Rethinking DNA

DNA Discovery, Extraction and Structure: A Critical Review

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The existence of DNA, its structure and its role are taught to us as facts; recognized and approved by all scientific establishments. But what if I told you that DNA started as a concept. Not DNA itself, but scientists' need to find the secret of life within our tissue, within the cells, and that the first DNA extraction became the perfect basis for the development of all sorts of theories, concepts, models and tools e.g. chromosomes, genes, RNA, PCR, GMO, epigenetics, CRISPR etc.

Currently DNA is presented to us as a double helix chain structure which carries our genetic code and instructions for the development, functioning and growth of all living organisms. But how exactly was all this established? This article will cover the history of DNA, which will include DNA isolation, isolation of its components, structure and many critical thoughts and questions that occurred during the literature review.

While going through this article, it's good to have at the back of your mind how delicate and sensitive DNA's physical and molecular structure is as postulated by the science, a structure that can be easily damaged by heat, chemicals and radiation.

Content:

- DNA EXTRACTION
- DNA COMPONENTS

- DNA STRUCTURE
- FINAL THOUGHTS AND CONCLUSION

In 1869 Johannes Friedrich Miescher, physician and biologist, was the first scientist to “isolate” nucleic acid which he, then, named nuclein.
Miescher was attracted to the new, evolving science of biochemistry, a science where chemical substances were applied on biological matter. Per biochemistry, the reaction of the biological matter to chemicals, procedures and the generated byproducts were giving clues of the composition and structure of cells and their content. Miescher believed that cells contained something vital within them which also was involved in the heredity process. Hoppe-Seyler, a biochemist and laboratory owner, suggested Miescher to concentrate on leukocytes (white blood cells) for his experiments. Miescher followed Hoppe-Seyler suggestion and collected leukocytes from the pus on fresh surgical bandages obtained from a nearby clinic.

Miescher isolated the leucocytes by soaking and washing the bandages in a sodium sulfate solution and filtering them through a sheet. To remove the wall of the cells and the cytoplasm he washed the leucocytes several times using a hydrochloric acid solution. The nuclei collected from the previous steps were vigorously shaken in a

solution of ether to remove any leftovers of the cytoplasm. Sodium carbonate (an alkalizer) was added to the nuclei obtained from the previous stage and then an acidic solution. The nuclein, the DNA, was the solid part of the content in the tube, the “precipitate” in the solution. The precipitate was forming when acid was part of the solution but dissolved when alkali was added. This reaction, the solidification of a substance upon acidification and dissolution upon alkalization, had never been observed before.

To examine the composition of the precipitate, Miescher burned it. Based on the byproducts generated from the burning process he concluded that nuclein contained a large amount of phosphorus (in the form of phosphoric acid) and nitrogen, but not sulfur (sulfur is mainly found and linked to protein). Based on these findings but also on the precipitate’s reaction to acid and alkali chemicals, he declared that he has discovered a novel substance and stated that “according to known histochemical facts, I had to ascribe such material to the nuclei”.

Miescher’s research paper describing his experiments, “Ueber die chemische Zusammensetzung der Eiterzellen”, got published 2 years later in Medizinisch-Chemische Untersuchungen (Medical-Chemical Examinations) journal. The publisher of the journal, Hoppe-Seyler, repeated Miescher’s experiments and confirmed his findings. Hoppe-Seyler obtained leucocytes from dogs’ abdomen for his experiments. The dogs were cut in the abdominal area and lenses were inserted into these cuts. All dogs were killed within 14 days. Hoppe-Seyler examined the lenses and the surrounding area. A sample of substances obtained was studied under microscope, where he observed protoplasmic movements and constant changes in shape (“pleomorphism”). The rest of the collected matter was chopped, boiled (in water and in alcohol), acidified, alkalized, treated with artificial gastric fluid, ether and hot alcohol, and later burned to examine and document the byproducts. Per Hoppe-Seyler, yeast cells

have similar structure to pus cells. He subjected yeast cells to similar experiments as with dog's leucocytes with the ending solution being burned and the leftovers were boiled and simmered in alcohol.

Critical checkpoints:

1. What made Miescher and Hoppe-Seyler believe that acid wash destroys and eliminates only cell walls and cytoplasm, and leaves the nucleus and its content intact and perfectly preserved? Many chemicals have the ability to shrink cells, they dehydrate the cells, was this taken into consideration when observing the chemically treated leukocytes or nuclei?
2. Something very important to have in mind is that the content of cells is rarely visible under the microscope, especially back in 1860; and if visible only some components are, e.g. nucleus, mitochondria. Miescher's observation after the chemical treatment might be actually shrunken leukocytes.
3. If you check videos of leukocytes under microscope you will notice that the active and moving part of these cells is the cytoplasm. Leukocytes movement is performed by the substances within the cytoplasm; the nucleus stays inactive, simply changing shape based on the activity of the cytoplasm. I wonder what make a scientist believe that the key to life and heredity is held in something inactive, something so passive.
4. The definition of actual Extraction or Isolation is "removing the particle of interest from the rest of the matter". In Miescher's and Hoppe-Seyler's experiments there was no isolation at any point of the process, the best description of their experiments would be a chemical wash of human and dog excretions.
5. Miescher's and Hoppe-Seyler's research papers unfortunately do not contain any drawings of isolated cells, specifically the content they've

observed under the microscope before and after each step. They also don't mention the microscopes and magnification used for their observations.

6. Miescher determined that he obtained a novel substance, that might be nuclein through the following observations:

- The addition of an acid in the solution was forming a precipitate and an alkali was dissolving it.
- The "isolation" procedures produced almost zero amount of sulfur, a byproduct linked to protein, but a high amount of phosphoric acid.
- Basically, he concluded that he has discovered a novel substance based on the reaction of the obtained solution to the chemicals used and procedures employed, and not based on actual isolation and observation under the microscope of the content of the nucleus.

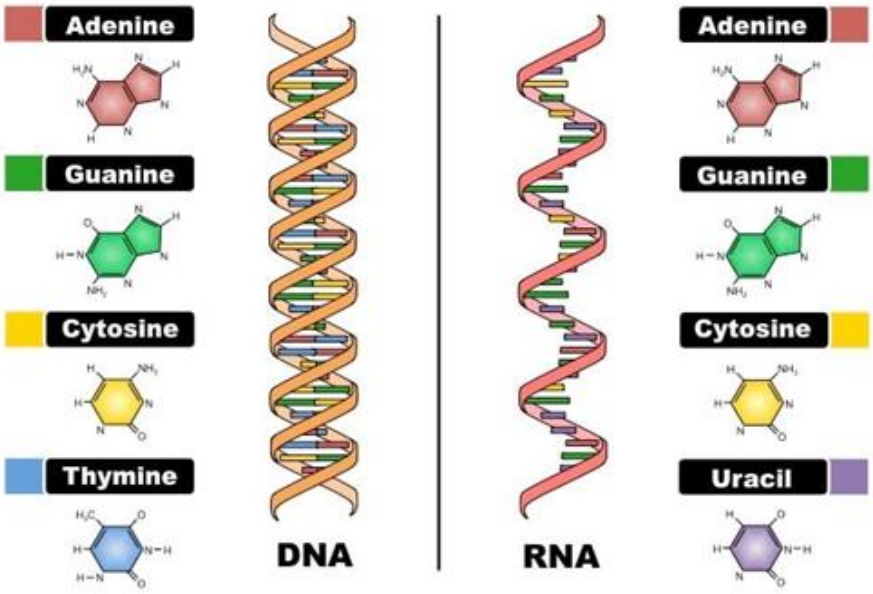
7. Phosphoric acid is a colourless liquid and nitrogen is a gas; both are quite hazardous. Finding these substances after chemical alkalization, acidification, boiling and burning of whatever is left says very little about the molecular structure of tissue, cells, nucleus and nuclein especially in their living state. Generally finding anything after the mentioned chemicals and steps says very little other than that spinning, boiling, heating, and burning chemically treated tissue produces hazardous substances.
8. Repeating the procedures and reaching the same results, i.e. Hoppe-Seyler's experiments, doesn't establish that a novel substance is found. The repetition establishes that treating similar matter with similar chemicals and employing similar procedures will produce the same byproducts.
9. While Miescher obtained leukocytes from pus on bandages, Hoppe-Seyler for some unknown reason decided to obtain leukocytes from dogs by placing lenses in their abdomen and later killing these dogs for extraction and examination. Since there is non-invasive and life

destructive way to obtain leukocytes, what is the reason to perform such harsh experiments? The extraction of different substances was performed through boiling dogs' body parts in alcohol, and/or caustic soda and then acidifying the mixture with acetic acid. Vitriol, soda solution and bismuth oxide were also added to test for any reaction. Hoppe-Seyler's experiment on dogs reminded me of Louis Pasteur experiments, where he also tortured dogs to develop the rabies vaccine in 1885.

10. Prior to DNA isolation, scientists were concentrated on the isolation of protein, which back then was believed to play a primary role in the formation of tissue. What Miescher and later Hoppe-Seyler actually did is changing the procedures of "isolation" by performing additional steps, adding chemicals and protein eating enzymes; in other words more chemicals and more steps produced different byproducts and as a result different conclusions.
11. What exactly made Miescher and Hoppe-Seyler believe that the participate was a nuclein and not a byproduct from the use of the hydrochloric acid or protein eating enzymes? Or that it was not chemically, heat treated debris of cells and/or nucleuses?
12. Per my understanding, studying either alive or dead matter, is to observe it under microscope, name/label each particle or substance in it and try to identify its role by removing it from the matter for further observation, how it acts on its own and also observe what happens to the rest of the matter without it. I also would expect whatever is isolated to be compared to particles and substances isolated from other matter. In biochemistry what we actually see and what biochemists call "isolation" is the treatment of dead or living biological matter with chemicals and heat, observation of the chemical reaction and documentation of the byproducts generated from these procedures e.g. phosphoric acid, sulfur, nitrogen etc. "Isolation" of a novel substance will be declared if a substance in the test tube doesn't

react and doesn't produce the same byproducts in the same quantity with previously "identified" substances, basically a byproducts comparison. Personally, I would accept the chemical way to study matter if there were no microscopes available, and taking into account that during those times microscopes weren't that powerful as today. But with today's technology and the existence of electron microscope that can observe atoms, I don't understand why scientist still keep doing these chemical "isolation/extraction" experiments.

DNA COMPONETS



Between 1885 and 1901 German chemist Albrecht Kossel, determined that nucleic acid comprised of five compounds: adenine (A), cytosine (C), guanine (G), thymine (T) and Uracil (U) which are now considered to be the basic building blocks of DNA and RNA. Kossel was awarded with Nobel Prize in Physiology or Medicine in 1910 for his contributions in cell chemistry including for isolation of proteins and nucleic components.

Critical checkpoints:

1. None of Kossel's research papers on isolating the mentioned compounds is freely available, nor could I find some kind of a

summary and/or translation in other languages. Why discoveries that are taught as established facts and for which a person earned a Nobel Prize are not widely and freely shared? This makes me wonder how many scientists have ever read these research papers.

2. Have Kossel's findings ever been confirmed by others? Were his experiments ever re-performed? Did he perform control experiments to examine the effects of the procedures and chemicals used on the studied matter?

3. As per the short article "From poop to pus – the discovery of DNA", Kossel obtained these compounds through "chemical extraction" (similar processes to DNA extraction) using organs and body parts donated from a local slaughterhouse:

- Kossel supposedly isolated Guanine but from which body part it is not mentioned. Guanine was originally isolated from excrement of seabirds known as guano by a German chemist Julius Bodo Unger, in 1844 (I couldn't find any information about the methodology of isolation).
- Adenine was isolated from an ox's pancreas gland.
- Thymine was isolated from the thymus of a calf.
- Cytosine was isolated by hydrolysis of the calf thymus.

4. Based on the previous point, the assumption that cells and nuclei content and molecular structure are alike across species and other living matter has no actual basis other than being a theoretical assumption based on the Cell theory. Cell theory has several assumptions and issues on its own (I will analyze cell theory and tissue formation and degeneration in another article). Extracting substances from different body parts from different species using different methodologies and chemicals, is one of the major flaws in this whole concept of molecular composition and structure of nucleic acid. Lately scientists are discovering that the molecular composition

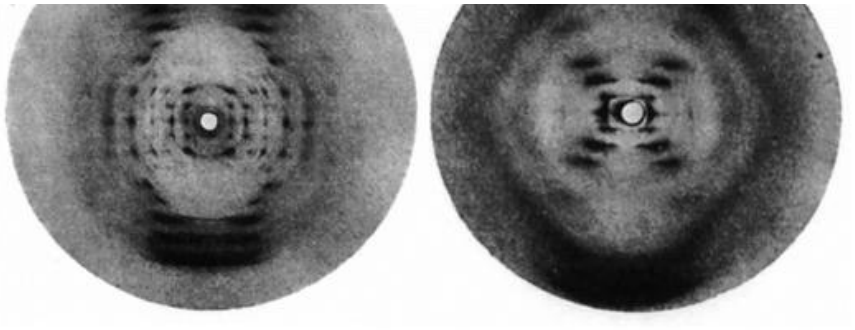
of DNA in one body part/tissue is not the same with another body part/ tissue e.g. "DNA Not The Same In Every Cell Of Body" and "Surprising science: Not all our cells have the same DNA".

5. Kossel used hydrolysis and decarboxylation in his experiments (basically heating the substances in various ways) and also chemicals like phosphotungstic acid, mercuric chloride and silver nitrate. We know that heat destroys and changes the composition and the structure of any matter (e.g. raw Vs cooked food, limestone Vs lime). In addition the chemicals used are quite harsh and hazardous to work with and their effect on the matter under study can only have destructive effects (e.g. Mercury chloride).

   So let's sum up Kossel's discoveries in order to move on: Kossel isolated the component of protein and DNA by applying heat and using harsh chemicals on different organs of animals. His findings are not confirmed by repetition of his experiments, by different isolation/ extraction methodology, or by using other body parts and species; his methodology and research papers are not freely available to the public regardless that his findings are taught as facts and he has received a Nobel Prize for them.

   Something interesting: Phoebus Levene is another chemist that is claimed to be the discoverer of DNA components. Levene worked briefly in Kossle laboratory, he was appointed a member of the Rockefeller Institute for Medical Research, and later the Head of "the center of bioorganic chemistry in America" department. Levene is claimed to be the discoverer of deoxyribose, the carbohydrate component of the backbone in DNA. He was the first one who tried to develop a chemical structure of DNA.

DNA STRUCTURE



A - DNA
non hydrated form of Na DNA

B - DNA
hydrated form of Na DNA

In May 1952 the famous X-ray diffraction image, Photo 51, of "Signer DNA" was produced using X-ray crystallography. The picture became the basis for modeling, the currently acceptable DNA structure. The picture was taken by Raymond Gosling under the supervision of Rosalind Franklin a chemist and X-ray crystallographer. The photographed DNA was a salt of a calf thymus (aka NaDNA) provided by a Swiss chemist Rudolf Signer.

The NaDNA was saturated with water to form a gel. Franklin and Gosling managed to extract a single DNA fiber which was exposed to x-rays for sixty-two hours and hydrogen gas was pumped through a salt solution to maintain the desired hydration of the fiber. Franklin labeled the obtained image "photo 51" which was a diffraction pattern of the hydrated form of NaDNA.

Franklin and Gosling published five research papers based on the two x-ray photos (a hydrated and a non-hydrated form of NaDNA) and used mathematical models to explain their findings:

- "The Structure of Sodium Thymonucleate Fibres. I. The Influence of Water Content", March 6 1953. This paper described the methodology used to photograph the NaDNA and the importance of humidity for high quality diffraction of NaDNA. In addition, they attempt to figure out the positioning of the molecules based on the humidity uptake and water content.
- "The Structure of Sodium Thymonucleate Fibres. II. The Cylindrically Symmetrical Patterson Function, March 6 1953. The article applies

Patterson function on the diffraction pattern generated by the non-hydrated NaDNA (aka A-DNA) in order to establish the structure and content of the NaDNA".

- "Molecular Configuration in Sodium Thymonucleate", April 25 1953. In this article the authors describe how humidly affects the diffraction of NaDNA and characterize the general features of the diffraction pattern. By taking into account the DNA molecules and by applying Patterson Function they suggest the form of DNA to be helical. This article was part of a combination of articles postulating the helical shape and molecular structure of DNA.
- "Evidence or 2-chain helix in crystalline structure of sodium deoxyribonucleate", July 25 1953. Another article discussing the x-ray diffraction and the effects of water and humidity; the Patterson function is used in order to support the 2-chain helical structure of NaDNA.
- "The Structure of Sodium Thymonucleate Fibres. III. The Three-Dimensional Patterson Function". October 29 1954. One more article on x-ray diffraction, effects of water and humidity and again the use of Patterson function to support, further, the helical structure of NaDNA.

Critical checkpoints:

1. In X-ray crystallography a beam of x-rays is shot at a crystal, the x-rays scatter based on the three-dimensional form of the crystal, and it provides a photo of a two-dimensional diffraction pattern. The interpretation of the diffracted photo is highly dependable on the observer's knowledge and experience. The observer will use mathematical model/s he/she thinks suits best in modeling the three-dimensional structure of the crystal. Before computers, it was up to the scientist to map the spots, determine their strength and density, basically to determine the essentials on which mathematical models will be applied to yield a three-dimensional structural of the crystal.

2. I've watched and read several articles on X-ray crystallography and found this video being an excellent explanation of how it works. At the same time this video was quite disturbing because:

- The diffraction pattern of a single spiral form is almost identical to the diffraction pattern of DNA. The two-chain helix form is suggested based on missing points in the photo 51. Basically, without those missing points the diffracted pattern of DNA would be identical to a single spiral form.

- The base pairs are not diffracted as they are claimed to be "transparent", their existence is assumed on the (also assumed) molecular structure of DNA. Basically, there are no evidence supporting the existence of base pairs other than the theoretical molecular structure of DNA.

3. From another experiment, "optical experiments using ballpoint pen spring" we also get a helical structure, but:

- The experiment, again, uses one spiral form to confirm a double spiral form; why doesn't anyone use double strand form to confirm double strand form?

- A structure with transparent matter within or a structure without matter within, will produce the same diffraction pattern.

4. Here is another confirmation of the assumed existence of paired bases in DNA structure: *"Franklin and Gosling account for the presence of the DNA bases in the molecule affect the X-ray diffraction pattern. They assume that the bases are evenly spaced apart. Using their equation and that assumption, Franklin and Gosling account for features they observe in Photo 51."* Basically, the interpretation of the diffraction pattern and the suggestion of the helical structure takes into account the invisible (actually assumed) base pairs. It should be stressed that the components of the base pairs have been isolated by Kossel, I'm not sure how someone can extract and isolate something

invisible.

5. Franklin et al. research papers concluded that NaDNA structure was crystalline, at least one of its forms took the shape of a helix, and many water molecules could cling to it. In addition, the structure depends on the state of hydration. Basically, from all the pictures taken, mathematical models used, observations and assumptions they've concluded that the structure might be helical (i.e. sometimes) and it tends to attract water to it. I'm not sure how this conclusion can be considered as evidence of double chain helical form of all DNA (in all living organisms) since Franklin's x-rays were derived from NaDNA only. DNA from other sources and matter weren't examined by Franklin.
6. We should be aware that there is no perfect symmetry in nature, so trying to predict a shape of an object as tiny as DNA using mathematical models might not be the most appropriate way in doing so.
7. Although "Molecular Configuration in Sodium Thymonucleate" was part of a combination of articles establishing DNA's 2-chain helical structure, in this paper Franklins and Gosling stated that their X-ray data alone cannot prove that DNA is helical. But it's on their x-ray images Wilkin, Crick and Watson postulated that the DNA is a 2-chain helical structure.
8. The NaDNA was exposed to hydrogen gas and x-rays for 62 hours in order to generate picture 51. It is interesting that a fragile and sensitive structure like DNA withstands such a treatment. I'm not sure if and how hydrogen gas can affect the DNA structure but we know that x-ray is considered an invasive and distractive method of studying matter, especially living matter. X-ray has a damaging effect on the tissue and its content, including DNA. How do we know that the x-ray images obtained are not images of the damaged and distorted DNA?

Maybe the missing spots that suggest the existence of 2-chain, are the consequence of the damaging effect of x-ray? Below are some articles on the distractive effect of x-rays:

- Types of DNA Damage
- Radioprotective agents to prevent cellular damage due to ionizing radiation
- X-ray radiation-induced damage in DNA monitored by online Raman
- X-ray radiation damage to biological samples: recent progress

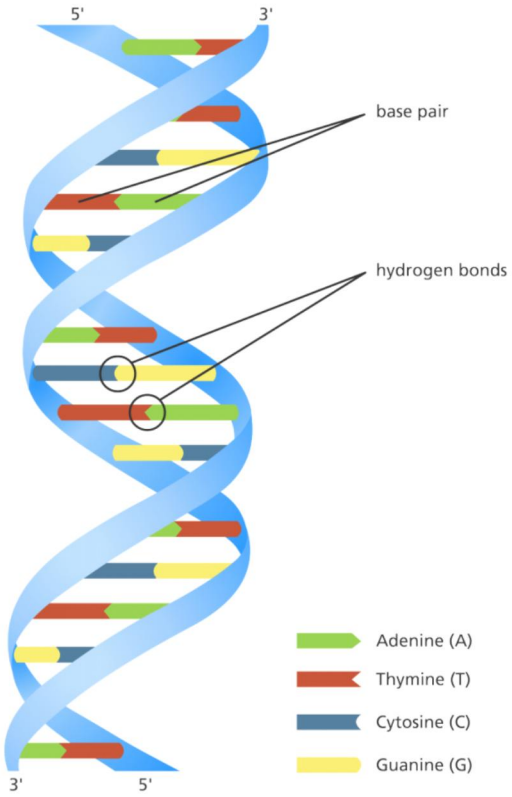
9. The same single fiber of NaDNA was actually exposed to x-ray for more than 62 hours as the same fiber was hydrated, dehydrated and re-hydrated again to obtain different diffraction photos: *"It seems, therefore, that drying does not break the phosphate-phosphate links but, if anything, cements them more strongly. The removal of water stresses and distorts the structure, destroying its regularity, while leaving the basic three-dimension skeleton intact. The effect on the X-ray diagrams maybe compared with that of strong thermal agitation".*
10. The research paper "Evidence of 2-chain helix in crystalline structure of sodium deoxyribonucleate" is a very technical article which tries, once again, to prove the 2-chain helical structure of NaDNA by using cylindrical Paterson fraction and also tries to approximate the number of nucleotides by estimating the density and water absorption-content. Additionally, the paper assumes the positioning of nucleotides without any reference for this assumption.
11. I'm kind of puzzled on why Signer's research paper on isolation of NaDNA is not translated, freely available, not taught and not used as the basis for DNA extraction since Signer was praised for obtaining high quality and quantity of DNA. Per Signer's research paper *"DNA is known to exist in the form of long-chain molecules of very high molecular weight; when sufficient precautions to avoid degradation are taken, values up to 8 million are obtained".* So here we have

Franklin et al. preparing, photographing and expecting results that will show some kind of long chain form based on extraction methodology never re-performed by anyone else.

12. Signer's DNA was received in a dry form while we know that Miescher and Hoppe-Seyler's DNA extraction experiments and even the current DNA extraction protocols require the DNA to be resuspended in a chemical solution to prevent DNA's degradation. Generally, the DNA pallet (dry form) is acceptable to be stored for short periods in a refrigerator or in a freezer. How exactly Signer's DNA stayed in perfect shape without this last step is unknown. This puzzles me even more, since Signer's method of extraction is one step less i.e. saves time, yields high quality and quantity of DNA and does not require special storage conditions. Why then aren't the modern extraction protocols based on Signer's methodology?
13. Gosling and Franklin prepared the DNA fibers for photography by saturating NaDNA with water to form a gel, a method which is described in "Physical studies of nucleic acid, Wilkins & Gosling, 1951". This is another paper not available for free and seems to be a method specific to NaDNA and not to other DNA samples. I wonder what made NaDNA to form a gel when saturated with water? This doesn't happen with the DNA that gets resuspended in water nowadays, this indicates that either the NaDNA contained additional molecular/chemical component which was forming into gel when hydrated or Wilkins and Gosling accept water added some kind of gel forming compound.
14. Here is a quick summary of all the mentioned points:

- All observations, assumptions and conclusions were derived from examining NaDNA, a sample of dry form of DNA from one source. Franklin didn't compare her finding to DNA obtained from other sources which means we cannot be sure that DNA from other sources looks like NaDNA.

- The 2-chain helical structure is suggested and assumed based on missing spots in the x-ray diffraction pattern of the hydrated form of NaDNA (B-DNA), mathematical models and invisible base pairs. These suggestions were not confirmed by examining DNA extracted from other sources.
- Existence of base pairs and their composition are assumed based on presumed molecular structure of DNA (molecular structure will be discussed in the next timeline event).
- The use of X-ray damages the structure of any tissue and its content, the diffraction pattern of NaDNA might be a diffraction of a damaged NaDNA.



On April 25 1953, the journal “Nature” published three articles about DNA two-chain helical structure under the heading “Molecular Structure of Nucleic Acids”:

- “A Structure of Deoxyribose Nucleic Acid” by Francis Crick and James D. Watson pg737-738. Crick and Watson were suggesting a two-

chain helical and molecular structure of DNA based on Frankin's et al. x-ray diffraction pictures of NaDNA and research performed by others. This article was characterized as *"a turning point in science"* as it became widely accepted as the accurate description and function of DNA. Since then, RNA, genetics, molecular biology in general, are based on Crick and Watson's suggestions.

- "Molecular structure of Dexyonpentose Nuclaid Acid" by Wilkins et al. pg 738-740. A paper proposing the helical structed of DNA based on unpublished x-ray diffraction pictures and on Bessel Function, a mathematical model.
- "Molecular Configuration in Sodium Thymonucleate" by Franklin et al. pg 740-741. Already discussed in pervious timeline event.

Critical checkpoints:

1. It is interesting that these three articles are not available for free by nature.com; why research suggesting the currently widely accepted structure of DNA isn't available freely to the public? Many bodily fluid tests, medical drugs, medical procedures, modern research are all based on DNA discovery and its structure. Shouldn't people have free access to the foundation on which molecular biology is based and medical procedures we are sometimes subjected to?
2. Watson and Crick never conducted x-ray crystallography themselves, nor any other type of photography of any matter or actual lab work on DNA. The helical structure of DNA was assumed based on theoretical, molecular structure of DNA and derived from the speculation of research and work performed by others. They theorized a structural model of DNA and then were searching for evidence to support this theoretical model.
3. Watson and Crick start their article by stating: "…*The purpose of this communication is to describe, in a preliminary way, some of the*

experimental evidence for the polynucleotide chain configuration being helical, and ***existing in this form when in the natural state***". There is absolutely no evidence that the natural form and state of DNA is helical. Unprocessed, unheated and untreated with chemicals DNA was never, ever observed under any microscope.

4. The article is clearly a "suggestion" of helical structure based on many, too many assumptions. The lack of scientific evidence and research and the number of words like "suggestion", "assumption" etc. would place the article under the science fiction genre rather that scientific article:

- *"We wish to* ***suggest*** *a structure for the* ***salt*** *of deoxyribose nucleic acid*." The salt of a DNA, the highly chemically treated and processed dry form of DNA obtained from the thymus of a calf.
- *"We* ***believe*** *that the material which gives the X-ray diagrams is the salt, not the free acid".* Science is based on experiments, believing in something suggests some kind of form of a religion or a cult. If they wanted to be scientifically correct, they would try to support their belief with experiments.
- *"We* ***wish to put forward*** *a radically different structure for the salt of deoxyribose nucleic acid"*
- *"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…".* They've assumed the form of DNA so it can match the theoretical, molecular structure of DNA.
- *"One of the pair* ***must be*** *a purine and the other a pyrimidine for bonding to occur"* why it must be like that is not explained.
- *"If it is* ***assumed*** *that the bases only occur in the structure in the most plausible tautomeric forms…"*
- *"****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).” Although they don’t mention how this was found, what they are referring to is “Chargaff’s Rule” supposedly developed by Erwin Chargaff who later became increasingly outspoken about the failure of the field of molecular biology, claiming that molecular biology was “running riot and doing things that can never be justified”. Erwin Chargaff using various chemicals and procedures managed to extract the base pair components (similar methods to Kossel) and compared the quantities obtained, including molar ratio of A-T (Adenine-Thymine) to G-T (Guanine-Cytosine); this comparison, A-T to G-T, was then taken as a hint of base pair mechanism, in reality Erwin Chargaff never suggested such a bonding mechanism. The research paper describing the mentioned findings was published in Nature journal August 15, 1953, almost four months after Crick and Watson’s article. Per Wikipedia Chargaff met Crick and Watson in 1952 and shared his discoveries.

- *“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”*
- *“It has been **found experimentally** 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.*” For some reason they, again, avoid referencing the research done by Erwin Chargaff.
- ***“We have made the usual chemical assumptions**. namely, that each chain consists of phosphate diester groups joining ß-D-deoxyribofuranose residues with 3’,5’ linkages”.* I wonder if these assumptions were ever proven or scientists continue to make “the usual chemical assumptions”?
- *“The sequence of bases on a single chain, **does not appear** to be*

restricted in any way"

- *"It has not escaped our notice that the specific pairing we have **postulated** immediately **suggests** a possible copying mechanism for the genetic material".* This suggestion has absolutely no basis, logic or evidence.
- *"The previously published X-ray data on deoxy-ribose 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 stereo-chemical arguments**."* Basically the previously published x-ray data doesn't confirm their theoretical molecular and the physical structure of DNA, their theories derived from published and unpublished data, their theories need to be proven by experiments and that they are not aware of the conclusions derived by the articles following their article.
- *"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 have also been **stimulated** by a knowledge of the general nature of the **unpublished experimental results and ideas**…"* How do we know that unpublished results and ideas have any real basis?

5. Watson and Crick mention that the (assumed) pairing mechanism implies a possible mechanism of DNA replication. How exactly does a theoretical molecular structure imply a replication mechanism? There are so many flaws in their suggestion:

- Molecular structure of DNA & NaDNA are assumed.
- Base Pairing mechanism is assumed.

- Base pairs, in general, are assumed and have never been seen by any method of observation (while they have supposedly been isolated by Albrecht Kossel between 1885 and 1901).
- Basically, they suggest replication based on unproven assumptions. Can anyone determine a replication method of unseen and unproven particles based on unseen and unproven particles?

6. The DNA form was originally drawn by Crick's wife "*based on their mathematical analysis of a pattern of spots revealed by a process called X-ray crystallography — for the April 1953 issue of the journal Nature."* As previously mentioned, Watson and Crick did not perform any DNA x-ray crystallography themselves and per their article they haven't applied or used any mathematical analysis to support their claims.

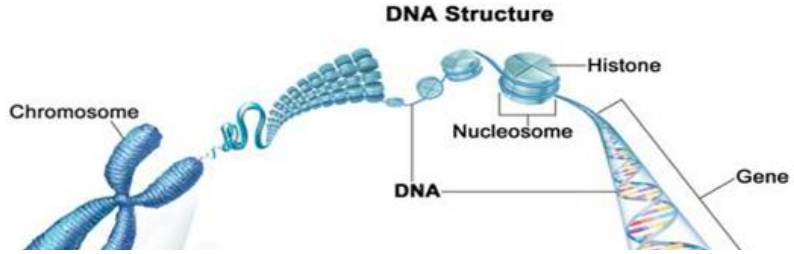
7. Some critical issues with the "Molecule structure of Dexyonpentose Nuclaid Acid" by Wilkins et al.:

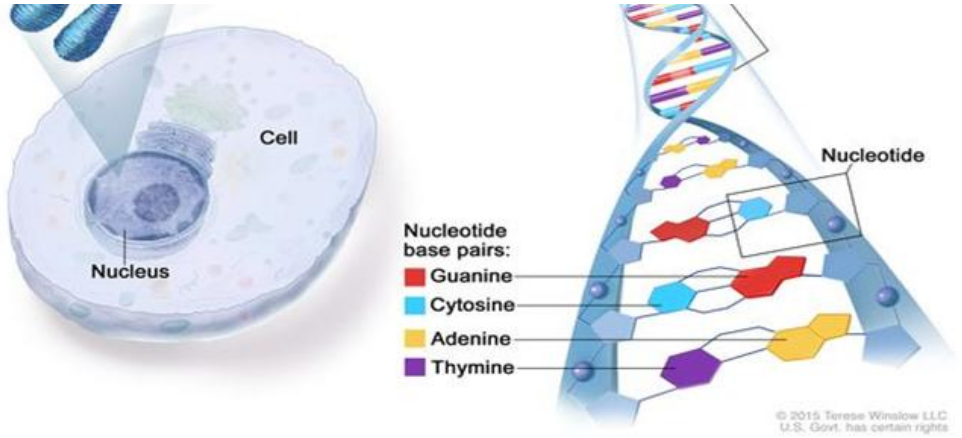
- "…some of the experimental evidence for the polynucleotide chain configuration being helical and existing in this form when in the natural state". To support this statement, at the end of their article, in the section "Structure in Vivo" (in living state, part of living organism) they mention that centrifugated trout semen produced the same diffraction pattern with dried, rehydrated or washed sperm heads. X-rays of centrifuged bacteriophage produced main features of paracrystalline sodium nucleate diffraction pattern. A dried form of once "active" deoxypentose nucleic has the same crystalline structure with some of the samples of NaDNA. Although they mention that treated matter produce similar diffraction patterns to matter if treated differently, all matter under study were treated in one way or another, the matter weren't in their living state and all were exposed to x-ray damaging effect. Fish sperm heads observed under electron microscope have actually a spherical shape.

- They mention that they have obtained similar photographs from calf and pig thymus, wheat germ, herring sperm, human tissue and T2 bacteriophage but these photographs are not shared publicly anywhere, neither the methodology of extraction and photography. The article contains an x-ray picture of e. coli. which is kind of similar but not similar enough to NaDNA. We might have had a better understanding if diffraction pattern of helical structure were compared to non-helical structure. Were these structures ever confirmed through other ways (e.g. electron microscopy) in order to make sure that the interpretation of the x-ray diffraction patterns is accurate?
- *"the whole diffraction pattern is modified by the form factor of the nucleotide"* basically the interpretation of the diffraction pattern takes into consideration the theoretical molecular structure of DNA including the invisible base pairs.
- *"The structure of deoxypentose nucleic acid is* ***the same in all species****"*. Is it? How exactly was this established and confirmed?
- *"The sequence of different nitrogen bases along the chain is not made visible"*, i.e. the base pairs are not visible.
- The conclusion that the structure is double helix and not one helix is based on intensity of certain spots of the diffraction and the absence of reflation on or near meridian.

  Just to sum everything up: what we see in all three articles is the need to back up the theoretical molecular structure of DNA by theoretical form of DNA and vice versa.

THOUGHTS AND CONCLUSION





So here we are, 150 years since the first DNA extraction, 140 years since DNA's components isolation, almost 70 years since DNA x-rays diffraction pictures and the introduction of the double helix form and molecular structure. The method of DNA extraction hasn't changed much since DNA discovery. In reality anyone can extract DNA nowadays by buying a DNA extraction kit (there are plenty of brands), some expensive equipment and by following suppliers' instructions. Chemicals got relabeled to buffers and every time a buffer is added, the mixture of the matter containing the buffer gets centrifugated. After repeating the mixing and spinning two to four times the extracted DNA gets re-suspended in a buffer, synthetic alcohol or ultra-pure water.

After this dive into the rabbit hole of DNA history, unfortunately I'm left with more questions than answers, with the main one being:

- What makes scientists believe that the inactive part of the cell, the nucleus, contains the vital information of "life" and the tissue formation?
- What makes scientists believe that components extracted from chemically treated tissue of one specie represent the content of all cells, nuclei, and nucleic acid of all species?
- Why the extraction components (adenine, cytosine, guanine and thymine) and the DNA x-ray crystallography are not re-performed in order to re-confirm the findings?
- Why Signer's protocols of extracting large amounts of perfectly

preserved DNA that can be stored in room temperature (up until today) are not re-performed and not practiced?

- The components of the base pairs were isolated (by Kossel) but per x-ray and electron microscope they are invisible. I'm not sure how exactly someone can extract and isolate something invisible and determine their position in molecular and physical structures. Molecular biology hasn't merged with quantum physics yet, as far as I'm aware.
- Why vital research papers describing the methodology of extraction of DNA and its component are not freely shared with some being totally missing? How many scientists actually read them?
- Why DNA extraction protocols of branded extraction kits vary from one another? Do different brands produce the same results if compared? Did anyone ever compare results obtained from one brand to another? What control experiments do the kits' manufacturers perform?
- What about the extraction protocols themselves, the harsh chemicals, detergents, synthetic alcohols, centrifugation, heating, boiling, cooking, cooling? Nothing natural and living can withstand these procedures but a sensitive and delicate DNA and its components residing in the inactive part of the cell, that represent the "code of life", can?
- What about control experiments? Of each procedure? Currently scientists use water as control because water is assumed that it doesn't contain DNA, but water also doesn't contain solid matter to go through all these procedures.
- Was the interpretation of x-ray crystallography pattern ever compared to pictures generated by electron microscope when studying same matter, tissue, cells, DNA? To confirm that both methods generate same forms?

- What makes scientists believe that life derives and propagates from a chemical or molecular composition of DNA? Why do they believe that treating dead or dying tissue with chemicals will provide answers on how tissue and life forms, replicates or propagates? Can we really derive to something meaningful after these chemical treatments and procedures? Can anything "living" or "vital" survive such a process and provide an explanation on how life "works"?
- Do scientists ever question the procedures and methodology they perform? And in general, what are they doing exactly?
- What evidence do we have on what is seen under the microscope (chemically treated, "fixed" and dyed dead tissue) exists, acts and has the same structure and functioning as when in a living state and a part of living tissue? Harold Hillman has documented quite well the effects of chemicals and dyes used for observing neurons under microscope: The Effects of Staining Procedures – Harold Hillman, 1987.

  It is interesting that since the two x-ray diffraction pictures of NaDNA in 1950, we only have two more images of DNA. One published on June 26, 2012 and the second on November 28, 2012, with both looking like one chain helix form. With DNA being claimed as the code of life and basis for so many, later, discoveries, I would imagine researches and students be eager to observe DNA under microscope. Why wouldn't this be a standard part of a molecular biology course? Something so fundamental on which so many things are based e.g. genes, chromosomes, proteins, RNA, etc.

  Why not to use Signer's DNA (still available at the college), Wilkins' technique of DNA fiber isolation and the most powerful electron microscope, a microscope that can generate images of atoms? Just to reconfirm the so many assumptions made by Crick and Watson. Some will argue that DNA is too sensitive and the radiation of the electron microscopy can damage its delicate structure. But if this is the

case why then is it assumed that:

- that exposing NaDNA to the x-rays for days in order to obtain a diffraction pattern will not damage the NaDNA structure?
- the obtained picture is of a well preserved NaDNA i.e. of a non damaged NaDNA? Atoms are not sensitive but DNA consisting of atoms is?

I don't question the existence of heredity, heredity is a fact, and we see it with our own eyes, in our parents, in us, in our children, generally in all creatures. If it is Medel's principles of inheritance or/and Darwin's natural selection mechanism, I'm not sure, those are also theories, theories containing unproven assumptions.

One of the most striking findings of mine is that control experiments are not performed, to consider or eliminate the effects of the chemicals and of the procedures.

I have a hard time understanding why scientists, biologists and chemists, believe that studying dead tissue treated with chemicals and applying mathematical models will lead to some kind of discovery. What exactly makes them believe that they are dealing with a novel substance and not with tissue debris derived from reaction between dead tissue, chemicals used and procedures applied?

Harold Hillman, neurobiology scientist, who used to challenge the mainstream science on the procedure employed to extract and study matter, once said in one of his interviews: *"I think it is absolutely essential that people should understand the methods by which the things they believe were discovered, because a lot of people seems somehow to think what they believe in, is independent on how it was found out… people actually don't know, if you stop [i.e. ask] the average person, an average biologists, how do you know that the DNA is in nuclei, the majority of them would say, we know about, would say, by subcellular fractionation, and you say have you ever*

considered what happens in subcellular fractionation, they haven't". Basically, what he tries to point out is that scientists believe that what they find is independent from the method employed to find it, they do not examine the effects the chemicals and the procedures have on the matter of study.

What molecular biologists and biochemists call isolation is actually identification and documentation of the byproducts generated after application of chemicals and some kind form of heat on biological matter. They compare the generated byproducts to byproducts of previously "isolated" matter and if the identified and documented byproducts, their quantity and composition do not match to anything already documented then they will call it a novel substance. This applies not only to DNA but also to different types of Protein, Vitamins, RNA etc.

If DNA is not what it's supposed to be and if it's not responsible for anything ascribed to it then I wonder how much basis and substance the discoveries, theories and technology based on it have? e.g. genetics, CRISP, GMO, viruses, RNA and mRNA technology? I've already done some research on Protein, RNA and PCR where I found similar chemicals, procedures and assumptions performed and made.

I don't erase the fact that there is something, somethings that "instructs" or "initiates" the formation and the process of "life", that there might be something behind all of this. Is it a chemical substance/s or chemical reaction? I doubt it, especially after this literature investigation. If it's god or some kind of immaterial force or power, I can't confirm neither erase such a thought. Personally, I don't think there is something material, quantifiable, or chemical behind our consciousness, instincts and the manifestation of life.

Maybe I'm biased by reading Antoine Bechamp's work and whatever I

could find on Gaston Naessens but I believe studying Bechamp's microzymas (or Naessens somatids) can answer a lot of questions about life, microorganisms, tissue, health and dis-eases that scientist are so eagerly trying to answer, or are paid/funded to answer.

I might not be a scientist and don't have much experience in this field other than some school experiments but after doing this literature research I've concluded that no matter how much scientists try to explain life with chemicals reactions, numbers and alphabetical labeling, physical and mathematical models, they will fail to find anything meaningful. Dead or decomposing matter which is chemically treated can only reveal what and how something destroys and kills life not what creates it and how; and secondary, it looks like a very destructive and cruel branch of science. I don't feel that whatever scientists find in their test tubes after all the mentioned procedures holds any answers to life, but it definitely shows how chemicals and unnatural procedures destroy and kills anything living.

If I needed to describe in one sentence all that I've read to write this article it would be: "let's mix dead or living matter with chemicals, spin, boil, burn and document what happens".

Sincerely,

Tam

PS: Miescher "nuclein" got relabeled to "nucleic acid" by Richard Altmann. "Nucleic acid" represents Deoxyribonucleic Acid (DNA) and ribonucleic acid (RNA).

Some unreferenced articles that I found interesting and which helped in my research:

- Friedrich Miescher and the discovery of DNA
- The DNA Riddle: King's College, London, 1951-1953
- Photograph 51, by Rosalind Franklin (1952)

- The “scientific catastrophe” in nucleic acids research that boosted molecular biology