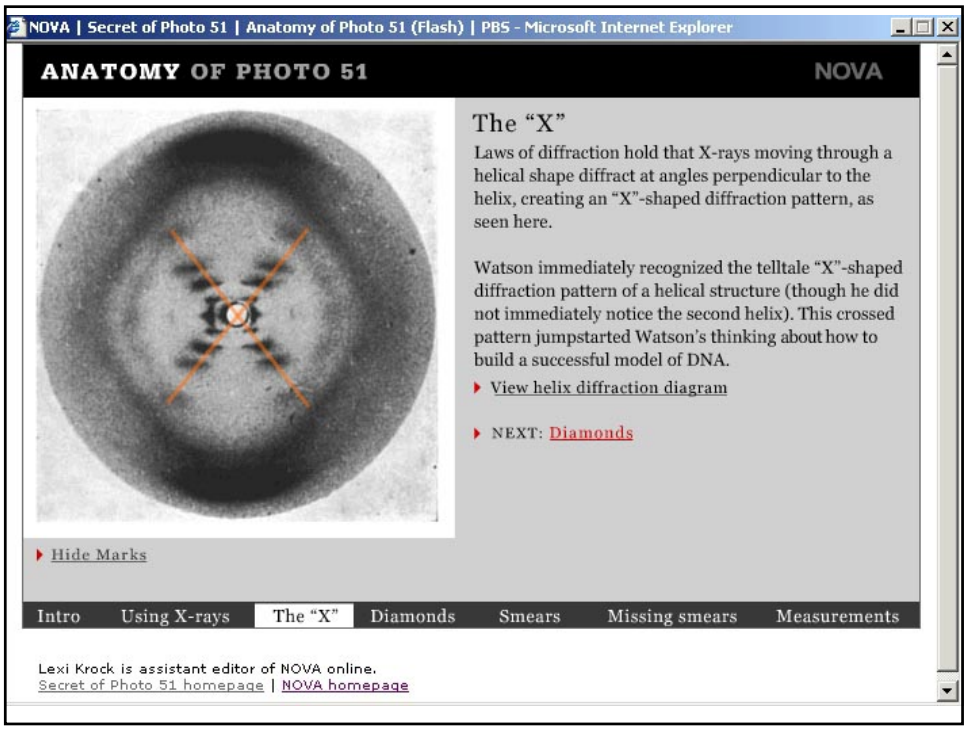
NEXT: The "X"

Intro | Using X-rays | The "X" | Diamonds | Smears | Missing smears | Measurements

Lexi Krock is assistant editor of NOVA online.
Secret of Photo 51 homepage | NOVA homepage



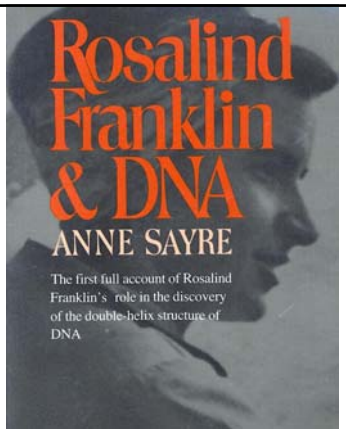
The secret of photograph 51



p. 190

Rosalind has been robbed, little by little; it is a robbery against which I protest. And so this book has been written. Robert Frost said it better,

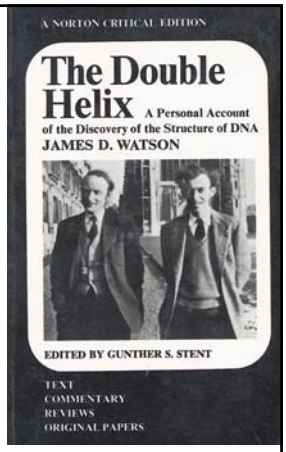
> Of all crimes the worst
> Is to steal the glory . . .
> Even more accursed
> Than to rob the grave



1975

Rosy, of course, did not directly give us her data. For that matter, no one at King's realized they were in our hands.

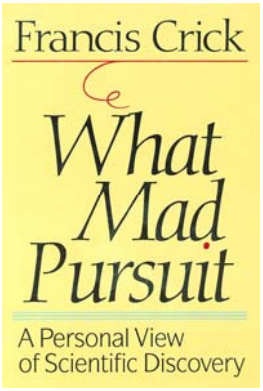
The minute I saw the picture my mouth fell open and my pulse began to race.



1968
1980

p. 68

People have discussed the handicap that Rosalind suffered in being both a scientist and a woman. Undoubtedly, there were irritating restrictions – she was not allowed to have coffee in one of the faculty rooms reserved for men only – but these were mainly trivial, or so it seemed to me at the time.



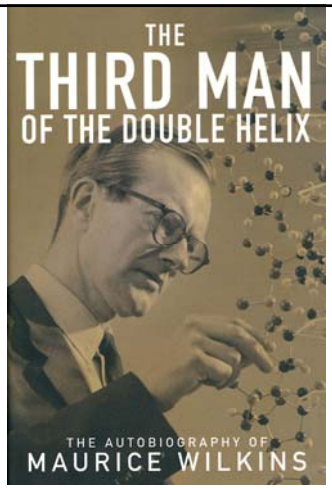
1988

p. 69

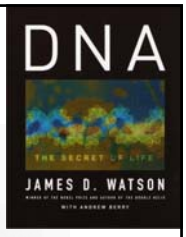
Then Randall changed his mind and suggested that, as the DNA fiber work (which Maurice had been doing) had become interesting, it might be better if she worked on that. I doubt if Rosalind know very much about DNA before Randall suggested that she work on it.

p. 129

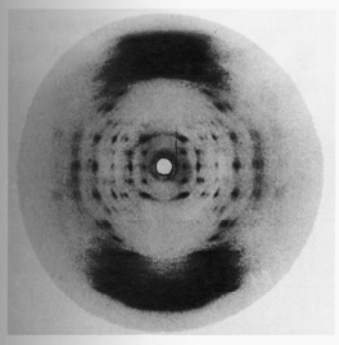
While I was away, Rosalind Franklin had taken up her new post at King's. . . I had arranged for Raymond (Gosling) to work with Rosalind because I thought that as a research student he should be supervised by an X-ray expert.

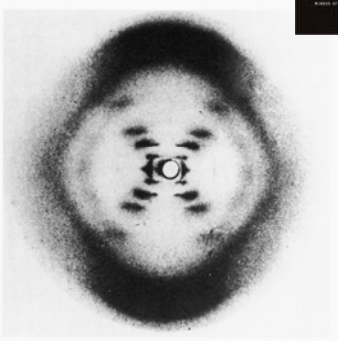


2003



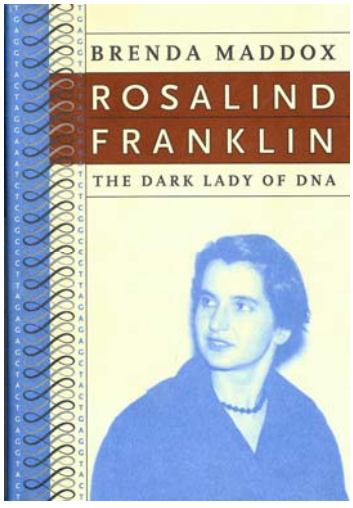
The Double Helix





X-ray photos of the A and B forms of DNA from, respectively, Maurice Wilkins and Rosalind Franklin. The differences in molecular structure are caused by differences in the amount of water associated with each DNA molecule.

2002

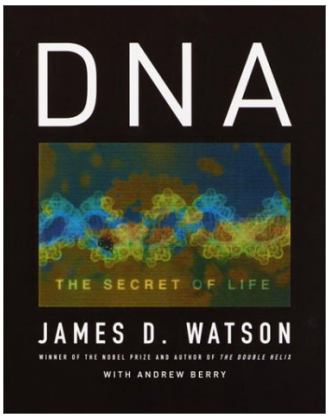


I think you will be interested to know that our dark lady leaves us next week… at last the decks are clear and we can put all hands to the pumps! …It won't be long now…M

"There's a myth which is, you know, that Francis and I basically stole the structure from the people at King's. I was shown Rosalind Franklin's x-ray photograph and, Whooo! that was a helix, and a month later we had the structure, and Wilkins should never have shown me the thing. I didn't go into the drawer and steal it, it was shown to me, and I was told the dimensions, a repeat of 34 angstroms, so, you know, I knew roughly what it meant and, uh, but it was that the Franklin photograph was the key event. It *was*, psychologically, it mobilized us..."

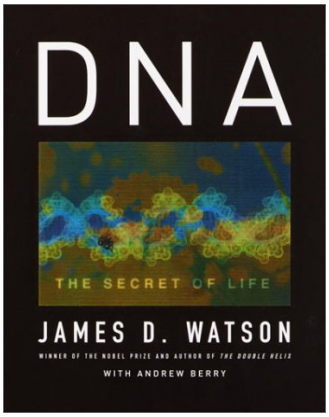
James Watson, Center for Genomic Research Inauguration, Harvard. September 30, 1999.

2003



p. 50-51 [Wilkins] showed me a photograph obtained more than six months earlier by Franklin's graduate student Raymond Gosling…until that moment I didn't know a B form even existed…Franklin had put that picture aside, preferring to concentrate on the A form…

2003



p. 51 She had decided to move on to avoid the unpleasantness at King's. Before leaving, she had been ordered to stop further work with DNA and had already passed on many of her diffraction images to Wilkins.

Was Dr. Franklin robbed of the credit she deserved?

Major Elements of Responsible Conduct of Research

Subject protection

-appropriate use of humans and animals in research

Research integrity

-data management, sharing and ownership
-authorship and publication practices
-peer review
-mentoring
-collaborative research

Fiscal Accountability

-proper use of research funds
-conflict of interest

Environmental Health and Safety Issues

-training and compliance

http://www.courses.vcu.edu/rcr/