1. PŘEDNÁŠKA

2013-14

Nucleic acids

Historical view

Emil Paleček

Institute of Biophysics, Acad. Sci. CR v.v.i., 612 65 Brno
Czech Republic

The Road to DNA started in Brno

G.J. Mendel
1866

F. Miescher
Tübingen 1871

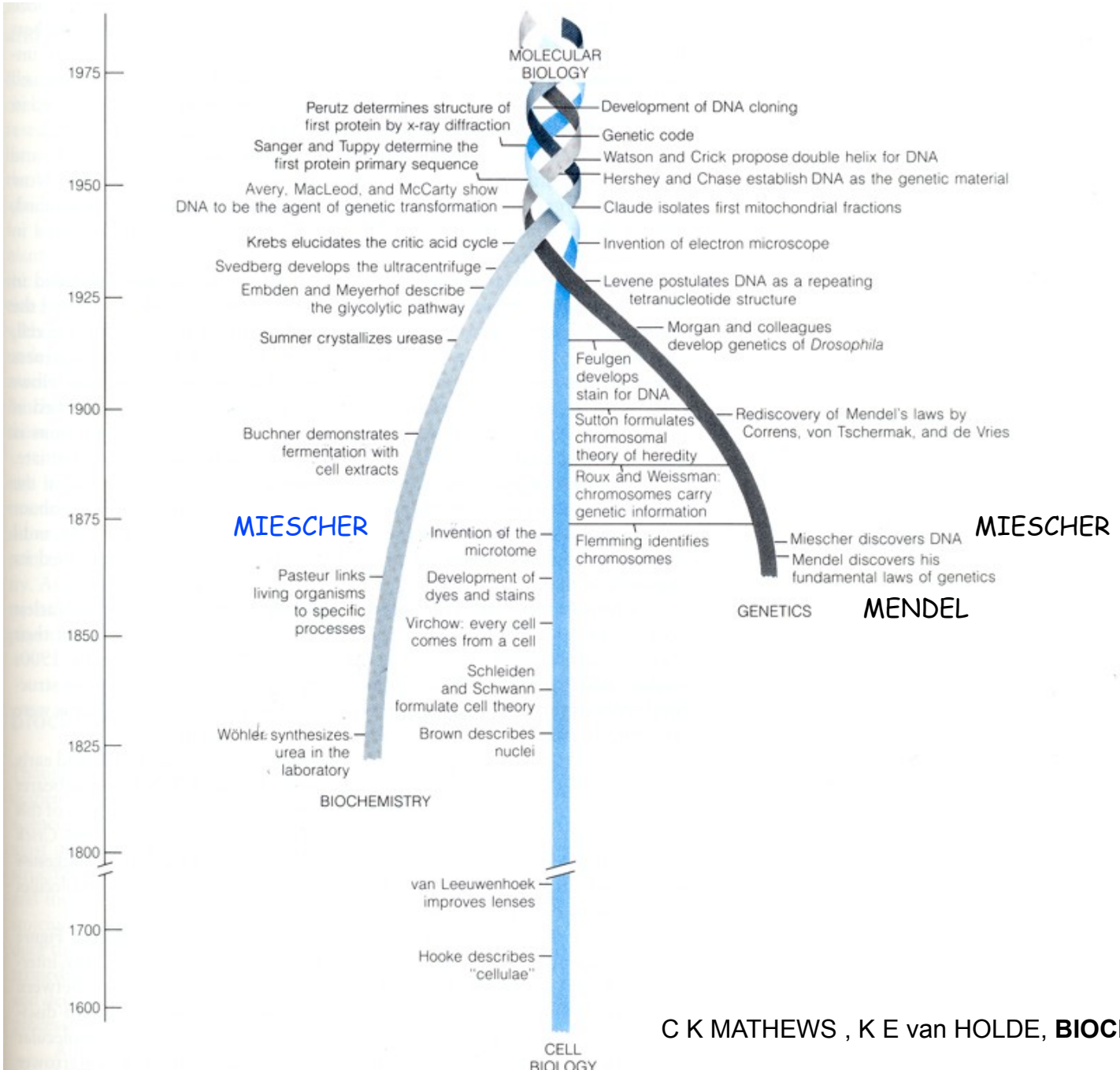
NUCLEIC ACIDS

"NUCLEIN" Isolation
Chemical nature and spatial organization
STRUCTURE

F. MIESCHER, TÜBINGEN
1871

"ELEMENTS OF HEREDITY"
Biological **FUNCTION**

G. J. MENDEL, BRNO
1866



C K MATHEWS , K E van HOLDE, **BIOCHEMISTRY,** 1990

Figure 1.2
Interweaving of the historical tradition of biochemistry, cell biology, and genetics. These three disciplines, which originally were considered to be quite separate, have become intertwined to yield a true molecular biology, the subject matter of present-day biochemistry.

Timeline of DNA

1865: **Gregor Mendel** discovers through breeding experiments with peas that traits are inherited based on specific laws (later to be termed "Mendel's laws"). By mentioning Elements of Heredity he predicts DNA and genes (published 1866)
1866: Ernst Haeckel proposes that the nucleus contains the factors responsible for the transmission of hereditary traits.
1869: **Friedrich Miescher** isolates DNA/NUCLEIN for the first time.
1871: The first publications describing DNA (nuclein) **by F Miescher, Felix Hoppe-Seyler**, and P. Plosz are printed.

1882: Walther Flemming describes **chromosomes** and examines their behavior during cell division.
1884–1885: Oscar Hertwig, Albrecht von Kölliker, Eduard Strasburger, and August Weismann independently provide evidence that the cell's **nucleus contains the basis for inheritance**.
1889: Richard Altmann renames **nuclein** to **nucleic acid**.
1900: Carl Correns, Hugo de Vries, and Erich von Tschermak **rediscover Mendel's Laws**.

1902: T Boveri and W Sutton postulate that the **heredity units** (called genes as of 1909) are located **on chromosomes**.
1902–1909: A Garrod proposes that **genetic defects** result in the loss of enzymes and hereditary metabolic diseases.
1909: Wilhelm Johannsen uses the word **gene** to describe units of heredity.
1910: T H **Morgan** uses fruit flies (**Drosophila**) as a model to study heredity and finds the **first mutant** with white eyes.
1913: Alfred **Sturtevant** and Thomas Hunt **Morgan** produce the first **genetic linkage map** (for the fruit fly Drosophila).

1928: Frederick **Griffith** postulates that a **transforming principle** permits properties from one type of bacteria (heat-inactivated virulent Streptococcus pneumoniae) to be transferred to another (live nonvirulent Streptococcus pneumoniae).
1929: P **Levene** identifies the **building blocks of DNA,** incl. four bases adenine (A), cytosine (C), guanine (G), thymine (T) .
1941: George **Beadle** and Edward **Tatum** demonstrate that **every gene is responsible for the production of an enzyme**.
1944: Oswald T. **Avery**, Colin **MacLeod**, and Maclyn **McCarty** demonstrate that Griffith's **transforming principle is not a protein, but** rather **DNA**, suggesting that DNA may function as the genetic material

1949: Colette and Roger **Vendrely** and A **Boivin** discover that the nuclei of **germ cells contain half the amount of DNA** that is found in somatic cells. This parallels the reduction in the number of chromosomes during gametogenesis and provides further evidence for the fact that DNA is the genetic material.
1949–1950: Erwin **Chargaff** finds that the DNA base composition varies between species but determines that the bases in DNA are always present in fixed ratios: the **same number of A's as T's and the same number of C's as G's.**
1952: Alfred **Hershey** and Martha **Chase** use viruses (bacteriophage T2) to confirm DNA as the genetic material by demonstrating that during infection viral DNA enters the bacteria while the viral proteins do not and that this DNA can be found in progeny virus particles.

1953: Rosalind **Franklin** and Maurice **Wilkins** use **X-ray analyses** to demonstrate that **DNA** has a regularly repeating **helical structure.**
1953: James **Watson** and Francis **Crick** discover the molecular structure of DNA: a **double helix** in which A always pairs with T, and C always with G.
1956: Arthur **Kornberg** discovers **DNA polymerase**, an enzyme that replicates DNA.
1957: Francis **Crick** proposes the **central dogma** (information in the DNA is translated into proteins through RNA) **1958**: Matthew **Meselson** and Franklin **Stahl** describe how DNA replicates (semiconservative replication).

1960-63: Julius **Marmur** and Paul **Doty** show separation of DNA strands and reformation of DNA double-helical structure – DNA **renaturation/hybridization**
1961–1966: Robert W. **Holley**, Har Gobind **Khorana**, Heinrich **Matthaei**, Marshall W. **Nirenberg**, and colleagues **crack the genetic code**.
1968–1970: Werner **Arber**, Hamilton **Smith**, and Daniel **Nathans** use **restriction enzymes** to cut DNA in specific places for the first time.
1972: **Paul Berg** uses restriction enzymes to create the first piece of **recombinant DNA**.
1977: Frederick **Sanger**, Allan Maxam, and Walter **Gilbert** develop **methods to sequence DNA**.

1982: The first drug (human insulin), based on recombinant DNA, on the market.
1983: Kary **Mullis** invents **PCR** as a method for amplifying DNA in vitro.
1990: Sequencing of the human genome begins.
1995: First complete sequence of the genome of a free-living organism (the bacterium Haemophilus influenzae) is published.
1996: The complete genome sequence of the first eukaryotic organism—the yeast S. cerevisiae—is published.

1998: Complete genome sequence of the first multicellular organism—the nematode worm Caenorhabditis elegans—is published.
1999: Sequence of the **first human chromosome (22)** is published.
2000: The complete sequences of the genomes of the **fruit fly Drosophila** and the **first plant—Arabidopsis**—are published.
2001: The complete sequence of the **human genome** is published.
2002: The complete genome sequence of the first mammalian model organism—the **mouse**—is published.

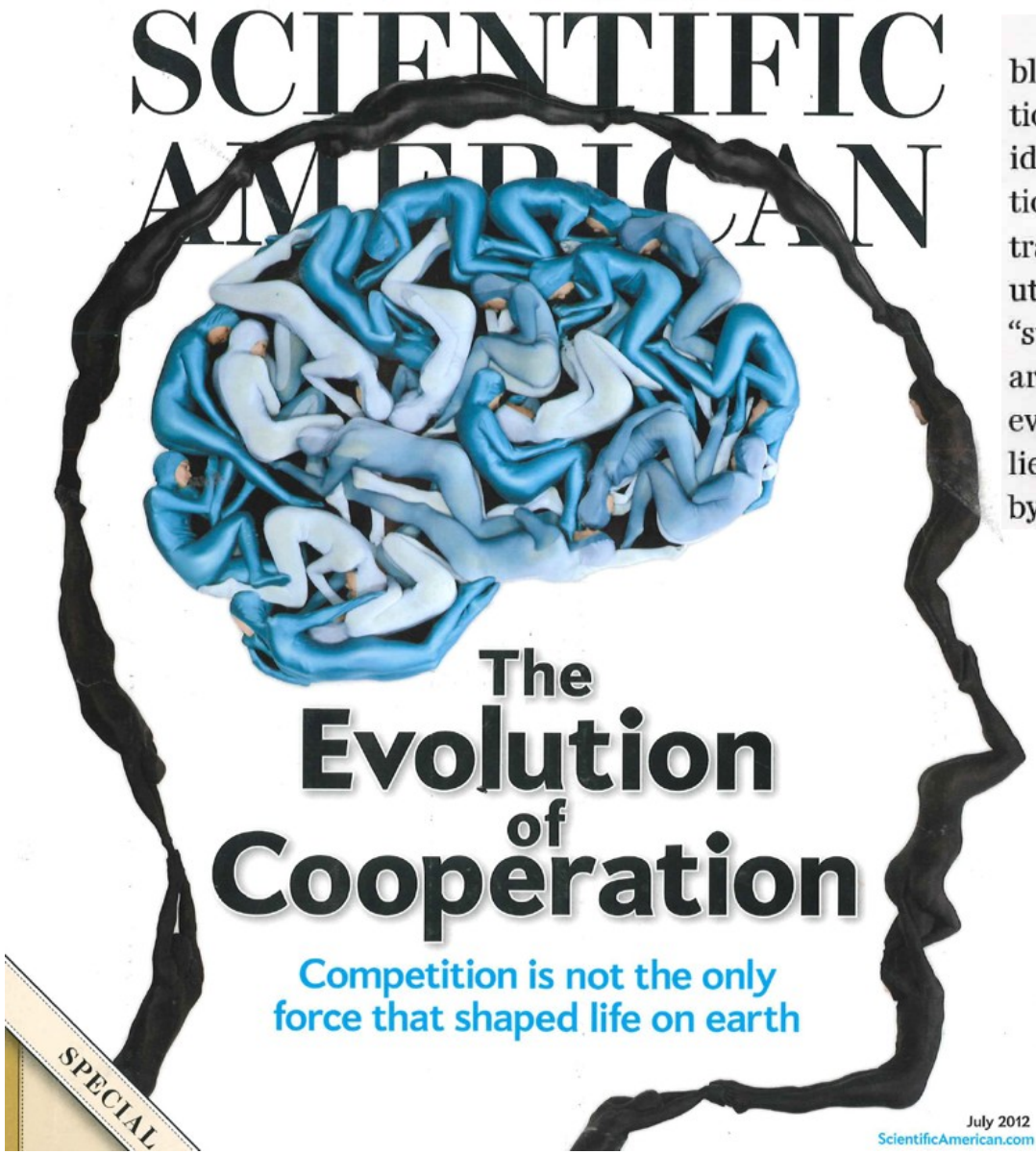
Darwin C. 1859: Book - On the Origin of Species by Means of Natural Selection
Mendel G. 1866
Miescher F. 1871 papers

Charles Darwin - Important claims:
A. Universal Common Descent - Tree of Life - the first one-celled organism, representing the root or trunk of the Tree, gradually developed and changed over many generations into new and more complex forms, representing the branches

B. Natural Selection as a mechanism responsible for the branching pattern
Variations in living forms arise at random
Nature selects the adaptive ones
Adaptive organism survive and reproduce
Inherited adaptations may cause population changes

Darwin understand neither how genetic traits were passed to the progeny nor how the variations arose. He is a founder of Evolution Biology

At present: - Natural Selection as a mechanism for relatively simple processes is fully confirmed but also cooperation played a significant role
- Universal Common Descent - Tree of Life and the role of natural selection in the origin of species are questioned



For decades biologists have fretted over cooperation, scrambling to make sense of it in light of the dominant view of evolution as "red in tooth and claw," as Alfred, Lord Tennyson so vividly described it. Charles Darwin, in making his case for evolution by natural selection—wherein individuals with desirable traits reproduce more often than their peers and thus contribute more to the next generation—called this competition the "struggle for life most severe." Taken to its logical extreme, the argument quickly leads to the conclusion that one should never ever help a rival and that an individual might in fact do well to lie and cheat to get ahead. Winning the game of life—by hook or by crook—is all that matters.

Far from being a nagging exception to the rule of evolution, cooperation has been one of its primary architects

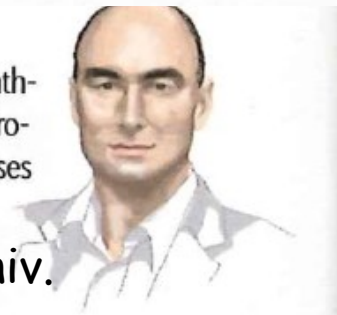
IN BRIEF

People tend to think of evolution as a strictly dog-eat-dog struggle for survival. In fact, cooperation has been a driving force in evolution.

There are five mechanisms by which cooperation may arise in organisms ranging from bacteria to human beings.

Humans are especially helpful because of the mechanism of indirect reciprocity, which is based on reputation and leads us to help those who help others.

Martin A. Nowak is a professor of biology and mathematics at Harvard University and director of the Program for Evolutionary Dynamics. His research focuses on the mathematical underpinnings of evolution.



Math & Biology, Vienna Univ.

I FIRST BECAME INTERESTED in cooperation back in 1987, as a graduate student studying mathematics and biology at the University of Vienna. While on a retreat with some fellow students and professors in the Alps, I learned about a game theory paradox called the Prisoner's Dilemma that elegantly illustrates why cooperation has so flummoxed evolutionary biologists. The dilemma goes like this: Imagine that two people have been arrested and are facing jail sentences for having conspired to commit a crime. The prosecutor questions each one privately and lays out the terms of a deal. If one person rats on the other

BASICS

Natural Defection

A game theory paradox called the Prisoner's Dilemma illustrates why the existence of cooperation in nature is unexpected. Two people face jail sentences for conspiring to commit a crime. Their sentences depend on whether they elect to cooperate and remain silent or defect and confess to the crime [*see payoff table below*]. Because neither knows what the other will do, the rational choice—the one that always offers the better payoff—is to defect.

		INDIVIDUAL 2: COOPERATE (remain silent)	INDIVIDUAL 2: DEFECT (confess)
INDIVIDUAL 1: COOPERATE (remain silent)		2 years in jail 2 years in jail	4 years in jail 1 year in jail
INDIVIDUAL 1: DEFECT (confess)		1 year in jail 4 years in jail	3 years in jail 3 years in jail

The Prisoner's Dilemma seduced me immediately with its power to probe the relation between conflict and cooperation. Eventually my Ph.D. adviser, Karl Sigmund, and I developed techniques to run computer simulations of the dilemma using large communities rather than limiting ourselves to two prisoners. Taking these approaches, we could watch as the strategies of the individuals in these communities evolved from defection to cooperation and back to defection through cycles of growth and decline. Through the simulations, we identified a mechanism that could overcome natural selection's predilection for selfish behavior, leading would-be defectors to instead lend helping hands.

We started with a random distribution of defectors and cooperators, and after each round of the game the winners would go on to produce offspring who would participate in the next round. The offspring mostly followed their parents' strategy, although random mutations could shift their strategy. As the simulation ran, we found that within just a few generations all the individuals in the population were defecting in every round of the game. Then, after some time, a new strategy suddenly emerged: players would start by cooperating and then mirror their opponents' moves, tit for tat. The change quickly led to communities dominated by cooperators.

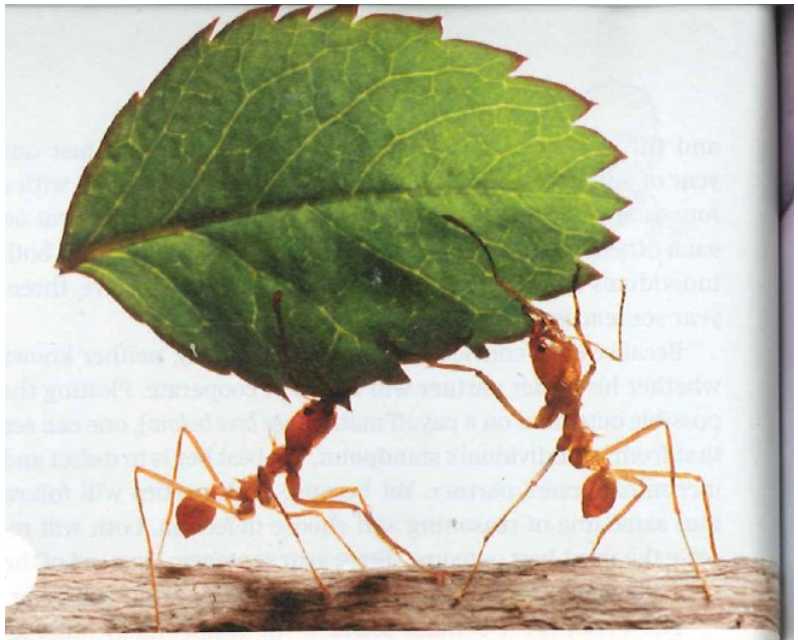
This mechanism for the evolution of cooperation among individuals who encounter one another repeatedly is known as direct reciprocity. Vampire bats offer a striking example. If a bat

In addition to direct reciprocity, I later identified four more mechanisms for the evolution of cooperation. In the several thousand papers scientists have published on how cooperators

A second means by which cooperation may find a foothold in a population is if cooperators and defectors are not uniformly distributed in a population—a mechanism termed spatial selection. Neighbors (or friends in a social network) tend to help one another, so in a population with patches of cooperators, these helpful individuals can form clusters that can then grow and thus prevail in competition with defectors. Spatial selection also operates among simpler organisms. Among yeast cells, cooperators make an enzyme used to digest sugar. They do this at a cost to themselves. Defector yeast, meanwhile, mooch off the cooperators' enzymes instead of making their own. Studies conducted by Jeff Gore of the Massachusetts Institute of Technology and, independently, by Andrew Murray of Harvard University have found that among yeast grown in well-mixed populations, the defectors prevailed. In populations with clumps of cooperators and defectors, in contrast, the cooperators won out.

DIRECT RECIPROCITY

Random distribution vs. **non-uniform** distribution of defectors and cooperators



HELPING OUT: Leaf-cutter ants work together to carry foliage back to their nest (*1*). Cells regulate their own division to avoid causing cancer (*2*). Lionesses cooperatively rear their young (*3*). Japanese macaques groom each other and thus burnish their reputations in their social group (*4*).

MORE TO EXPLORE

Five Rules for the Evolution of Cooperation. Martin A. Nowak in *Science*, Vol. 314, pages 1560–1563; December 8, 2006.

Super Cooperators: Altruism, Evolution, and Why We Need Each Other to Succeed. Martin A. Nowak, with Roger Highfield. Free Press, 2012.

SCIENTIFIC AMERICAN ONLINE

View a slide show of cooperative species at ScientificAmerican.com/jul2012/cooperation

Horizontal gene transfer - cell conglomerate instead of single cell ancestor

On the evolution of cells

Carl R. Woese*

Department of Microbiology, University of Illinois at Urbana-Champaign, 601 South Goodwin Avenue, B103 Chemical and Life Sciences Laboratory, Urbana, IL 61801-3709

Contributed by Carl R. Woese, May 3, 2002

A theory for the evolution of cellular organization is presented. The model is based on the (data supported) conjecture that the dynamic of horizontal gene transfer (HGT) is primarily determined by the organization of the recipient cell. Aboriginal cell designs are taken to be simple and loosely organized enough that all cellular componentry can be altered and/or displaced through HGT, making HGT the principal driving force in early cellular evolution. Primitive cells did not carry a stable organismal genealogical trace. Primitive cellular evolution is basically communal. The high level of novelty required to evolve cell designs is a product of communal invention, of the universal HGT field, not intralineage variation. It is the community as a whole, the ecosystem, which evolves. The individual cell designs that evolved in this way are nevertheless fundamentally distinct, because the initial conditions in each case are somewhat different. As a cell design becomes more complex and interconnected a critical point is reached where a more integrated cellular organization emerges, and vertically generated novelty can and does assume greater importance. This critical point is called the "Darwinian Threshold" for the reasons given.

The evolution of modern cells is arguably the most challenging and important problem the field of Biology has ever faced (1, 2). In Darwin's day the problem could hardly be imagined. For much of the 20th century it was intractable. In any case, the problem lay buried in the catch-all rubric "origin of life"—where, because it is a biological not a (bio)chemical problem, it was effectively ignored. Scientific interest in cellular evolution started to pick up once the universal phylogenetic tree, the framework within which the problem had to be addressed, was determined (refs. 3 and 4; Fig. 1). But it was not until microbial genomics arrived on the scene that biologists could actually do much about the problem of cellular evolution.

Initial attempts to frame the issue have typically been in the classical Darwinian mode, and the focus to date has been almost exclusively on modeling the evolution of the eukaryotic cell. The reason, of course, is clear—the appeal of the endosymbiosis concept. Because endosymbiosis has given rise to the chloroplast and mitochondrion, what else could it have done in the more remote past? Biologists have long toyed with an endosymbiotic (or cellular fusion) origin for the eukaryotic nucleus, and even for the entire eukaryotic cell (4–10). These classical explanations have three characteristics: they (*i*) invoke cells that are basically *fully evolved*; (*ii*) evolve the essential eukaryotic cell well *after* its archaeal and bacterial counterparts (as has always been connoted by the term "*pro*karyote"); and (*iii*) focus attention on eukaryotic cellular evolution, which implies that the evolutions of the "prokaryotic" cell types, the archaeal and bacterial, are of a *different character*—simpler, and, it would seem, less interesting. We cannot expect to explain cellular evolution if we stay locked into the classical Darwinian mode of thinking.

The universal phylogenetic tree in one sense brought classical evolution to culmination. Darwin had said: "The time will come . . . when we shall have very fairly true genealogical trees of each great kingdom of nature" (11). A century later the universal phylogenetic tree based on molecular (rRNA) sequence comparisons did precisely that and went the further, final step to unify all of the "great kingdoms" into one single "empire" (3). The central question posed by the universal tree is the nature of the entity (or state) represented by its root, the fount of all extant life. Herein lies the door to the murky realm of cellular evolution.

Experience teaches that the complex tends to arise from the simple, and biologists have assumed it so in the case of modern cells. But this assumption is usually accompanied by another not so self-evident one: namely that the "organism" represented by the root of the universal tree was equivalent metabolically and in terms of its information processing to a modern cell, in effect was a modern cell. Such an assumption pushes the real *evolution* of modern cells back into an earlier era, which makes the problem not directly addressable through genomics. *That* is not a scientifically acceptable assumption. Unless or until facts dictate otherwise, the possibility must be entertained that some part of cellular evolution *could* have occurred during the period encompassed by the universal phylogenetic tree.

There is evidence, good evidence, to suggest that the basic organization of the cell had not yet completed its evolution at the stage represented by the root of the universal tree. The best of this evidence comes from the three main cellular information-processing systems. Translation was highly developed by that stage: rRNAs, tRNAs, and the (large) elongation factors were by then all basically in near modern form; hence, their universal distributions. Almost all of the tRNA charging systems were in modern form as well (12). But, whereas the majority of ribosomal proteins are universal in distribution, a minority of them is not. A relatively small cadre is specific to the bacteria, a somewhat larger set common and confined to the archaea and eukaryotes, and a few others are uniquely eukaryotic.

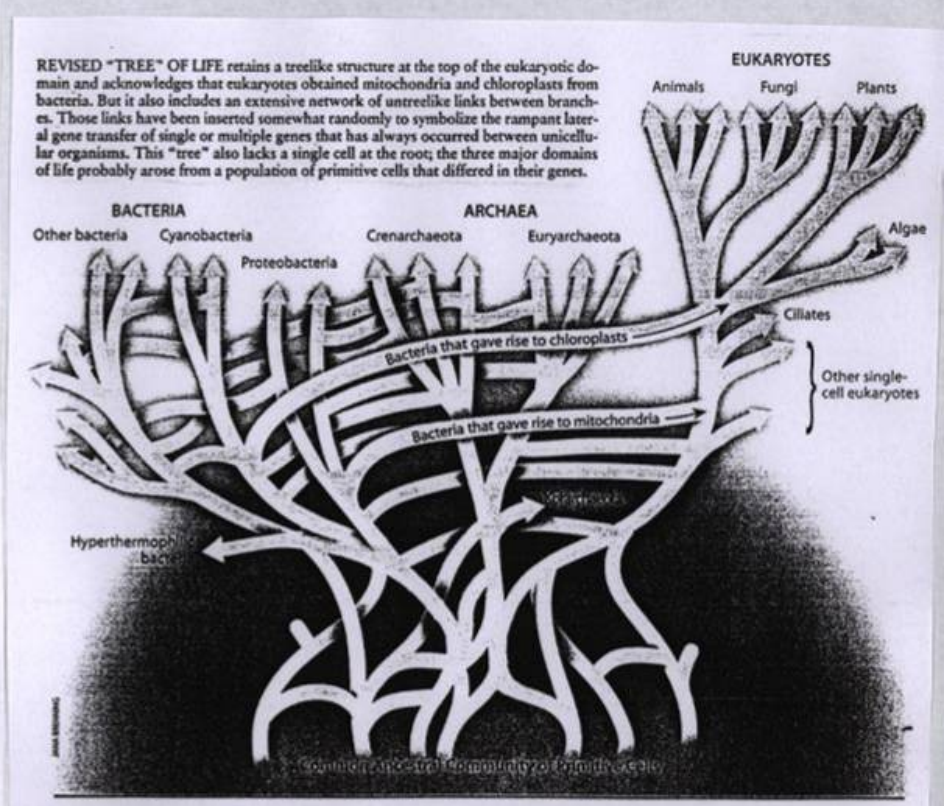
Almost all of the universal translational proteins (as well as those in transcription) show what is called the *canonical pattern*, i.e., the bacterial and archaeal versions of the protein are remarkably different from one another, so much so that their difference is distinguished as one of "genre" (12). Except for the aminoacyl-tRNA synthetases the corresponding eukaryotic versions are virtually all of the archaeal genre (12). Why canonical pattern exists is a major unanswered question (3). In the overall it would seem that translation, although highly developed at the root of the universal tree, subsequently underwent idiosyncratic modifications in each of the three major cell types.

Transcription seems to have been rather less developed at the root of the universal tree. The two largest (the catalytic) subunits of the DNA-dependent RNA polymerase, β and β′ in bacterial nomenclature, are universal in distribution. But the remaining bacterial subunit (α) is only partially so. Bacterial α exists in two copies in the bacterial polymerase. Its archaeal/eukaryotic counterpart comprises two distinct proteins, each present in single copy in the enzyme and (portions of) each showing homology to (somewhat different) portions of bacterial α and *vice versa* (13). A structural difference of this magnitude must represent at least some functional distinction. The archaeal transcription apparatus also contains additional (smaller) subunits, none of which are found in bacteria but all of which occur in eukaryotes (13). [As in the case of translation, the (three) eukaryotic mechanism(s) contain additional eukaryote-specific small subunits.] Bacterial transcription initiation does not re-

Abbreviations: HGT, horizontal gene transfer; SMA, supramolecular aggregate.

*E-mail: carl@phylo.life.uiuc.edu.

www.pnas.org/cgi/doi/10.1073/pnas.132268999



REVISED "TREE" OF LIFE retains a treelike structure at the top of the eukaryotic domain and acknowledges that eukaryotes obtained mitochondria and chloroplasts from bacteria. But it also includes an extensive network of untreelike links between branches. Those links have been inserted somewhat randomly to symbolize the rampant lateral gene transfer of single or multiple genes that has always occurred between unicellular organisms. This "tree" also lacks a single cell at the root; the three major domains of life probably arose from a population of primitive cells that differed in their genes.

The Author

W. FORD DOOLITTLE, who holds degrees from Harvard and Stanford universities, is professor of biochemistry and molecular biology at Dalhousie University in Halifax, Nova Scotia, and director of the Program in Evolutionary Biology of the Canadian Institute for Advanced Research.

Further Information

- THE UNIVERSAL ANCESTOR. Carl Woese in the *Proceedings of the National Academy of Sciences*, Vol. 95, No. 12, pages 6854–6859; June 9, 1998.
- YOU ARE WHAT YOU EAT: A GENE TRANSFER RACHET COULD ACCOUNT FOR BACTERIAL GENES IN EUKARYOTIC NUCLEAR GENOMES. W. Ford Doolittle in *Trends in Genetics*, Vol. 14, No. 8, pages 307–311; August 1998.
- PHYLOGENETIC CLASSIFICATION AND THE UNIVERSAL TREE. W. Ford Doolittle in *Science*, Vol. 284, pages 2124–2125; June 25, 1999.

ESSAY

Putting the pieces together

Biology's next revolution

The emerging picture of microbes as gene-swapping collectives demands a revision of such concepts as organism, species and evolution itself.

Nigel Goldenfeld and Carl Woese

One of the most fundamental patterns of scientific discovery is the revolution in thought that accompanies a new body of data. Satellite-based astronomy has, during the past decade, overthrown our most cherished ideas of cosmology, especially those relating to the size, dynamics and composition of the Universe.

Similarly, the convergence of fresh theoretical ideas in evolution and the coming avalanche of genomic data will profoundly alter our understanding of the biosphere — and is likely to lead to revision of concepts such as species, organism and evolution. Here we explain why we foresee such a dramatic transformation, and why we believe the molecular reductionism that dominated twentieth-century biology will be superseded by an interdisciplinary approach that embraces collective phenomena.

The place to start is horizontal gene transfer (HGT), the non-genealogical transfer of genetic material from one organism to another — such as from one bacterium to another or from viruses to bacteria. Among microbes, HGT is pervasive and powerful — for example, in accelerating the spread of antibiotic resistance. Owing to HGT, it is not a good approximation to regard microbes as organisms dominated by individual characteristics. In fact, their communications by genetic or quorum-sensing channels indicate that microbial behaviour must be understood as predominantly cooperative.

In the wild, microbes form communities, invade biochemical niches and partake in biogeochemical cycles. The available studies strongly indicate that microbes absorb and discard genes as needed, in response to their environment. Rather than discrete genomes, we see a continuum of genomic possibilities, which casts doubt on the validity of the concept of a 'species' when extended into the microbial realm. The uselessness of the species concept is inherent in the recent forays into metagenomics — the study of genomes recovered from natural samples as opposed to clonal cultures. For example, studies of the spatial distribution of rhodopsin genes in marine microbes suggest such genes are 'cosmopolitan', wandering among bacteria (or archaea) as environmental pressures dictate.

Equally exciting is the realization that viruses have a fundamental role in the biosphere, in both immediate and long-term

ZAHER.

memory of a community's genetic information, contributing to the system's evolutionary dynamics and stability. This is hinted at, for example, by prophage induction, in which viruses latent in cells can become activated by environmental influences. The ensuing destruction of the cell and viral replication is a potent mechanism for the dispersal of host and viral genes.

It is becoming clear that microorganisms have a remarkable ability to reconstruct their genomes in the face of dire environmental stresses, and that in some cases their collective interactions with viruses may be crucial to this. In such a situation, how valid is the very concept of an organism in isolation? It seems that there is a continuity of energy flux and informational transfer from the genome up through cells, community, virosphere and environment. We would go so far as to suggest that a defining characteristic of life is the strong dependency on flux from the environment — be it of energy, chemicals, metabolites or genes.

Nowhere are the implications of collective phenomena, mediated by HGT, so pervasive and important as in evolution. A computer scientist might term the cell's translational apparatus (used to convert genetic information to proteins) an 'operating system', by which all innovation is communicated and realized. The fundamental role of translation, represented in particular by the genetic code, is shown by the clearly documented optimization of the code. Its special role in any form of life leads to the striking prediction that more powerful early forms of HGT.

Refinement through the horizontal sharing of genetic innovations would have triggered an explosion of genetic novelty, until the level of complexity required a transition to the current era of vertical evolution. Thus, we regard as regrettable the conventional concatenation of Darwin's name with evolution, because other modalities must also be considered.

This is an extraordinary time for biology, because the perspective we have indicated places biology within a context that must necessarily engage other disciplines more strongly aware of the importance of collective phenomena. Questions suggested by the generic energy, information and gene flows to which we have alluded will probably require resolution in the spirit of statistical mechanics and dynamical systems theory. In time, the current approach of post-hoc modelling will be replaced by interplay between quantitative prediction and experimental test, nowadays more characteristic of the physical sciences.

Sometimes, language expresses ignorance rather than knowledge, as in the case of the word 'prokaryote', now superseded by the terms archaea and bacteria. We foresee that in biology, new concepts will require a new language, grounded in mathematics and the discoveries emerging from the data we have highlighted. During an earlier revolution, Antoine Lavoisier observed that scientific progress, like evolution, must overcome a challenge of communication: "We cannot improve the language of any science without at the same time improving the science itself; neither can we, on the other hand, improve a science without improving the language or nomenclature which belongs to it." Biology is about to meet this challenge. ■

Nigel Goldenfeld is in the Department of Physics and Institute for Genomic Biology, University of Illinois at Urbana-Champaign, 1110 West Green Street, Urbana, Illinois 61801, USA. Carl Woese is in the Department of Microbiology and Institute for Genomic Biology, 601 South Goodwin Avenue, Urbana, Illinois 61801, USA.

FURTHER READING
Frigaard, N., Martinez, A., Mincer, T. & DeLong, E. Nature 439, 847–850 (2006).
Sullivan, M. et al. PLoS Biol. 4, e234 (2006).
Pedulla, M. et al. Cell 113, 171–182 (2003).
Vetsigian, K., Woese, C. & Goldenfeld, N. Proc. Natl Acad. Sci. USA 103, 10696–10701 (2006).

CONNECTIONS

Thus we regard as regrettable the conventional concatenation of Darwin's name with evolution, because other modalities must also be considered

EVOLUČNÍ BIOLOGIE
- rychle se vyvíjející vědecká disciplina

vedle ní existuje IDEOLOGIE EVOLUCIONISMU

PODLE DARWINISTY M. RUSE NENÍ

BOJ EVOLUCIONISMU S KREACIONISMEM

BOJEM VĚDY S NÁBOŽENSTVÍM ALE

BOJEM NÁBOŽENSTVÍ S NÁBOŽENSTVÍM

M. Ruse, The Evolution-Creation Struggle
HARVARD UNIVERSITY PRESS , 2005

JOHANN GREGOR MENDEL

* 1822 in Hynčice (Moravia, Austro-Hungarian Empire)
\+ 1884 in Brno (buried at Central Cemetery in Brno)

discovered through breeding experiments with peas that traits are inherited based on specific laws (later to be termed "Mendel's laws"). By mentioning Elements of Heredity he predicted DNA and genes (published 1866, lecture in Brno 1965)

In the 1950´s Mendelism declared to be a reactionary teaching (LYSENKO, LEPESHINSKAYA)

Mendel statue removed and its destruction ordered
Brno geneticist J. Kříženecký jailed
His pupil V. Orel forced to work manually in industry

1964 attempts to rehabilitate Mendel
Academicians B. Němec (biologist) and F. ŠORM (biochemist, President of the Czechoslovak Academy of Sciences) backed by Soviet Academicians. Dealing between N. Khrushtchov, A. Novotný (President of Czechoslovakia), F. Šorm and biologist J. Pospíšil (later the Party Secretary) resulted in the decision to organize an international conference in 1968 (100 anniversary of publication of Mendel´s paper) in Brno (F. Šorm warned by Novotný that his attempts may result in the end of his career if the action will get out of control). Beginning of Mendel´s Museum in Brno

A milestone not only in the approach of Party and State to Mendel but also a beginning of rehabilitation of SCIENCE against the COMMUNIST IDEOLOGY

Brno Augustinians 1860-62 Abbot C. Napp

Mendel's Medal,
Moravian Museum, Brno

Abbot G. Mendel

Teachers of Brno gymnasium (High School)

G J MENDEL, priest, teacher,
scientist and abbot
in BRNO

THE STATUE STORY

In 1906 Dr. Hugo Iltis, the gymnasium professor in Brno organized an international collection to build the Mendel's Statue in Brno. Created by a French sculpturer T. Charlemont the Statue was errected at the Mendel Square in 1910

In 1956 Mendel's Statue was ordered by the Regional Authorities to be destroyed. The workers who were supposed to the job decided not to do it because they believed that the statue was nice. Moreover it would be difficult to destroy it.

After February 1948 Soviet „Lysenkism" (T. D. Lysenko 1896-1974) strongly affected biology in Czechoslovakia. After Stalin death (1953) attempts were made by soviet scientists (particularly by physists and chemists) to substitute Lysenko's „materialistic biology" for normal science and by the end of 1950's plans were made to organize in Brno International Mendel Memorial Symposium. In 1962 Lysenko's work was criticized by the Soviet Academy but still in September 1964 N.S. Khrushtchov raised objections against the Mendel Symposium in 1965 in Brno. During his visit in Prague he dealt with the President A. Novotny who finally agreed with the meeting organization after the President of the Academy F. Sorm personally guaranteed that the Symposium will not be politically misused. (F. Sorm was well informed about the activities of the influential Soviet scientist to rehabilitate fully the genetics - Soon after his visit of this country N.S. Khrushtchov was removed from his position).

Before the Symposium the Director of the Institute of Biophysics prof. F. Hercik was entrusted by the Academy to help with the organization of the Mendel International Meeting in Brno. To fulfill his duties he turned to the City Authorities asking to move the Mendel's Statue to the Abbey garden. As his request was ignored he asked his graduate students J. Koudelka and B. Janík to move the Statue from the Abbey yard to the garden. Both fellows were quite strong young men but they found the marble Statue too heavy.

1844 - 1895 Friedrich MIESCHER

1. sdělení v r. 1871

Žák **Hoppe-Seylera** v **Tübingen** se zabýval izolací jaderných komponent (z hnisajících buněk, které získával z tamnější chirurgie). Buňky hydrolyzoval pepsinem-HCl a po třepání s eterem izoloval jádra jako separovanou vrstvu na dně nádoby. Z tohoto materiálu **„nuklein“** - reagoval kysele, rychle se rozpouštěl ve zřeď. louhu a obsahoval velké množství P.

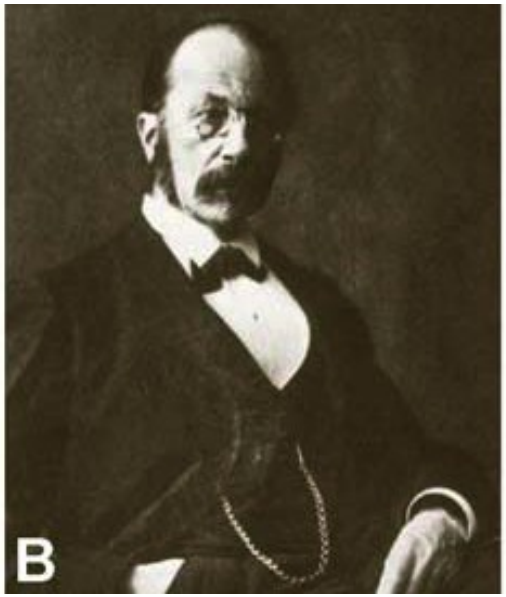
Vysoký obsah P byl považován za velmi pozoruhodný - jediná tehdy známá organická látka obsažená v tkáni - lecitin. Když F.M. předložil práci k publ. shledal ji H.S. tak překvapující, že ji odmítl uveřejnit, dokud ji sám neprověřil.

F.M. se pak vrátil do Baselu, kde nalezl **vhodnější materiál k izolaci nukleinu v hlavičkách spermií lososa** - z nich **nuklein o vysoké m.v.** a zásaditý materiál bílkovinné povahy, který nazval **protamin**; obsah P v nukleinu 9,59 %.

Purinové base (**A,G**) objevili **Piccard a Kossel (1874-85) U 1885, Altman** nazval nuklein poprvé **nukleová kyselina**, NK (**nukleinsäure**) (1889); **koncem 19. století** identifikován **T** a vzápětí **C**.

Kolem roku **1930** již známy **DNA** (thymus) a **RNA** (kvasnice) i jejich základní složení. Ve čtyřicátých letech - **DNA v jádře**, **RNA v cytoplazmě a jádře**.

F. Miescher

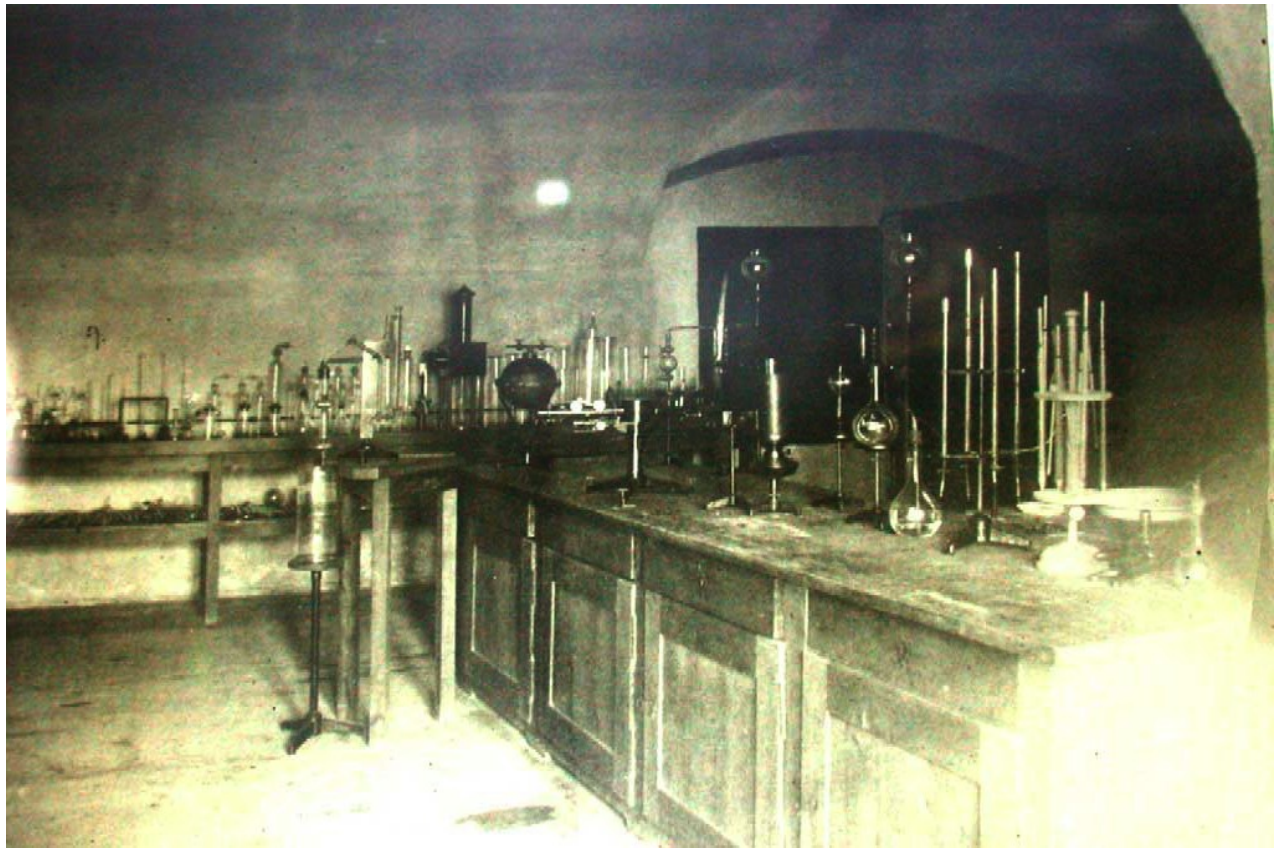


W. His
(FM's uncle)

F. Hoppe-Seyler
(supervisor)

A. STRECKER

Fig. 1. Friedrich Miescher and his mentors. (A) Friedrich Miescher (1844–1895) as a young man. (B) Wilhelm His (1831–1904), Miescher's uncle. His still is famous for his work on the fate of cells and tissues during embryonic development and for his insights into neuroembryology. He, for example, discovered neuroblasts and coined the term bdendriteQ (Finger, 1994; Shepherd, 1991). (C) Felix Hoppe-Seyler (1825–1895), one of the pioneers of physiological chemistry (now biochemistry). Hoppe-Seyler performed seminal work on the properties of proteins, most notably hemoglobin (which he named), introduced the term **proteid** (which later became **protein**), and worked extensively on fermentation and oxidation processes as well as lipid metabolism (Perutz, 1995). He was instrumental in founding Germany's first independent institute for physiological chemistry (in 1884) and in 1877 founded and edited the **first journal of biochemistry, the Zeitschrift fu¬r Physiologische Chemie**, which still exists today as Biological Chemistry. (D) Adolf Strecker (1822–1871), a leading figure in chemistry in the mid-19th century and professor at the University of Tubingen from 1860 to 1870. Among other achievements, he was the **first to synthesize amino acid (alanine** from acetaldehyde via its condensation product with ammonia and hydrogen cyanide) in a reaction known today as **Strecker synthesis** (Strecker, 1850). (E) Carl Ludwig (1816–1895), a protagonist in the field of physiology in the second half of the 19th century. His focus was the physiology of the nervous system and its sensory organs. In 1869, he founded Leipzig's Physiological Institute.

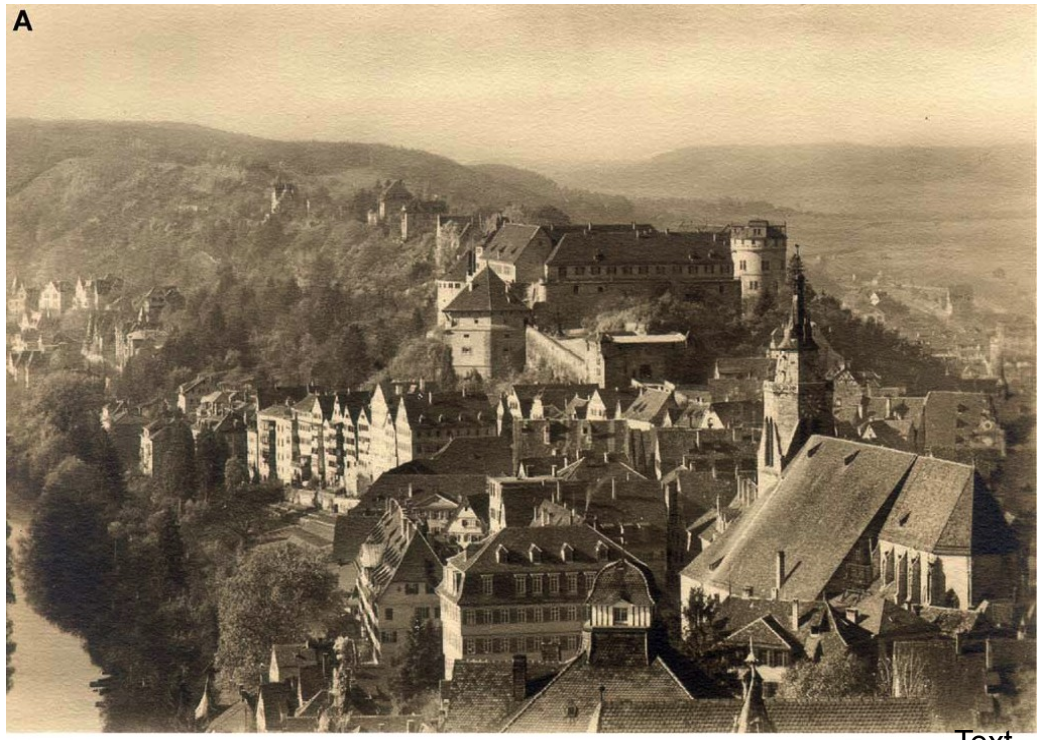


Hoppe-Seyler's laboratory around 1879

Fig. 2. Photograph of Felix Hoppe-Seyler's laboratory around 1879. Prior to becoming the chemical laboratory of Tübingen University in 1823, this room was Tübingen castle's laundry. Here, Hoppe-Seyler had made ground-breaking discoveries regarding the properties of hemoglobin. This achievement was a significant step for later investigations into the properties and functions of this and other proteins. Photography by Paul Sinner, Tübingen.

F. Miescher's laboratory

Fig. 4. The laboratory in the former kitchen of the castle in Tübingen as it was in 1879. It was in this room that Miescher had discovered DNA 10 years earlier. The equipment and fixtures available to Miescher at the time would have been very similar, with a large distillation apparatus in the far corner of the room to produce distilled water and several smaller utensils, such as glass desiccators and a glass distillation column on the side board. Photography by Paul Sinner, Tübingen.



Text

Tübingen castle

A, in Miescher's time

B, at present

FIRST PROTOCOL

Before attempting the isolation of cells from the pus on surgical bandages, Miescher took great care to ensure that his source material was fresh and not contaminated. He painstakingly examined it and discarded everything that showed signs of decomposition, either in terms of smell, appearance under the microscope, or by having turned acidic. A great deal of the material he could obtain did not meet these strict requirements (Miescher, 1871d). Those samples that did were subsequently used to isolate leucocytes.

In a first step, Miescher separated the leucocytes from the bandaging material and the serum (Miescher, 1869a, 1871d). This separation posed a problem for Miescher. Solutions of NaCl or a variety of alkaline or alkaline earth salt solutions used to wash the pus resulted in a “slimy swelling” of the cells, which was impossible to process further (His, 1897b). (This “slimy swelling” of the cells was presumably due to high-molecular-weight DNA, which had been extracted from cells that had been damaged.) Only when Miescher tried a dilute solution of sodium sulfate [a mixture of one part cold saturated Glauber’s salt (Na2SO4d 10 H2O) solution and nine parts water] to wash the bandages did he manage to successfully isolate distinct leucocytes, which could be filtered out through a sheet to remove the cotton fibers of the bandaging. Miescher subsequently let the washing solution stand for 1–2 h to allow the cells to sediment and inspected the leucocytes microscopically to confirm that they did not show any signs of damage.

Having isolated the cells, Miescher next had to separate the nuclei from the cytoplasm. This had never been achieved before and Miescher had to develop new protocols. He washed the cells by rinsing them several (6–10) times with fresh solutions of diluted (1:1000) hydrochloric acid over a period of several weeks at “wintry temperatures” (which were important to avoid degradation). This procedure removed most of the cells’ bprotoplasm,Q leaving behind the nuclei. The residue from this treatment consisted in part of isolated nuclei and of nuclei with only little fragments of cytoplasm left attached. Miescher showed that these nuclei could no longer be stained yellow by iodine solutions, a method commonly used at the time for detecting cytoplasm (Arnold, 1898; Kiernan, 2001).

He then vigorously shook the nuclei for an extended period of time with a mixture of water and ether. This caused the lipids to dissolve in the ether while those nuclei, still attached to cytoplasm, collected at the water/ether interface. By contrast, the clean nuclei without contaminating cytoplasm were retained in the water phase. Miescher filtered these nuclei and examined them under a microscope. He noticed that in this way he could obtain completely pure nuclei with a smooth contour, homogeneous content, sharply defined nucleolus, somewhat smaller in comparison to their original volumes (Miescher, 1871d).

Miescher subsequently extracted the isolated nuclei with alkaline solutions. When adding highly diluted (1:100,000) sodium carbonate to the nuclei, he noticed that they would swell significantly and become translucent. Miescher then isolated a yellow solution of a substance from these nuclei. By adding acetic acid or hydrochloric acid in excess, he could obtain an insoluble, flocculent precipitate (DNA). Miescher noted that he could dissolve the precipitate again by adding alkaline solutions.

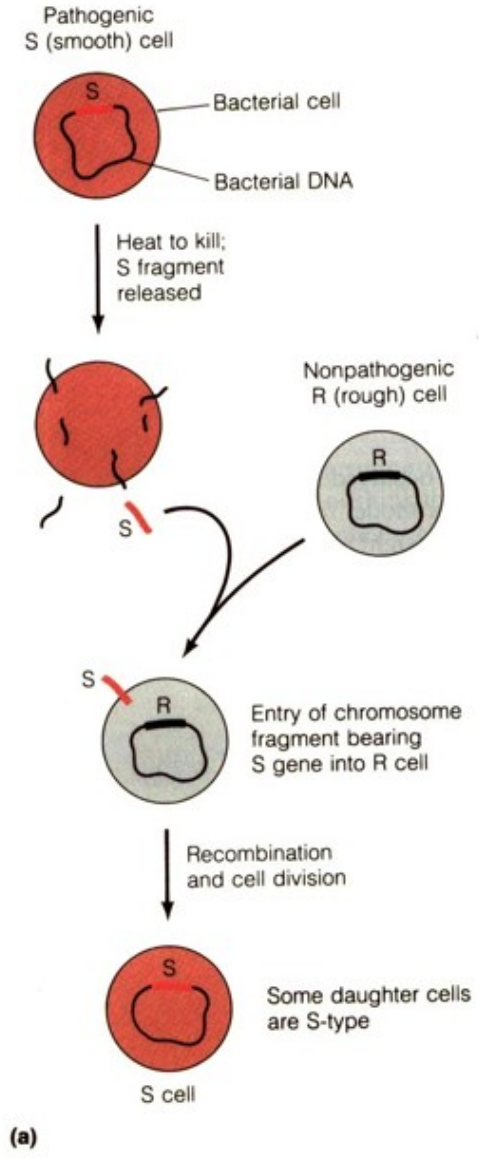
Although this protocol allowed Miescher for the first time to isolate nuclein in appreciable purity and quantities, it was still too little and not pure enough for his subsequent analyses. He consequently improved on this protocol until he established the protocol detailed in Box 2, which enabled him to purify sufficient amounts of nuclein for his first set of experiments on its elementary composition.

M. SECOND PROTOCOL TO ISOLATE DNA

A key concern of Miescher's was to get rid of contaminating proteins, which would have skewed his analyses of the novel substance. "I therefore turned to an agent that was already being used in chemistry with albumin molecules on account of its strong protein-dissolving action, namely, **pepsin** solutions (Miescher, 1871d). Pepsin is a proteolytic enzyme present in the stomach for digesting proteins. Miescher used it to separate the DNA from the proteins of the cells' cytoplasm. He extracted the pepsin for his experiments from pig stomachs by washing the stomachs with a mixture of 10 cc of fuming hydrochloric acid and one liter of water and filtering the resulting solution until it was clear. In contrast to his earlier protocol, Miescher first washed the pus cells (leucocytes) three or four times with warm alcohol to remove lipids. He then let the residual material digest with the pepsin solution between 18 and 24 h at 37–45 C. After only a few hours, a fine gray powdery sediment of isolated nuclei separated from a yellow liquid. Miescher continued the digestion process, changing the pepsin solution twice. After this procedure, a precipitate of nuclei without any attached cytoplasm formed. He shook the sediment several times with ether in order to remove the remaining lipids. Afterwards, he filtered the nuclei and washed them with water until there was no longer any trace of proteins. He described the nuclei isolated in this way as naked. The contours were smooth in some cases or slightly eaten away in others (Miescher, 1871d). Miescher washed the nuclei again several times with warm alcohol and noted that the nuclear mass cleaned in this way exhibited the same chemical behavior as the nuclei isolated with hydrochloric acid. Miescher subsequently extracted the isolated nuclei using the same alkaline extraction protocol he had previously employed on the intact cells (see Box 1) and, when adding an excess of acetic acid or hydrochloric acid to the solution, again obtained a precipitate of nuclein.

Fig. 5. Glass vial containing nuclein isolated from salmon sperm by Friedrich Miescher while working at the University of Basel. The faded label reads Nuclein aus Lachssperma, F. Miescher (Nuclein from salmon sperm, F. Miescher). Possession of the Interfakult-res Institut fqr Biochemie (Interfacultary Institute for Biochemistry), University of Tubingen, Germany; photography by Alfons Renz, University of Tubingen.

Fig. 6. This picture of Friedrich Miescher in his later years is the frontispiece on the inside cover of the two volume collection of Miescher's scientific publications, his letters, lecture manuscripts, and papers published posthumously by Wilhelm His and others (His et al., 1897a,b).



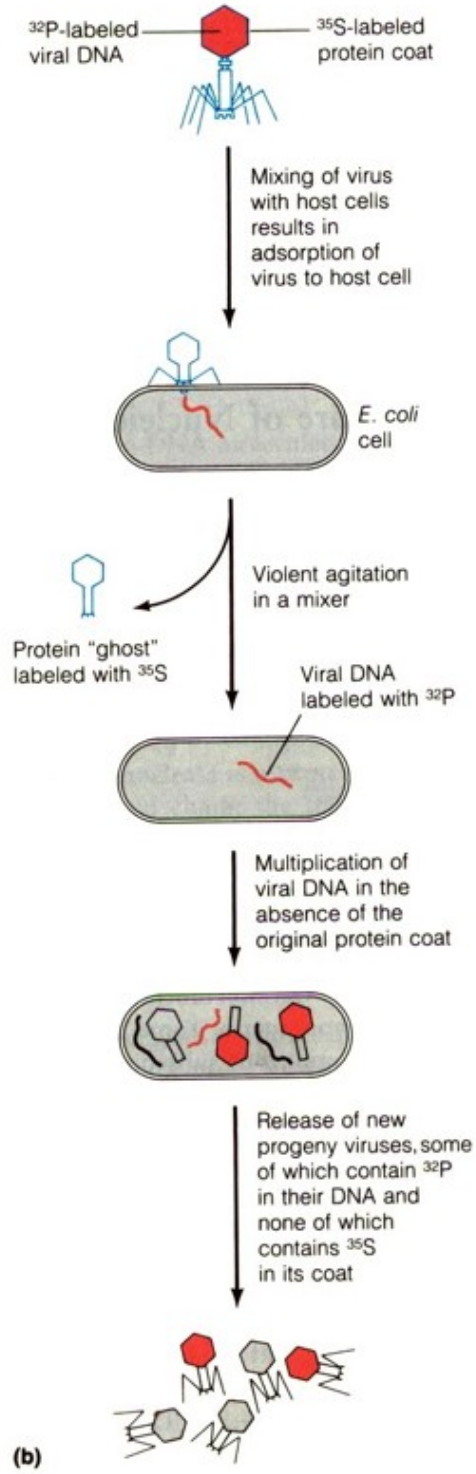


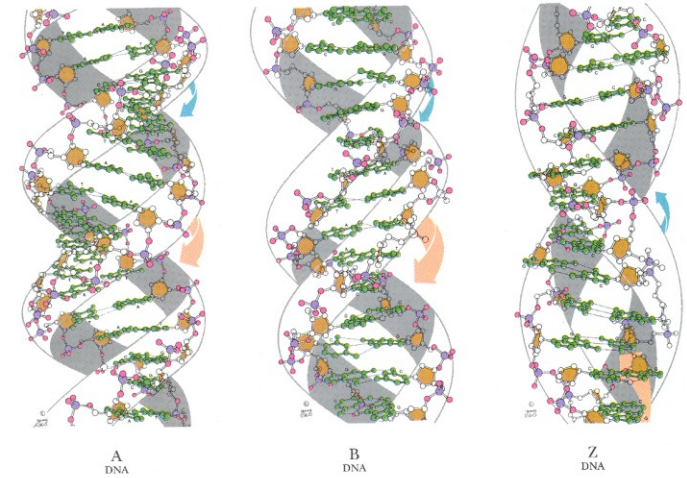
Figure 4.8
Crucial experiments that demonstrated DNA as the genetic substance. (a) The experiment of Avery et al. showing that nonpathogenic pneumococci could be made pathogenic by transfer of DNA from a pathogenic strain. (b) The experiment of Hershey and Chase showing that it is transfer of the DNA from a bacteriophage to a bacterium that gives rise to new bacteriophages.

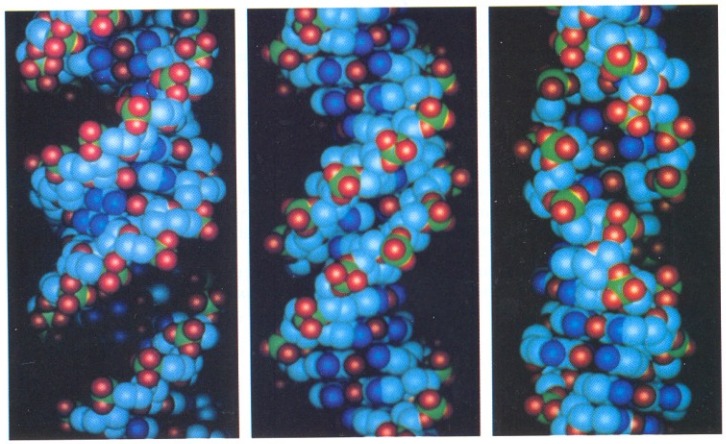
(a) 1944: Oswald T. **Avery**, Colin **MacLeod**, and Maclyn **McCarty** demonstrate that Griffith's **transforming principle is not a protein, but** rather **DNA**, suggesting that DNA may function as the genetic material

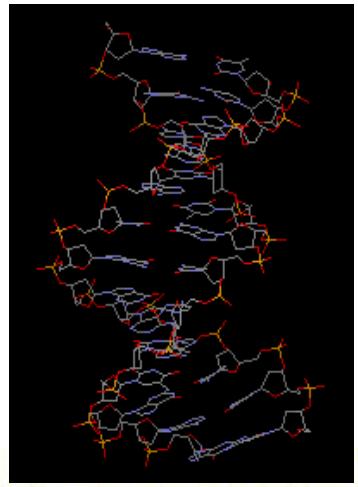
(b) 1952: Alfred **Hershey** and Martha **Chase** use viruses (bacteriophage T2) to confirm DNA as the genetic material by demonstrating that during infection viral DNA enters the bacteria while the viral proteins do not and that this DNA can be found in progeny virus particles.

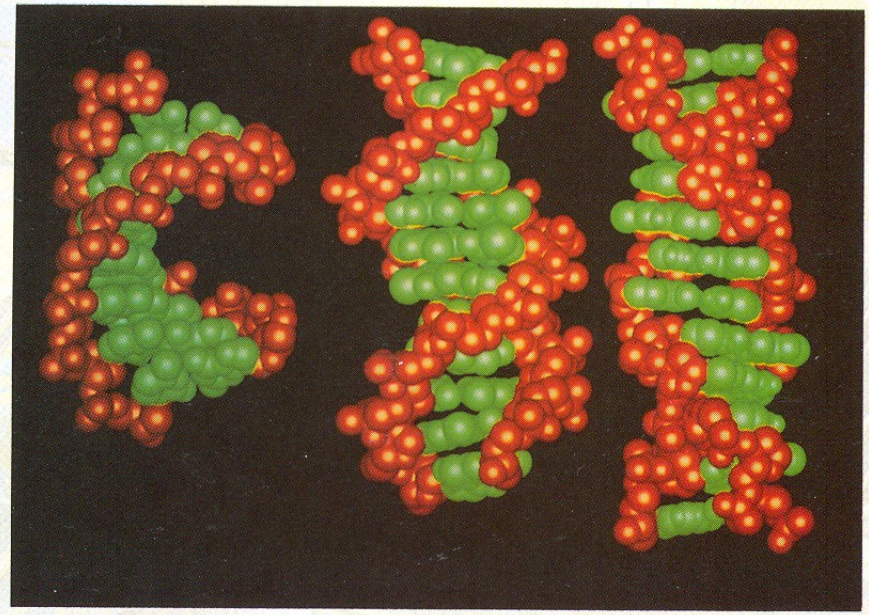
A, B and left-handed Z-DNA as we know them now

How did we arrive to them ?









Double helical conformations of DNA: (left) *A-DNA*, (center) *B-DNA*, (right) *Z-DNA*.

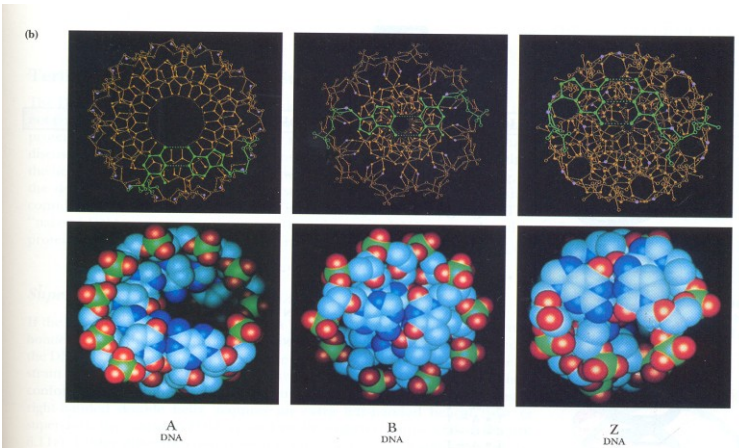
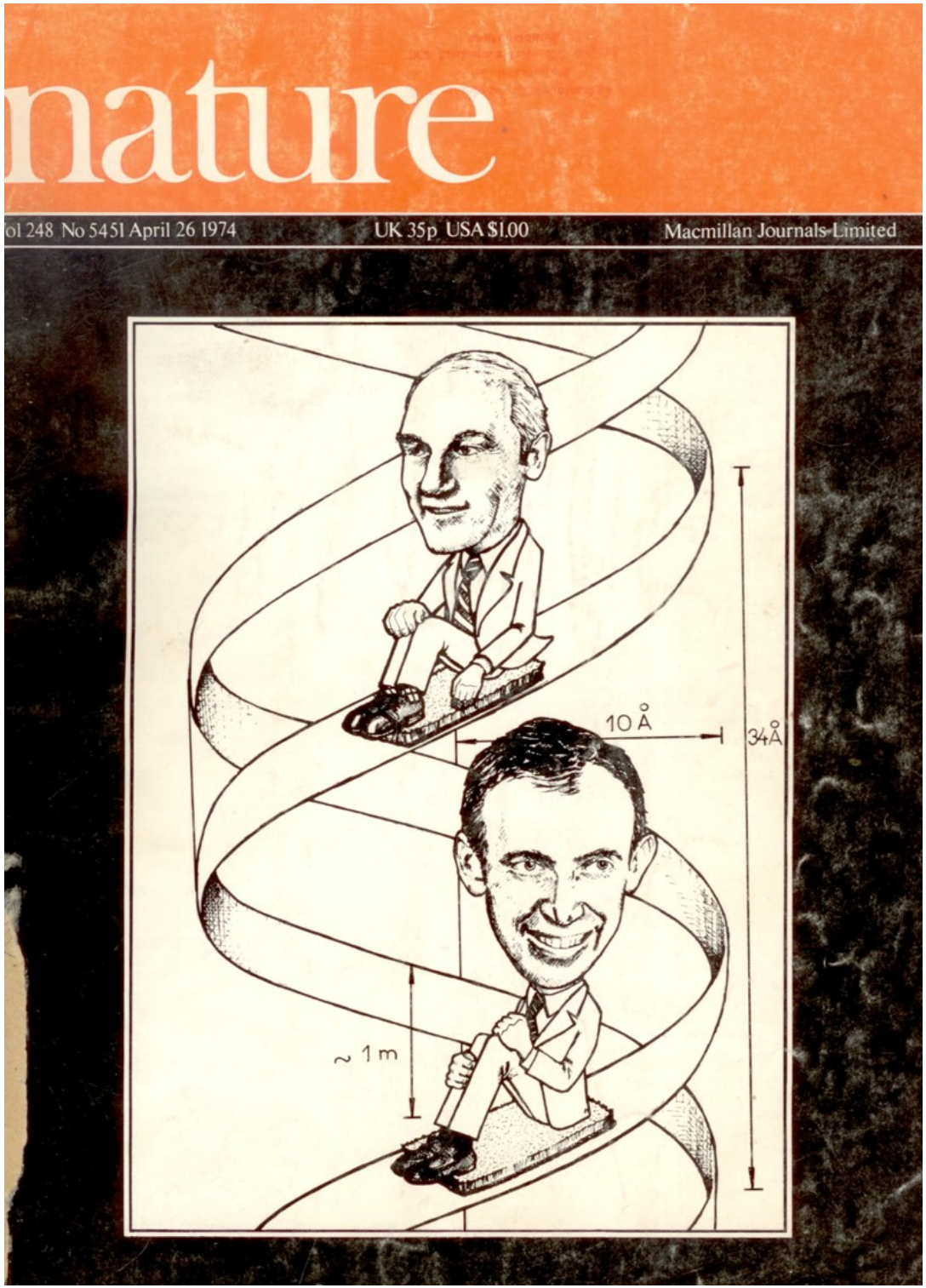


FIGURE 6.9
A comparison of the A, B, and Z forms of DNA. Part (a) shows side views of all



21st Anniversary:
The DNA Double Helix
Comes of Age

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 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 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.

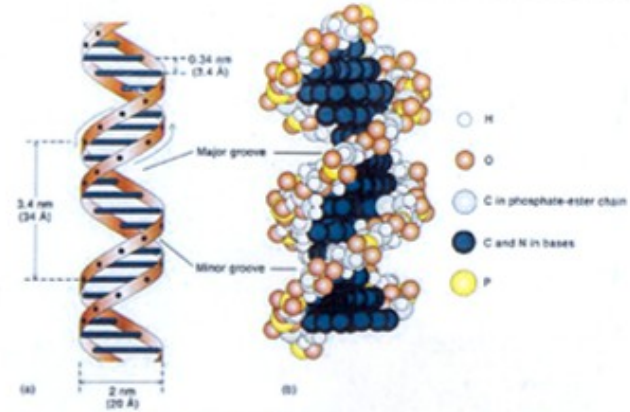
J. D. WATSON
F. H. C. CRICK

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

X-RAY FIBER ANALYSIS OF DNA

represented the main evidence for the Watson-Crick double helix model

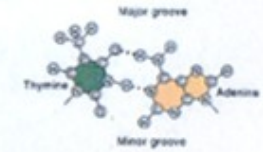
This method enabled analysis of high-molecular DNA, but provided only few basic parameters of the helix, such as



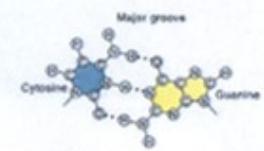
distance between base pairs

number of base residues per turn

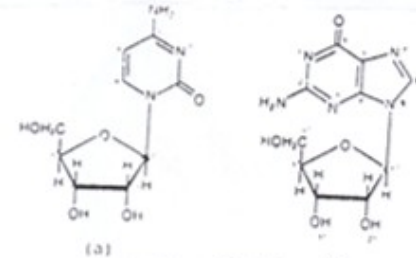
Further data were derived from model building considering the laws of structural chemistry



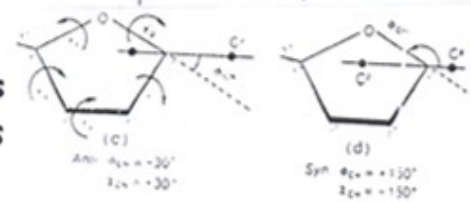
Base pairing from physical-chemical measurements



Sugar configuration (PUCKER)

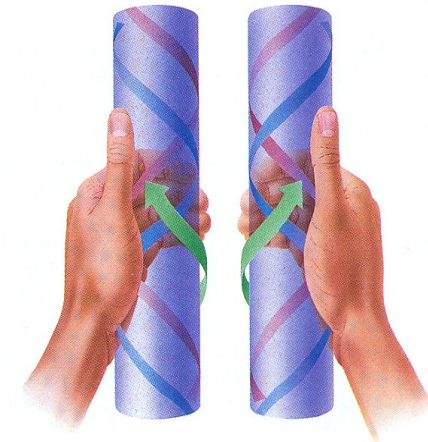


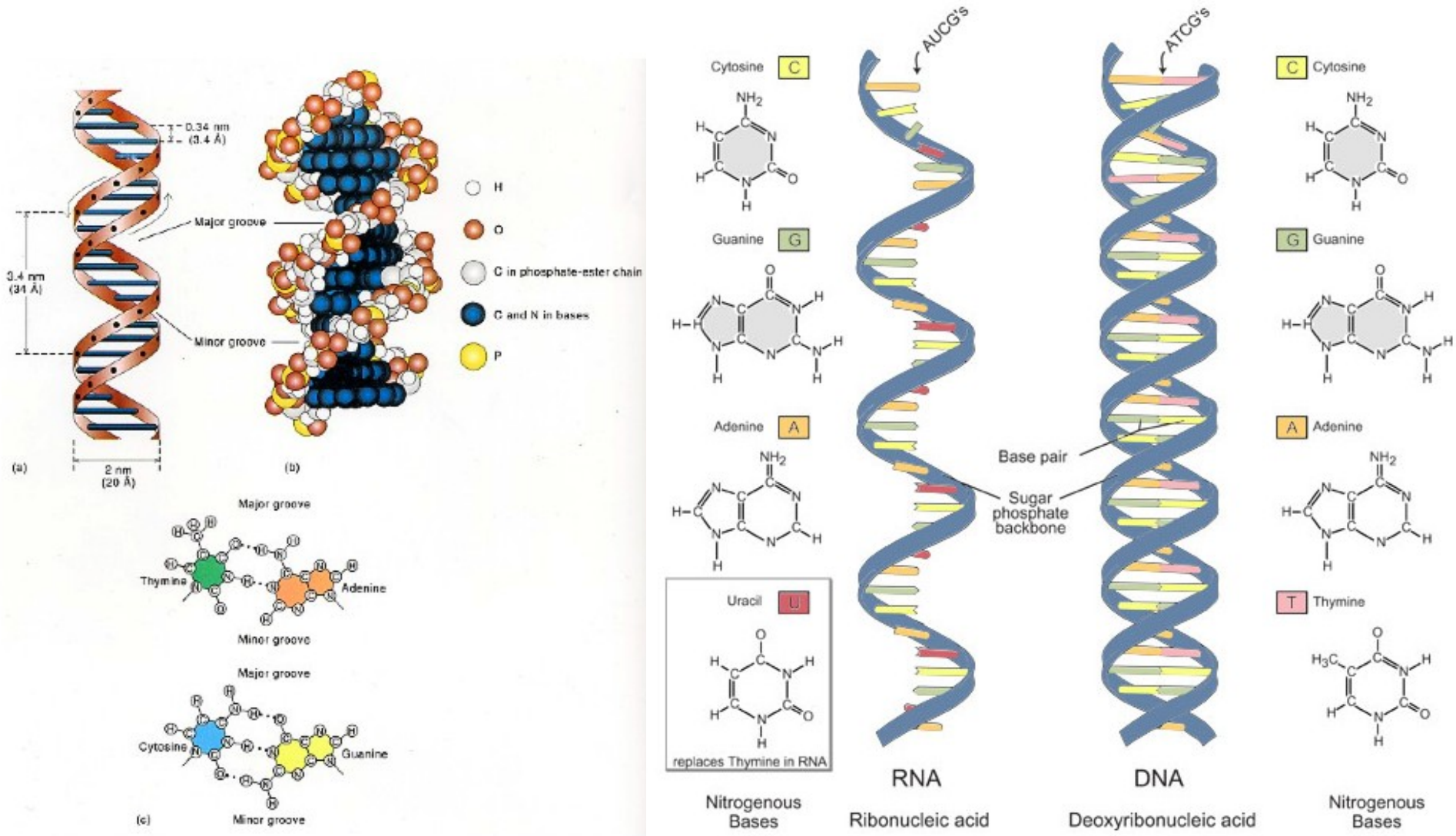
Angles of the glycosidic bonds were fixed within certain limits



Handedness of the helix

The direction of rotation was guessed and then subjected to testing





DNA is a polyanionic biomacromolecule with bases in its interior and sugar-phosphate backbone on the surface. At neutral pH it carries one negative charge per nucleotide. Below pH 5 and and above pH 9 ionization of bases become important

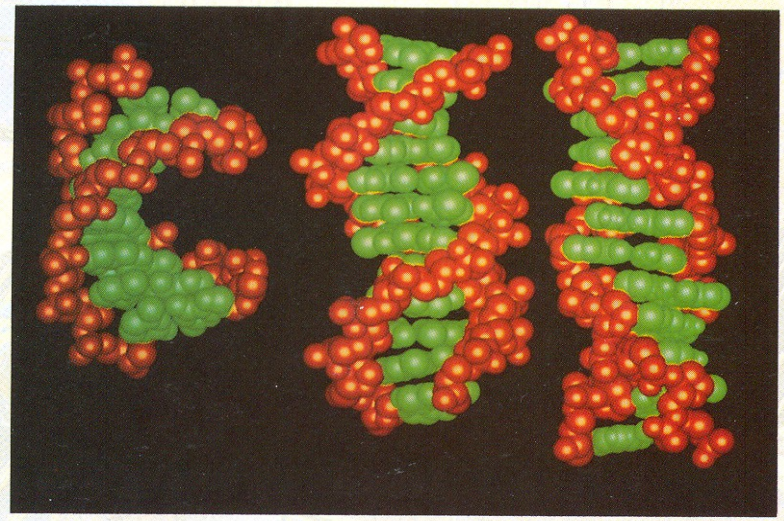
Parameters of DNA structures

TABLE 1
Comparison of A-, B-, and Z-DNA

Helix sense	A-DNA[a] right-handed	B-DNA[a] right-handed	B′-DNA[b] right-handed	Z-DNA[c] left-hande
Base pairs per turn	11	10	10	12 (6 dime
Helix twist (°)	32.7	36.0	34.1, 36.8	−10, −50
Rise per base pair (Å)	2.9	3.4	3.5, 3.3	3.7
Helix pitch (Å)	32	34	34	45
Base pair tilt (°)	13	0	0	−7
P distance from helix axis (Å)	9.5	9.3	9.1	6.9, 8.0
Glycosidic orientation	*anti*	*anti*	*anti*	*anti, syn*
Sugar conformation	C3′-*endo*	Wide range	C2′-*endo*	C2′-*endo*, C3 *endo*[d]

[a] Numerical values for each form were obtained by averaging the global parameters of corresponding double-helix fragments.
[b] B′-DNA values are for a double helix backbone conformation alternating between conform tional states I and II.
[c] The two values given correspond to CpG and GpC steps for the twist and P distance valu to cytosine and guanosine for the others.
[d] Two values correspond to the two conformational states. From Kennard, O. and Hunter, W. *Q. Rev. Biophys.*, 22, 3427, 1989. With permission.

A B Z



Double helical conformations of DNA: (left) *A-DNA*, (center) *B-DNA*, (right) *Z-DNA*.

DNA structures from X-ray crystal analysis

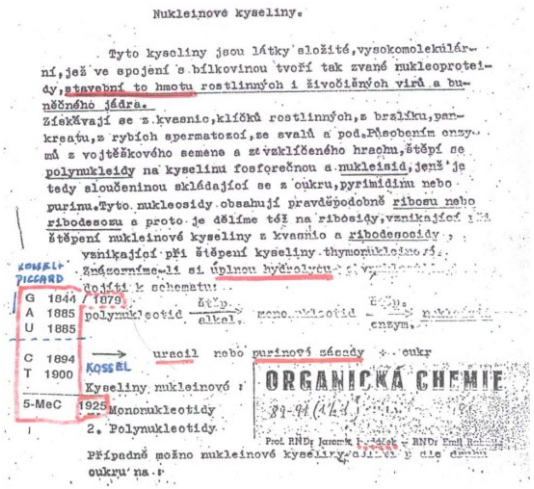
DNA double helix is polymorphic depending on the nucleotide sequence

TABLE 2
Average Helical Parameters for Selected Right-Handed Structures

	Helix twist (°)	Rise per base pair (Å)	Base pair tilt (°)	Propeller twist (°)	Groove width (Å) Minor	Groove width (Å) Major	Displacement Da (Å)
A-form							
d(GGTATACC)	32	2.9	13	10	10.2	6.3	4.0
d(GGGCGCCC)	32	3.3	7	12	9.5	10.1	3.7
d(CTCTAGAG)	32	3.1	10	11	8.7	8.0	3.6
r(GCG)d(TATACGC)	33	2.5	19	12	10.2	3.2	4.5
r(UUAUAUAUAUAUAA)	33	2.8	17	19	10.2	3.7	3.6
Fiber A-DNA	33	2.6	22	6	11.0	2.4	4.4
B-form							
d(CGCGAATTCGCG)	36	3.3	2	13	5.3	11.7	−0.2
d(CGCGAATTBrCGCG)	36	3.4	−2	18	4.6	12.2	−0.2
Fiber B-DNA	36	3.4	2	13	6.0	11.4	−0.6

BrC = 5-bronecytosimo.
Adapted from Kennard, O. and Hunter, W. N., *Q. Rev. Biophys.*, 22, 327, 1989. With permission.

1953


Nukleinové kyseliny.

Tyto kyseliny jsou látky složité, vysokomolekulární, jež ve spojení s bílkovinou tvoří tak zvané nukleoproteidy, stavební to hmotu rostlinných i živočišných virů a buněčného jádra.
Získávají se z kvasnic, klíčků rostlinných, z brzlíku, pankreatu, z rybích spermatozoí, se svalů a pod. Působením enzymů z vojtěškového semene a ze vyklíčeného hrachu, štěpí se polynukleidy na kyselinu fosforečnou a nukleisid, jenž je tedy sloučeninou skládající se z cukru, pyrimidinu nebo purinu. Tyto nukleosidy obsahují pravděpodobně ribosu nebo ribodesosu a proto je dělíme též na ribosidy, vznikající
Štěpení nukleinové kyseliny z kvasnic a ribodesosidy
vznikající při štěpení kyseliny thymonukleinové
Zaměříme-li si úplnou hydrolýzu
dojíti k schematu:
G 1844 / 1879
A 1885 polynukleotid štěp. alkal. mono-nukleotid štěp. enzym.
U 1885
C 1894 → uracil nebo purinový základ + cukr
T 1900
Kyseliny nukleinové
5-MeC 1925 Mononukleotidy
2. Polynukleotidy
Případně možno nukleinové kyseliny
cukru na

KOSSEL
PICCARD
KOSSEL
ORGANICKÁ CHEMIE

A paragraph dealing with nucleic acids from a text book of Organic Chemistry (in Czech) is shown. Briefly, it says nucleic acids (NA's) form complexes with proteins which are the building blocks of plant and animal viruses and of cell nucleus. Total hydrolysis of NA's proceeds according to the following scheme:

alkaline hydrolysis enzym. digestion

Polynucleotide → mononucleotide → uracil or purine bases

Considering that uracil and adenine were discovered in 1885 and G in 1844 while C in 1894 and T in 1900, our lectures on NA's were up-todate in 1885 but not in 1894

In courses of **Marxism-Leninism** (obligatory to all students)
we were tought that **G. Mendel was a burgeois reactionary pseudoscientist**.
Interestingly there was **not a single chemist** among us **who believed it**.
To my surprise there were some biologists who took this nonsense seriously

SCIENTOMETRIE / BIBLIOMETRIE

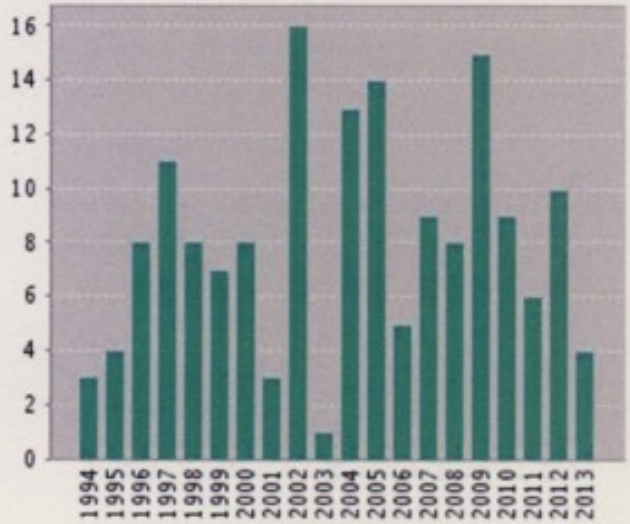
Citation Report Author=(Palecek E)

Timespan=All years. Databases=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-EXPANDED, IC.

This report reflects citations to source items indexed within Web of Science. Perform a Cited Reference Search to include citations to items not indexed within Web of Science.

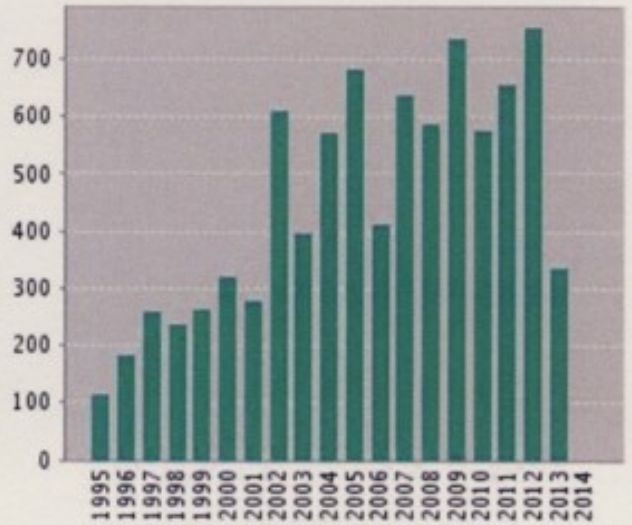
Research Professor

Published Items in Each Year



The latest 20 years are displayed.
View a graph with all years.

Citations in Each Year



The latest 20 years are displayed.
View a graph with all years.

Results found:	304	304 papers
Sum of the Times Cited [?] :	11227	11227 times cited
Sum of Times Cited without self-citations [?] :	7990	7990 without self
Citing Articles[?] :	4110	4110 citing articles
Citing Articles without self-citations [?] :	3837	3837 articles without self
Average Citations per Item [?] :	36.93	36,9 average per item
h-index [?] :	59	59 h-index

Results: **304** Page 1 of 31 Go Sort by: Publication Date -- newest to oldest

Use the checkboxes to remove individual items from this Citation Report
or restrict to items published between 1900 and 2014 Go

	2010	2011	2012	2013	2014	Total	Average Citations per Year
	578	658	756	337	0	11227	200.48
1. Title: **Electrochemical sensing of 2D condensation in amyloid peptides** Author(s): Kurzatkowska, Katarzyna; Ostatna, Veronika; Hamley, Ian W.; et al. Source: ELECTROCHIMICA ACTA Volume: **106** Pages: **43-48** DOI: **10.1016/j.electacta.2013.05.057** Published: **SEP 1 2013**	0	0	0	1	0	1	1.00
2. Title: **Enzymatic activity and catalytic hydrogen evolution in reduced and oxidized urease at mercury surfaces** Author(s): Cernocka, Hana; Ostatna, Veronika; Palecek, Emil Source: ANALYTICA CHIMICA ACTA Volume: **789** Pages: **41-46** DOI: **10.1016/j.aca.2013.06.014** Published: **JUL 30 2013**	0	0	0	0	0	0	0.00

Web of Science® *now* with books

<< Back to previous page

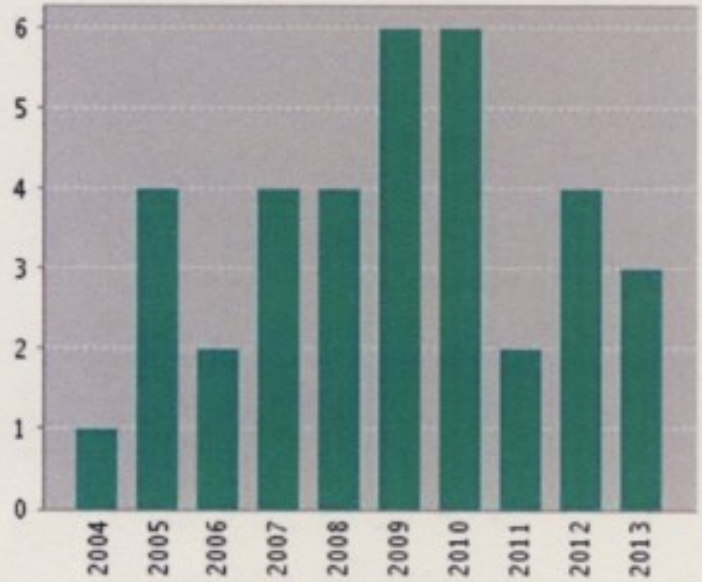
Assoc. Prof. Candidate

Citation Report Author=(Ostatna V)

Timespan=All years. Databases=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, BKCI-S, BKCI-SSH, CCR-EXPANDED, IC.

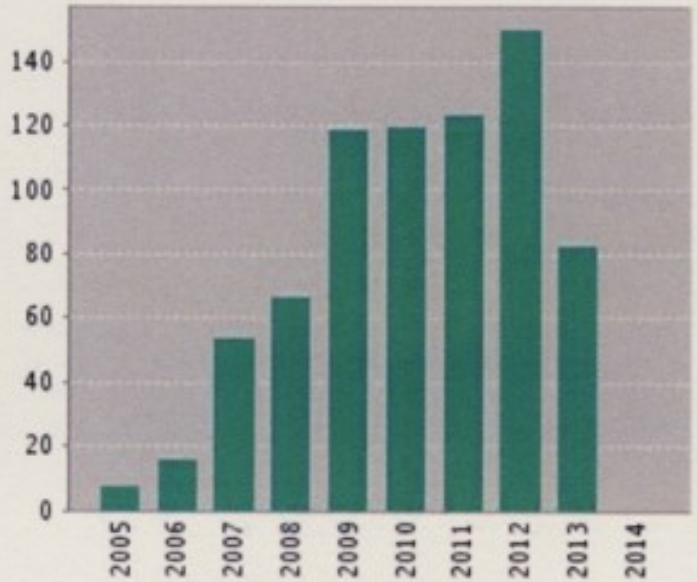
This report reflects citations to source items indexed within Web of Science. Perform a Cited Reference Search to include citations to items not indexed within Web of Science.

Published Items in Each Year



The latest 20 years are displayed.

Citations in Each Year



The latest 20 years are displayed.

Results found:	36	36
Sum of the Times Cited [?] :	741	741
Sum of Times Cited without self-citations [?] :	564	564
Citing Articles[?] :	413	
Citing Articles without self-citations [?] :	382	382
Average Citations per Item [?] :	20.58	20.58
h-index [?] :	18	18

Results: **36** Page 1 of 4 Go Sort by: Times Cited -- highest to lowest

Select Page | Add to Marked List (0) | Send to: my.endnote.com

1. Title: **Detection of aptamer-protein interactions using QCM and electrochemical indicator methods**
Author(s): Hianik, T; Ostatna, V; Zajacova, Z; et al.
Source: BIOORGANIC & MEDICINAL CHEMISTRY LETTERS Volume: **15** Issue: **2** Pages: **291-295** DOI: **10.1016/j.bmcl.2004.10.083** Published: **JAN 17 2005**
Times Cited: **99** (from Web of Science)
S·F·X | Full Text | [View abstract]

2. Title: **Influence of ionic strength, pH and aptamer configuration for binding affinity to thrombin**
Author(s): Hianik, Tibor; Ostatna, Veronika; Sonlajtnerova, Michaela; et al.
Conference: **18th International Symposium on Bioelectrochemistry and Bioenergetics/3rd Spring Meeting of the International-Society-of-Electrochemistry** Location: **Coimbra, PORTUGAL** Date: **JUN 19-24, 2005**
Sponsor(s): **Bioelectrochem Soc; Int Soc Electrochem**
Source: BIOELECTROCHEMISTRY Volume: **70** Issue: **1** Special Issue: **SI** Pages: **127-133** DOI: **10.1016/j.bioelechem.2006.03.012** Published: **JAN 2007**
Times Cited: **73** (from Web of Science)
S·F·X | Full Text | [View abstract]

3. Title: **Electroactivity of nonconjugated proteins and peptides. Towards electroanalysis of all proteins**
Author(s): Palecek, Emil; Ostatna, Veronika
Source: ELECTROANALYSIS Volume: **19** Issue: **23** Pages: **2383-2403** DOI: **10.1002/elan.200704033** Published: **DEC 2007**
Times Cited: **61** (from Web of Science)
S·F·X | Full Text | [View abstract]

4. Title: **Changes in interfacial properties of alpha-synuclein preceding its aggregation**
Author(s): Palecek, Emil; Ostatna, Veronika; Masarik, Michal; et al.
Source: ANALYST Volume: **133** Issue: **1** Pages: **76-84** DOI: **10.1039/b712812f** Published: **2008**
Times Cited: **41** (from Web of Science)
S·F·X | Full Text | [View abstract]

5. Title: **Native and denatured bovine serum albumin. D.c. polarography, stripping voltammetry and constant current chronopotentiometry**
Author(s): Ostatna, Veronika; Uslu, Bengi; Dogan, Burgu; et al.
Source: JOURNAL OF ELECTROANALYTICAL CHEMISTRY Volume: **593** Issue: **1-2** Pages: **172-178** DOI: **10.1016/j.jelechem.2006.03.037** Published: **AUG 1 2006**
Times Cited: **39** (from Web of Science)
S·F·X | Full Text | [View abstract]

6. Title: **Effect of the immobilisation of DNA aptamers on the detection of thrombin by means of surface plasmon resonance**
Author(s): Ostatna, Veronika; Vaisocherova, Hana; Homola, Jiri; et al.
Source: ANALYTICAL AND BIOANALYTICAL CHEMISTRY Volume: **391** Issue: **5** Pages: **1861-1869** DOI: **10.1007/s00216-008-2133-6** Published: **JUL 2008**
Times Cited: **33** (from Web of Science)
S·F·X | Full Text | [View abstract]

7. Title: **Covalent labeling of nucleosides with VIII- and VI-valent osmium complexes**
Author(s): Trefulka, Mojmir; Ostatna, Veronika; Havran, Ludek; et al.
Source: ELECTROANALYSIS Volume: **19** Issue: **12** Pages: **1281-1287** DOI: **10.1002/elan.200703848** Published: **JUN 2007**
Times Cited: **33** (from Web of Science)
S·F·X | Full Text | [View abstract]

8. Title: **Enzyme nanoparticles-based electronic biosensor**
Author(s): Liu, GD; Lin, YH; Ostatna, V; et al.
Source: CHEMICAL COMMUNICATIONS Issue: **27** Pages: **3481-3483** DOI: **10.1039/b504943a** Published: **2005**
Times Cited: **32** (from Web of Science)
S·F·X | Full Text | [View abstract]

9. Title: **Self-assembled monolayers of thiol-end-labeled DNA at mercury electrodes**
Author(s): Ostatna, Veronika; Palecek, Emil
Source: LANGMUIR Volume: **22** Issue: **15** Pages: **6481-6484** DOI: **10.1021/la061424v** Published: **JUL 18 2006**
Times Cited: **31** (from Web of Science)
S·F·X | Full Text | [View abstract]

10. Title: **Native, denatured and reduced BSA - Enhancement of chronopotentiometric peak H by guanidinium chloride**
Author(s): Ostatna, Veronika; Palecek, Emil

11. Title: **Voltammetry of osmium end-labeled oligodeoxynucleotides at carbon, mercury, and gold electrodes**
Author(s): Trefulka, Mojmir; Ferreyra, Nancy; Ostatna, Veronika; et al.
Source: ELECTROANALYSIS Volume: **19** Issue: **12** Pages: **1334-1338** DOI: **10.1002/elan.200703849** Published: **JUN 2007**
Times Cited: **27** (from Web of Science)
S·F·X | Full Text | [View abstract]

12. Title: **Constant current chronopotentiometry and voltammetry of native and denatured serum albumin at mercury and carbon electrodes**
Author(s): Ostatna, Veronika; Kuralay, Filiz; Trnkova, Libuse; et al.
Source: ELECTROANALYSIS Volume: **20** Issue: **13** Pages: **1406-1413** DOI: **10.1002/elan.200804206** Published: **JUN 2008**
Times Cited: **25** (from Web of Science)
S·F·X | Full Text | [View abstract]

13. Title: **Protein Structure-Sensitive Electrocatalysis at Dithiothreitol-Modified Electrodes**
Author(s): Ostatna, Veronika; Cernocka, Hana; Palecek, Emil
Source: JOURNAL OF THE AMERICAN CHEMICAL SOCIETY Volume: **132** Issue: **27** Pages: **9408-9413** DOI: **10.1021/ja102427y** Published: **JUL 14 2010**
Times Cited: **23** (from Web of Science)
S·F·X | Full Text | [View abstract]

14. Title: **Fabrication and Characterization of Solid Mercury Amalgam Electrodes for Protein Analysis**
Author(s): Juskova, Petra; Ostatna, Veronika; Palecek, Emil; et al.
Source: ANALYTICAL CHEMISTRY Volume: **82** Issue: **7** Pages: **2690-2695** DOI: **10.1021/ac902333s** Published: **APR 1 2010**
Times Cited: **23** (from Web of Science)
S·F·X | Full Text | [View abstract]

15. Title: **Ionic strength-dependent structural transition of proteins at electrode surfaces**
Author(s): Palecek, Emil; Ostatna, Veronika
Source: CHEMICAL COMMUNICATIONS Issue: **13** Pages: **1685-1687** DOI: **10.1039/b822274f** Published: **2009**
Times Cited: **23** (from Web of Science)
S·F·X | Full Text | [View abstract]

16. Title: **The detection of DNA deamination by electrocatalysis at DNA-modified electrodes**
Author(s): Ostatna, V; Dolinnaya, N; Andreev, S; et al.
Conference: **1st Workshop on New Trends in Nucleic Acid Based Biosensors** Location: **Univ Florence, Florence, ITALY** Date: **OCT 25-28, 2003**
Source: BIOELECTROCHEMISTRY Volume: **67** Issue: **2** Pages: **205-210** DOI: **10.1016/j.bioelechem.2004.07.008** Published: **OCT 2005**
Times Cited: **22** (from Web of Science)
S·F·X | Full Text | [View abstract]

17. Title: **Potential-dependent surface denaturation of BSA in acid media**
Author(s): Palecek, Emil; Ostatna, Veronika
Source: ANALYST Volume: **134** Issue: **10** Pages: **2076-2080** DOI: **10.1039/b912602c** Published: **2009**
Times Cited: **20** (from Web of Science)
S·F·X | Full Text | [View abstract]

18. Title: **Electrocatalytic Monitoring of Metal Binding and Mutation-Induced Conformational Changes in p53 at Picomole Level**
Author(s): Palecek, Emil; Ostatna, Veronika; Cernocka, Hana; et al.
Source: JOURNAL OF THE AMERICAN CHEMICAL SOCIETY Volume: **133** Issue: **18** Pages: **7190-7196** DOI: **10.1021/ja201006s** Published: **MAY 11 2011**
Times Cited: **18** (from Web of Science)
S·F·X | Full Text | [View abstract]

18x

h-index 18

19. Title: **Polylysine-Catalyzed Hydrogen Evolution at Mercury Electrodes**
Author(s): Zivanovic, Marko; Aleksic, Mara; Ostatna, Veronika; et al.
Conference: **International Conference on Modern Electroanalytical Methods** Location: **Sci Charles Univ Prague, Czech Chem Soc, Inst Phys Chem Acad Sci Czech Rep, Prague, CZECH REPUBLIC** Date: **DEC 09-13, 2009**
Sponsor(s): **European Soc Electroanalytical Chem; Int Soc Electrochem**
Source: ELECTROANALYSIS Volume: **22** Issue: **17-18** Pages: **2064-2070** DOI: **10.1002/elan.201000088** Published: **SEP 2010**
Times Cited: **14** (from Web of Science)
S·F·X | Full Text | [View abstract]

14x