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The chromosome resembles more a crystal than other cell organelles

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Abstract. Several organelles in the cell, such as mitochondria and chloroplasts, are limited by one or several membranes, whereas others, like ribosomes and nucleoli have no membranes. Their shape is decided by their inner atomic coherence. The mineral crystal has no delimiting membranes built by separate atoms. Atomic self-assembly determines its pattern. Remarkable is that the chromosome has no outer membrane limiting its pattern as seen in the light and electronic microscopes. Its pattern is also decided by the inner coherence of the atomic configuration of its DNA, RNA, and proteins. The chromosome appears to occupy an intermediate position between a mineral crystal and a cell organelle when its atomic configuration is considered.

Keywords: chromosome, crystal structure, DNA.

MOLECULAR BIOLOGY DID NOT ORIGINATE FROM NATURAL SCIENCE BUT WAS A RESULT OF THE INTERACTION BETWEEN CRYSTALLOGRAPHY AND PHYSICS

It is usually not realized that the field of Molecular Biology had not its origin in Natural Sciences but resulted from the interaction of crystallography with physics. Cell biologists lacked many times knowledge of these two fields of science or these were mainly foreign to their minds.

The pioneers were Max von Laue (1879-1969), William Bragg (1862-1942) and Lawrence Bragg (1890-1971). All three were physicists. von Laue demonstrated that X rays were electromagnetic waves. He then realized that the atoms in a crystal were in an ordered array, in accord with their external regularity. He passed a narrow beam of X-rays through a crystal of a copper compound and obtained a diffraction pattern of spots on a photographic film.

This experiment became the basis of future X-ray crystallography. It allowed to measure the interatomic distance in crystals of diamond, copper, and salts such as KCI. The ordered atomic interior of crystals became a reality.

A PHYSICIST INROAD INTO GENETICS. SCHRÖDINGER WAS LOOKING FOR THE SIZE OF THE GENE BEFORE THE STRUCTURE OF DNA WAS ELUCIDATED

Several years before the chemical structure of DNA was revealed, the structure of genes and their size, was already a preoccupation. Geneticists, like most biologists tend to be conservative, and for them to venture into the molecular organization of the chromosome was foreign to their minds. But physicists, who at that time were already dealing with the extremely small elementary particles, such as the neutrino, felt obliged to inquire into the physics of living matter. Besides, by that time, geneticists asserted that the gene was to be built of proteins, because they were complex structures that demanded complex molecules. Nucleic acids, such as DNA, were too simple atomic combinations to carry the genetic material.

The leading physicist Schrödinger (1944) (Nobel Laureate 1933) was a professor in Berlin but had left Germany when Hitler assured power in 1933. He gave a series of lectures in 1943, in Dublin, Ireland, that were written down in his classic work "What is Life. The Physical Aspect of the Living Cell" (1944). By that time DNA had been demonstrated as being the genetic material in bacteria (Avery et al. 1943) but their experiment was regarded by geneticists to be of marginal value because at that time it was not known whether bacteria had chromosomes.

ASSERTING THAT ORDER IS TO BE SEARCHED IN LIVING PROCESSES

Schrödinger's main contribution was to emphasize the cell's physical construction and function:

1 Where others saw disorder, in the construction of the cell, he looked for order and stated: "We have inherited from our forefathers the keen longing for unified, all-embracing knowledge".

2 For the first time he called the chromosome "an aperiodic crystal" and added that "in physics we have dealt hitherto only with periodic crystals". And expressed clearly: "The difference in structure is of the same kind as that between an ordinary wallpaper in which the same pattern is repeated again and again in regular periodicity and a masterpiece of embroidery, say a Raphael tapestry, which shows no dull repetition, but an elaborate, coherent, meaningful design traced by the great master".

3 He calculated the size of atoms, but as he pointed out, we could not see them at that time. They ought to be "between about 1/5000 and 1/2000 of the wave-length of yellow light". Atomic diameters would range between 1 and 2 angstrom.

4 Schrödinger emphasized as well that physical laws are only approximate since they rest on atomic statistics. "As we shall presently see, incredibly small groups or atoms, much too small to display exact statistical laws, do play a dominating role in the very orderly and lawful events within a living organism".

5 He calculated the size of a gene as being "the volume of a gene equal to a cube of side 300 angstrom, being probably a large protein molecule".

6 "The gene has been kept at a temperature of 98° F, during all that time. How are we to understand that it has remained unperturbed by the disordering tendency of the heat motion for centuries?". Actually we know today that this period extended for millions of years, since the ribosomal RNA genes present in bacteria are the same as those found in plants and humans, only with minor modifications of the molecular edifice.

7 "Life seems to be orderly and lawful behavior of matter, not based exclusively on its tendency to go over from order to disorder, but based partly on existing order that is kept up". He calls it a new principle, "the order from order principle".

THE CHROMOSOME'S DNA TURNS OUT TO BE MORE PERIODIC THAN SCHRÖDINGER COULD HAVE ENVISAGED. THE EUKARYOTIC CHROMOSOME ARCHITECTURE IS BASED ON HIGHLY REPETITIVE DNA

Already at the prokaryotic level the DNA shows repeated sequences at precise positions. Examples are the IS elements and transposons of these genomes. In eukaryotes, the relative amounts of single copy and repetitive DNAs of many genomes are known, and certain classes of satellite DNA occur in the centromere and telomere regions.

In plant chromosomes the bulk of their DNA is made up of about 30 different repeat sequences. These are the tandemly repeated satellite DNA sequences of the centromere, telomeres and elsewhere. There are also long swathes of retrotransposon sequences. In maize they are of such high copy number that they form clusters that stretch for megabases along the DNA (Brown 2017).

Half of the human genome consists of repetitive DNA. Sequences consisting of 150 to 300 base pairs in length are repeated many thousands of times, and so called *Alu* sequences (circa 300 base pairs) They are present more than a million times.

Table 1. Reproduction of DNA can be compared to minerals.

REPRODUCTION	
Without DNA	With DNA
Centrioles	Chromosomes
Minerals	Cells
CELL ORGANELLES	
With membrane	Without membrane
	Centrioles
Chloroplasts	Chromosomes
Mithocondria	Nucleolus
CELL AND CELL ORGANELLE	
Membrane	No membrane
Cell	
Cell membrane (By self-assembly)	Ribosome
Endoplasmic Reticulum	Chromosome
Nuclear Envelope	
Mitochondrion	
Chloroplast	

Hence, the problem is not one of periodicity but mainly of the ability to be a self-sustained entity maintained by its atomic coherence.

This obliges to consider the role of membranes in the establishment of order in chemical reactions as well as their role in the establishment of well defined order in their construction.

THE CELL IS A WORLD OF MEMBRANES

The cell started, by being enveloped in a thick layer that separates it sharply from the environment. Besides it harbors a series of different membrane types.

But life creates many side solutions that led the cell to produce organelles that are not enclosed in membranes. The *membranous* part of the. cell consists of: (1) cell or plasma membrane, (2) nuclear membrane, (3) rough endoplasmic reticulum, (4) smooth endoplasmic reticulum, (5) Golgi apparatus, (6) mitochondria, (7) chloroplasts (in plants), (8) lysosomes, (9) centrosomes. But there are also *non-membranous* cell organelle: (1) chromosomes, (2) ribosomes, (3) nucleoli.

1 The *cell membrane* has long been known to consist of two protein layers separated by a phospholipid bilayer which regulates substance transport in and out of the cell.
2 *The nuclear envelope* consists of two lipid bilayer membranes an inner and outer membrane building a perinuclear space. The outer nuclear membrane is continuous with the endoplasmic reticulum. This is a connection between membranes that puts in evidence the ability to extend their range to other non-membranous organelles. One of its characteristics is its many nuclear pores. Filament proteins, called lamins give structural support to the nucleus.
3 The *endoplasmic reticulum* is a network of flattened membrane-enclosed sacs (*cisternae*) and tubular structures. These are continuous with the outer nuclear membrane. Both the rough and smooth reticulum are found in most eukaryotic cells but not in red blood cells or spermatozoa.
4 *Mitochondria* have two membranes: outer membrane and inner membrane. The two membranes have distinct properties. Infoldings of the inner membrane build cristae and there is a fluid internal matrix.
5 The *chloroplast* is even more complex. It is limited by a double layer with an intermediate space. Following secondary endosymbiosis chloroplasts may possess three or four membranes.

THE NON-MEMBRANOUS ORGANELLES OF THE CELL

(1) CHROMOSOME: As late as the 1960s there was a debate among cytologists of wether the chromosome had a surrounding membrane, called matrix, or this supposed pellicle was only an artifact. Soon more accurate studies and the electron microscope disposed of this artifact. The chromosome has no membrane surrounding its structure.

This situation is not unique, other organelles too do not have membranes limiting their bodies. These are the ribosomes and the nucleoli.

(2) RIBOSOME: Ribosomes in bacteria and eukaryotes are macromolecular "machines" found within all living cells that perform protein synthesis by messenger RNA translation. They link amino acids together to form polypeptide chains following an order specified by the codons of messenger RNA.

Ribosomes consist of two major components: the small and large ribosomal subunits (30S and 50S). Each subunit consists of one or more ribosomal RNA molecules and many ribosomal proteins. Together with other molecules they build the translational apparatus. Amino acids are selected and carried to the ribosome by transfer RNA. The 30S component has mainly a decoding function, the 50S has a mainly catalytic function. Ribosomes are often associated with the intracellular membrane that make up the rough endoplasmic reticulum, but are an independent non-membranous edifice built by dozens of distinct proteins of variable number.

(3) NUCLEOLUS: Nucleoli have been studied in over 500 species of eukaryotes from algae to humans and they were found to be a very well defined spherical body containing vacuoles (Lima-de-Faria, 1973, 1979).

The chemical composition of the nucleolus has been well established.

The nucleolus is the largest structure in the nucleus of eukaryotic cells and is known as the site of ribosome biogenesis. It also has other functions participating in the formation of signal recognition particles and in the cell's response to stress.

Nucleoli are a large structural edifice made of proteins, DNA and RNA. They are formed at a specific site called the nucleolar organizing region and are formed only in specific chromosomes.

Nucleoli have vacuoles that are clear areas in their center. The nucleolus consists of three major components: a fibrillar center, a dense fibrillar component and a granular component. In plants, some species have high concentrations of iron in this organelle.

To generate the 18S RNA, 5.8S and 28S RNA, RNA modifying enzymes are brought to recognition sites by interaction with guide RNAs showing a most ordered process. An additional RNA molecule is the 5SRNA which is also necessary. The DNA sequence responsible for its formation lies outside the nucleolus organizer region being transcribed in the nucleoplasm.

Significant is that this spherical cell organelle maintains this most regular configuration in hundreds of different species as an independent edifice without membrane.

THE CHROMOSOME IS MORE SIMILAR TO A MINERAL CRYSTAL THAN TO OTHER CELL ORGANELLES. IT IS NOT LIMITED BY A MEMBRANE

A cell, a nucleus, a chloroplast, a mitochondrion, all are limited by well defined membranes that show a complex structure when analysed with the electron microscope. Membranes are in abundance all over the cell. The endoplasmic reticulum that fills the cytoplasm consists of a long series of membranes tightly stapled on each other that could have been used as well to put definite limits on the chromosome.

But this is not the case. In this respect the chromosome is like the nucleolus, which has its limits determined by its molecular structure. The nucleolus may in exceptional cases have a radial shape but in the most studied species it has a regular spherical structure.

Hence both the chromosome, the ribosome and the nucleolus are in this respect closer to mineral crystals, which have natural faces determined solely by their molecular configurations.

A crystal of quartz, or any other mineral has facets that are not covered by any limiting structure, they emerge solely as a result of the atomic interactions of their constituent molecules.

Hence, the chromosome's atomic construction is closer to that of a mineral crystal than to a cell organelle.

DNA ASSOCIATED PROTEIN ALSO CRYSTALLIZE

It may be recalled that DNA, and its associate proteins, could not have been identified as macromolecules, atom by atom, if they were not crystallized. It is only by reducing them to this ordered condition that their atomic structure and their special organization could be defined.

Their crystallization was possible for the simple reason that their atomic configurations are highly ordered.

DEFINITION OF A CRYSTAL

"A solidified form of substance in which the atoms or molecules are arranged in a definite repeating pattern so that the external shape of a particle or mass of the substance is made up of planed faces in a symmetrical arrangement" (Webster 1976). The definition of Klein and Hurlbut (1985) is: "any solid with an ordered internal structure regardless of whether it possesses external faces". And in a broader definition: "a homogenous solid possessing long-range, three dimensional internal order".

MINERALOGISTS POINT OUT THAT DNA IS ALSO A CRYSTAL

The definition of a crystal by Wenk and Bulakh states clearly that DNA is a crystal: "is a homogenous chemical compound with a regular and periodic arrangement of atoms. But crystals are not restricted to minerals: they comprise most solid matter such as sugar, cellulose, metals, bones and even DNA".

RIBOSOMES ALSO ASSUME A CRYSTAL FORM AS A RESULT OF THEIR ORDERED ATOMIC STRUCTURE

Viruses, which consist of nucleic acids and proteins, can become crystal structures but abandon this ordered configuration when they reproduce in the cell. Ribosomes can form crystalline structures as is the case in chicken, mouse, and other types of tissues (Morimoto et al. 1972). Ribosomes become crystalline when the cells are chilled to 5-15°. Chromosomes follow the same condition. They also become crystallized when their activity becomes minimal and are obliged to occupy a minimum of space.

ACTUALLY, THE CHROMOSOME BECOMES A CRYSTAL IN THE ANIMAL SPERM

The evidence just described is corroborated by a key observation that is usually not cited. The arrangement of DNA in sperm nuclei has been studied by X-ray diffraction and polarizing microscopy. During spermiogenesis the proteins gradually condense. They also acquire specific patterns which are typical of the arrangement.

The crystalline organization of the chromosomes is particularly evident in the spermatids of two grasshopper species, *Dissosteira carolina* and *Melanoplus femur rubrum*. During development the nuclear fibers form plates which are oriented longitudinally to the major axis of the nucleus. Later these lamellae coalesce into a "crystalline body" (Gall and Björk,1958) as described by the antlion. As the electron microscope sections show the pattern is most similar to that of ribosome crystals.

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