The Structure of Genes and Genomes

The genome of an organism is physically located on its chromosome(s).
Plasmids--accessory (and sometimes autonomous) fragments of DNA in the cytoplasm--are not part of the genome, and are considered to be genomes unto themselves.
Viruses, too, have a genome--though they are not capable of replicating it without the cellular machinery of a living host.

The History of DNA's Discovery…

1. Frederick Griffiths (1928) first reported the TRANSFORMATION of non-pathogenic (rough) Pneumococcus bacteria into pathogenic (smooth) bacteria when live rough population was exposed to an extract of dead, boiled smooth Pneumococcus.
No one immediately knew which part of the extract was responsible for this transformation.
The polysaccharides in the cell coat?
Proteins?
Nucleic acids?
Lipids?
All of these substances were present in the extract, and no one yet knew which of them caused transformation.
They knew however, that the Mystery Substance must have three important properties:

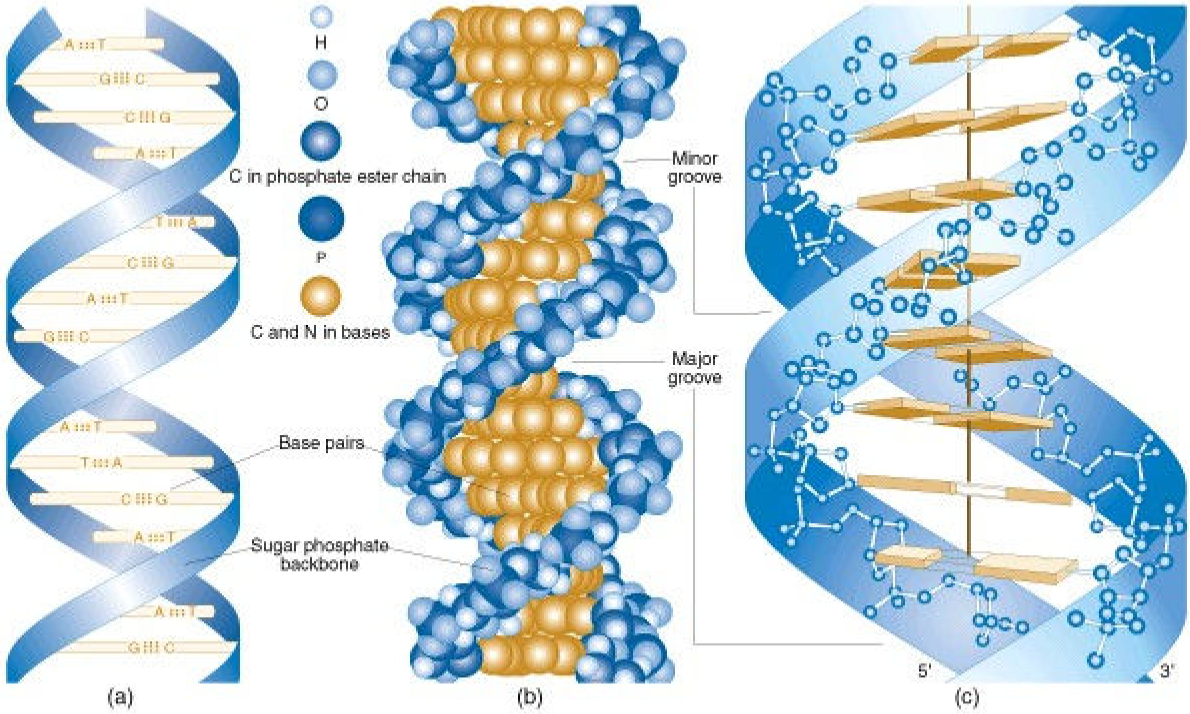
- It had to be duplicated whenever a cell divided, so it could be passed on unchanged.
- It had to be in the form of an informational code
- It had to be stable and--for the most part--resistant to change

2. Oswald Avery (1944) demonstrated that DNA was the substance responsible for bacterial transformation when he exposed Griffiths' extract to various substances, e.g.
lipases
proteases
RNase
DNase
carbohydrate-digesting enzymes
...that would inactivate/destroy one of the suspected compounds at a time.
Avery found that DNase (an enzyme which breaks down DNA) stopped the transformation process. Boiled DNase did not affect transformation.

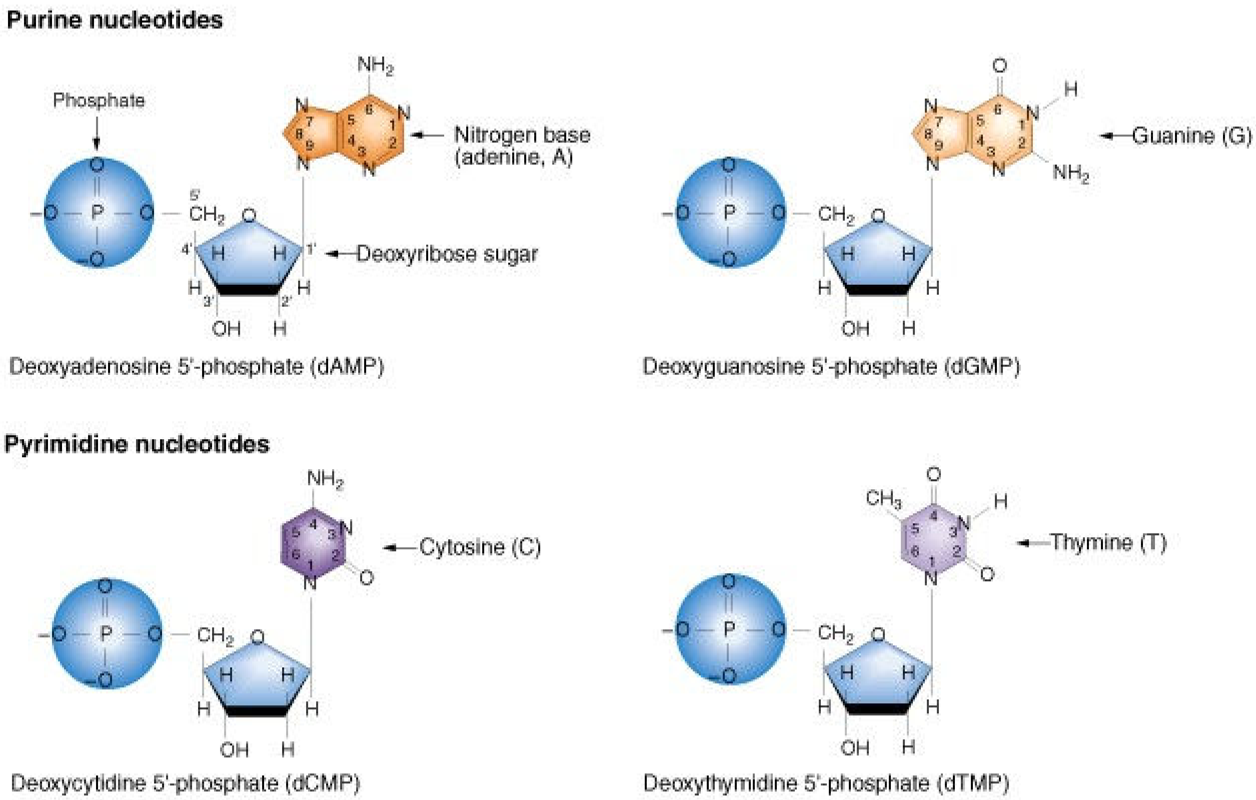
3. Edwin Chargaff (1950) noted that A and T were present in approximately equal quantities, as were G and C. (This is now known as "Chargaff's Rule")

4. Amazing x-ray crystallography by Rosalind Franklin (working in the lab of Maurice Wilkins) suggested a helical structure for DNA.

5. Watson and Crick (1953) used Franklin's data (not entirely with her consent) to cut and paste and finally came up with the helical model for which they are so famous today. THEY COULD NOT HAVE DONE IT WITHOUT ROSALIND FRANKLIN'S WORK. But they still get most of the credit.



DNA and RNA are polymers of nucleotides.



A nucleotide is composed of

- a sugar (deoxyribose in DNA; ribose in RNA)
- a phosphate group
- a nitrogenous base
- Adenine (purine)
- Guanine (purine)

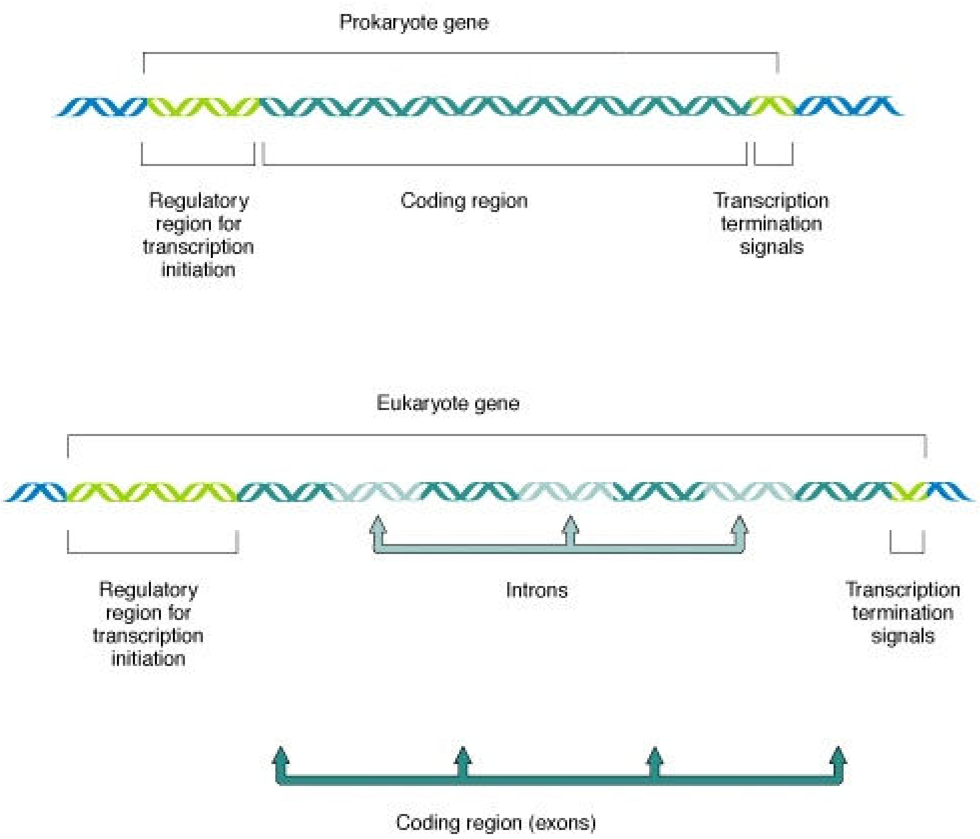
- Cytosine (pyrimidine)
- Uracil (pyrimidine - RNA)
- Thymine (pyrimidine - DNA)

The nucleotides are linked via PHOSPHODIESTER BONDS. The nitrogenous bases forming the "rungs" of the ladder are linked by HYDROGEN BONDS.

The structure of DNA

We already know that DNA can be transcribed into either informational (mRNA) or functional RNA (rRNA, tRNA, snRNA). It's also important that DNA not be transcribed constantly. This would be wasteful, and not allow cell differentiation during development of the organism.

Hence, every gene is flanked by REGULATORY REGIONS which allow it to respond to signals from its environment, attach to various other molecules, etc. and either turn "on" or "off" (or somewhere in between).



Also note that eukaryotic genes contain regions that are excised before translation (INTRONS) and others that are left behind and do encode information (EXONS). The number and size of these segments varies with species.

Genes on the chromosomes are separated by regions of DNA that do not appear to code for anything.

Some of these regions contain highly repetitive sequences called (conveniently) "repetitive DNA."

Repetitive DNA may be a result of mobile genetic elements: sections of DNA that copy themselves autonomously, and hop around the genome. (A remnant of ancestral "commensal" viruses?)
The function of repetitive DNA is still largely unknown, though some heritable diseases (e.g., Huntington's Disease) are associated with an abnormal number of repeats in specific locations. The more repeats a person has, the earlier the onset of the condition.

Plasmids

These are commensal or mutualistic segments of DNA found in bacteria that float separately from the chromosome and are not needed for basic maintenance of the bacterial cell.

- Plasmids cannot survive or replicate without their bacterial host.
- Plasmids may not be essential to host survival, but they can confer some real advantages, such as resistance to antibiotics, promoting bacterial genetic transfer, the ability to manufacture toxins exotoxins - secreted into the medium endotoxins - bound to the plasma membrane of the bacterium
- Plasmids may also sometimes be found in eukaryotic cells--usually plants and fungi.
- No eukaryotic plasmids are known to benefit the host cell, and some are pathogenic.
- Plasmid DNA is generally small, ranging from less than 10 kb to slightly more than 100.

Organelle DNA

- This is found in mitochondria (mtDNA) and chloroplasts (cpDNA).
- In any given cell, these organelles are usually (though not always) genetically identical.
- Organelle DNA is primarily there to govern the function of the organelles themselves.
- The organelle genome usually encodes the enzymes necessary for the energy transducing reactions (cellular respiration or photosynthesis) taking place in the organelle.
- Because they are intimately involved in energy transduction, mtDNA and cpDNA can have profound effects if they mutate. Errors in mtDNA, for example, can cause profound muscle weakness and other problems.
- Nuclear DNA also participates in manufacturing enzymes for organelle function; the organelles cannot function without nuclear DNA.
- However, the genes in the nucleus and the genes in the organelles are different from one another.

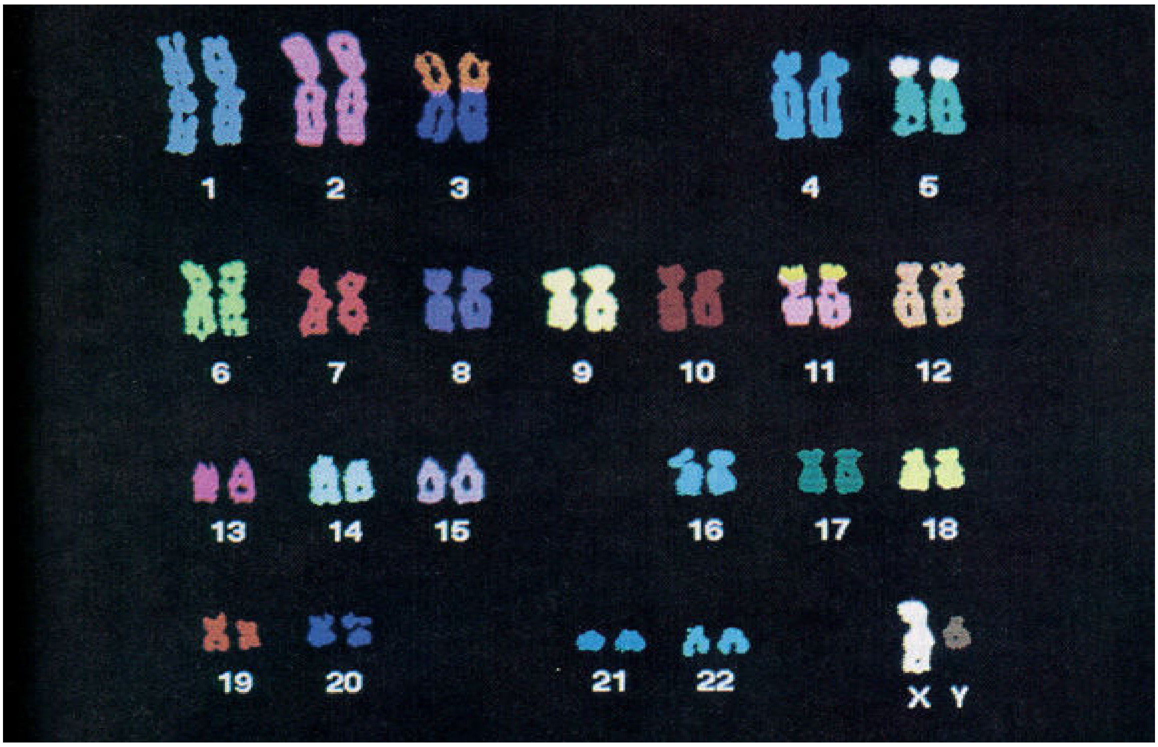
Prokaryote Genomes

- These are the genomes of the true bacteria, and usually (not always) they are present as a single, circular chromosome.

- The single chromosome is located in a large central area called the nucleoid (or nucleoid region). This is held together in a live bacterium, but falls apart when the bacterium is lysed (to yield a great, big string of DNA).
- Introns and exons exist in prokaryotes, but are very rare.
- Some bacterial genes code for proteins that are all used in the same function or process. Such genes are often located adjacent to each other on the chromosome, and are always transcribed together as a single mRNA that can be used for translation of all the proteins needed for that function or process.
- The entire functional group of genes is called an OPERON.
- The bacterial chromosome has a few associated proteins, but their function has not been completely elucidated.

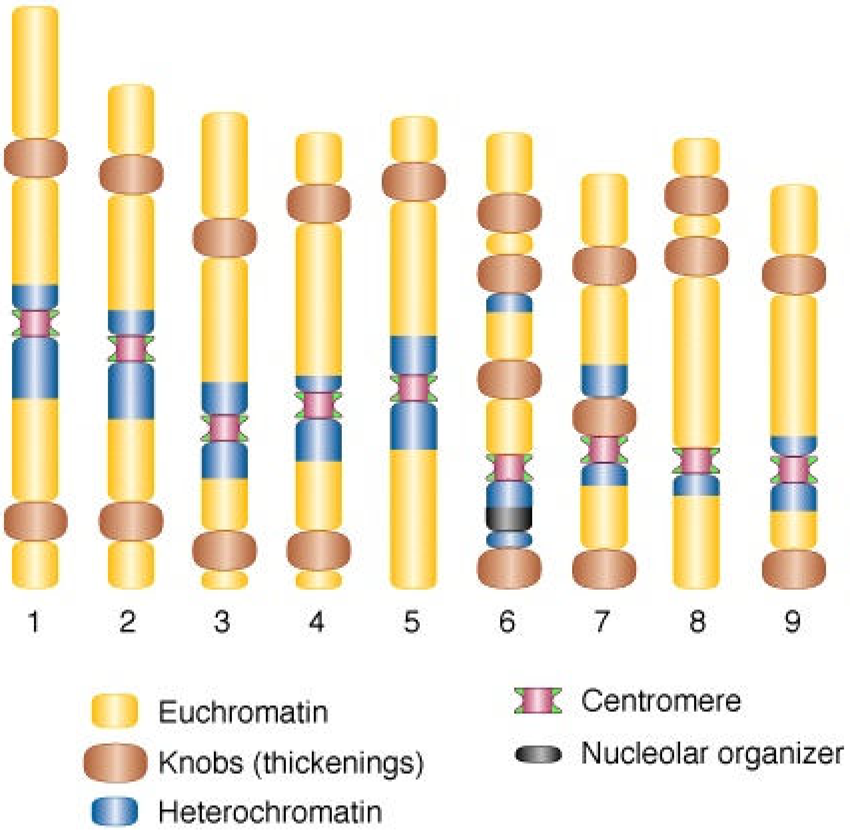
NUCLEAR GENOMES

- These are the chromosomes enclosed in the eukaryotic nucleus.
- Diploid (2n) cells contain two copies of the genome. Haploid (n) cells contain only one copy.
- n = the number of chromosomes in one complete copy of the genome.
- HOMOLOGOUS PAIRS of chromosomes are those which carry matching portions of the genome. Think of them as "mated pairs." They contain the same gene loci, though they may have different alleles of the genes at those loci.
- A chromosome that is not a sex chromosome is called an AUTOSOME
- A cell can be stopped in mid-mitosis, its metaphase chromosomes extracted and lined up in homologous pairs and photographed. Such a depiction of the chromosome complement is known as a KARYOTYPE. The karyotype yields important information, from chromosome number to physical markers on the chromosomes.



Useful physical properties of chromosomes include:

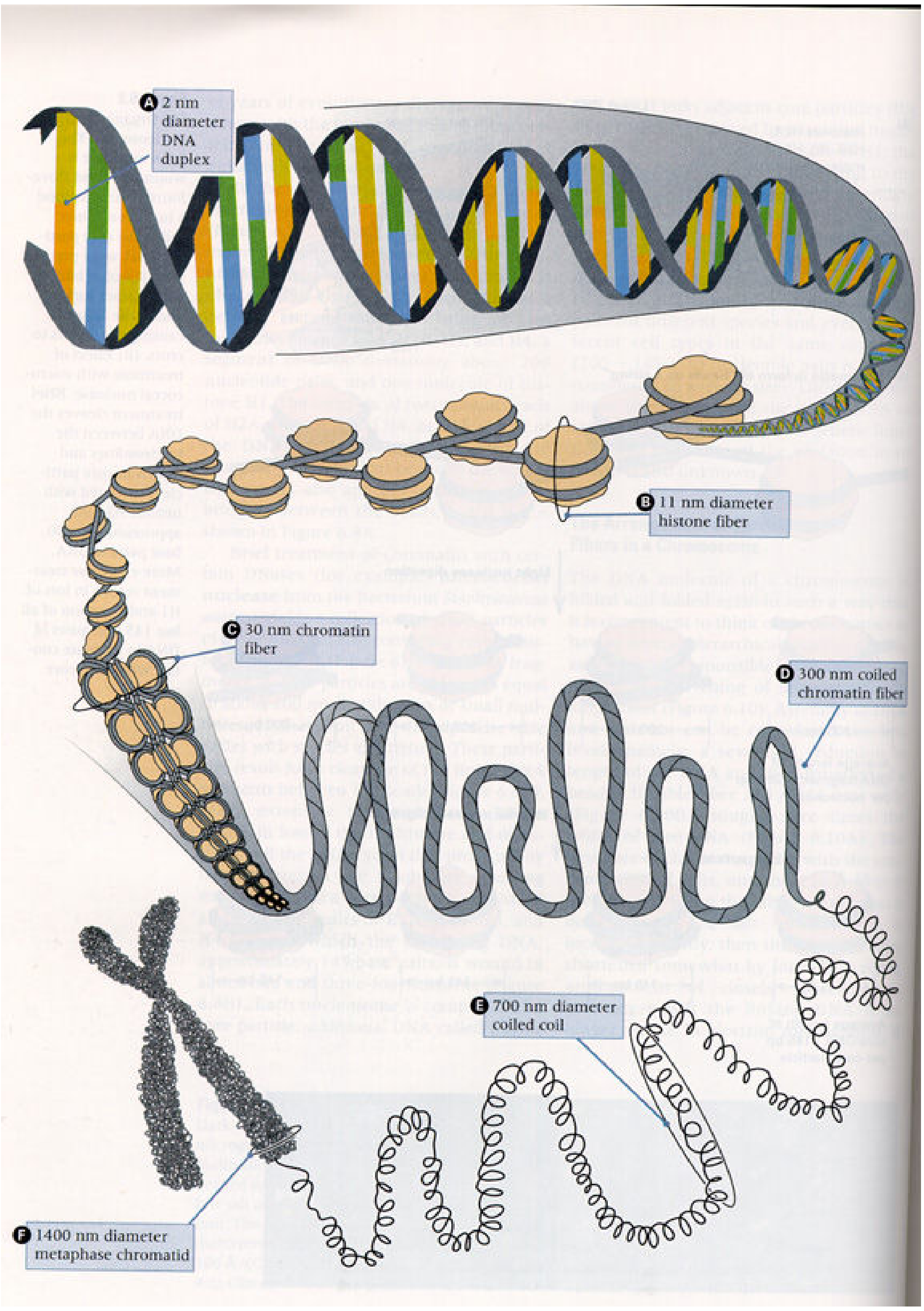
- size (relative to the others in the genome)
- position of centromere (location of the kinetochore, which is the proteinaceous structure to which sister chromatied attach during mitosis)
- telocentric (centromere at the end)
- acrocentric (centromere very close to the end)
- metacentric (centromere in the center)
- submetacentric - almost in the center
- chromomere patterns - function unknown. These are little thickenings along the chromosome, easily viewed during prophase of mitosis or meiosis. Especially large chromomeres are called "knobs."



- Heterochromatin patterns. Portions of the chromosome are generally present as either tightly coiled heterochromatin (not actively transcribed) and euchromatin (able to be transcribed). Certain stains can be used to show these regions, which have characteristic patterns.

Structure of the Eukaryotic Chromosome

Each eukaryotic contains one continuous, highly coiled and folded DNA molecule present in a protein/nucleic acid complex known as CHROMATIN.
DNA strand is wound on little lumps of DNA/histone called NUCLEOSOMES. These histones are octamers (composed of 8 subunit proteins, two of each of four types of histones).



A 2 nm diameter DNA duplex
B 11 nm diameter histone fiber
C 30 nm chromatin fiber
D 300 nm coiled chromatin fiber
E 700 nm diameter coiled coil
F 1400 nm diameter metaphase chromatid