

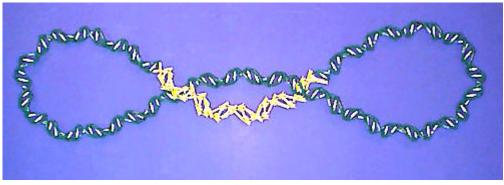
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K'NEX ® DNA Models

Developed by <u>Dr. Gary Benson</u> Department of Biomathematical Sciences Mount Sinai School of Medicine

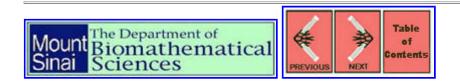
All photos by <u>Kevin Kelliher</u>. To download an Acrobat pdf version of this website <u>Click here</u>.

Simple and informative models of DNA can be built with **K'NEX** (a) brand constructors, found at most toy stores. These models, which take only a few minutes to build, illustrate many important physical properties of DNA including the major and minor grooves, antiparallel strands, right-handed and left-handed helices, positive and negative supercoiling, molecular flexibility, etc. More elaborate models can be built to illustrate complementary base pairing, transcription and replication. If *students* are allowed to build and manipulate the models, they will gain an intuitive sense of the physical properties of DNA which are essential to many cellular processes. These models can be used in either a high school or college setting. Instructions for building the models and illustrations of various properties of DNA are presented on the following pages. Either follow the pages in order or refer to the **table of contents** to find a particular topic.



Model of a negatively supercoiled, circular DNA molecule.

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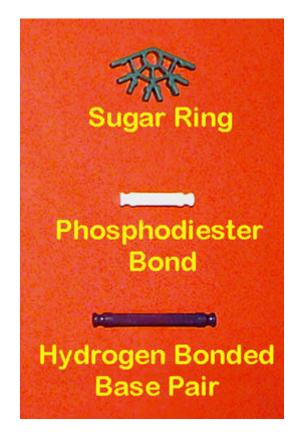
Building the helix



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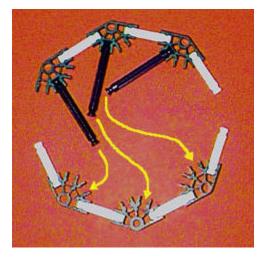
Building the helix

Models are built using a basic repetitive structure. Three pieces are required, the 135 degree green connectors, the white rods, and the blue rods. The green connectors serve as the **deoxyribose sugar** units of the helix backbone. **Phosphodiester bonds** linking the sugar units are represented by the white rods. **Hydrogen bonded base pairs** are represented by blue rods.

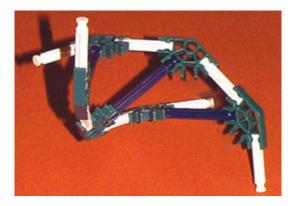


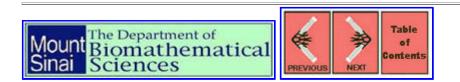
The connections for the simplest model are illustrated below. The double helix is composed of two backbones held together by hydrogen bonded bases. Each backbone is formed by joining green connectors in a chain using the white rods attached to the outer slots. The backbones are cross linked with the blue rods. Blue rod attachment should be at the third slot of the green connectors on each chain. Because the chains are anti-parallel, on one chain attachment should be at the **third slot from the left** and on the other chain, **third slot from the right**.

Building the helix



Follow the arrows above to produce the segment pictured below. When the second blue rod is attached, the two backbones will start to twist around each other.





Helix geometry

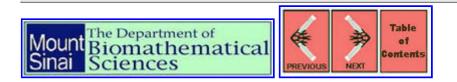


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Helix geometry

Once you have cross-linked seven or eight blue rods, pick a sugar ring (green connector) and follow its strand around the helix until you reach another sugar ring in the same orientation. This is one **helical turn** and it occurs after reaching the sixth green connector (start counting with the first connector after the one you picked). The model has six base pairs (blue connectors) per helical turn. In the normal form of DNA, there are ten base pairs in one helical turn. Hold your model vertically. Notice that the base pairs are inclined. The angle they make with horizontal is close to 20 degrees. In normal DNA, the base pairs are nearly horizontal (the incline is -6 degrees).



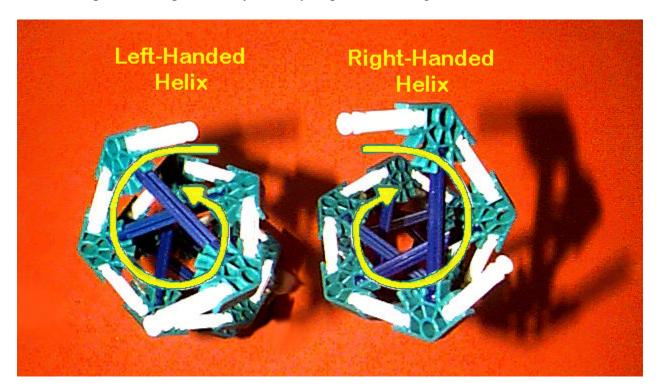


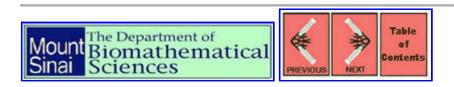


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Right-handed and left-handed helices

Is your model a right-handed helix or a left-handed helix? If you hold it pointing away from you and it twists clockwise moving away, it is right-handed, otherwise it is left-handed. These models are mirror images and can not be converted one into the other by rotation. The helix of normal DNA is right-handed. Left-handed helices have been produced experimentally and may be present in living cells.



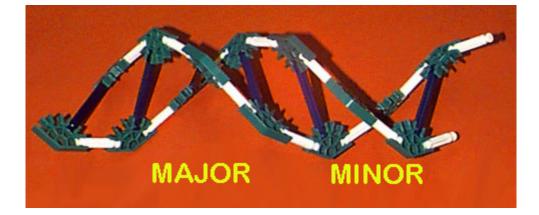


http://c3.biomath.mssm.edu/knex/right.left.hand.knex.html

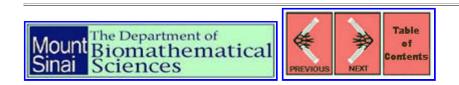


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Major and minor grooves



The strand backbones are closer together on one side of the helix than on the other. The **major groove** occurs where the backbones are far apart, the **minor groove** occurs where they are close together. The grooves twist around the molecule on opposite sides. Certain proteins bind to DNA to alter its structure or to regulate transcription (copying DNA to RNA) or replication (copying DNA to DNA). It is easier for these **DNA binding proteins** to interact with the bases (the internal parts of the DNA molecule) on the major groove side because the backbones are not in the way.



Anti-parallel strands

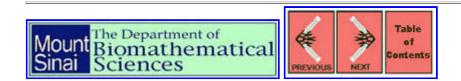


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Anti-parallel strands



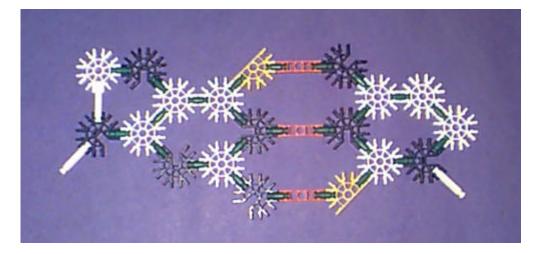
The DNA molecule is composed of two strands held together by hydrogen bonds. A single strand is different at its two ends. One end is called 5' (5 prime), the other is called 3' (3 prime). The names come from the notation for the two sugar carbon atoms which participate in the phosphodiester bonds. The different strands in the helix run in opposite (anti-parallel) directions. At each end of the double helix, one strand is 5' and the other is 3'. In the illustration, the 3' end is shown with a red arrowhead and the 5' end with the yellow connector.

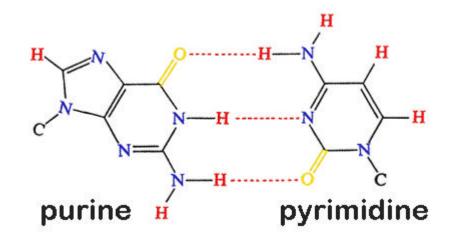




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Base pairs





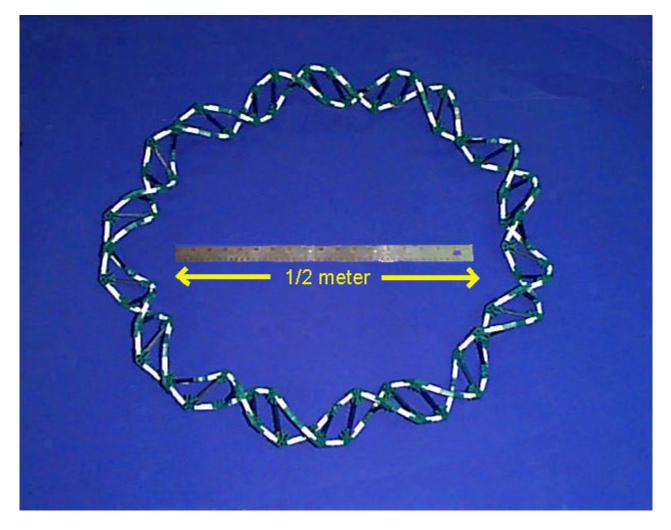
Attached to each sugar ring is a **nucleotide base**, one of the four bases **Adenine** (A), **Guanine** (G), **Cytosine** (C), and **Thymine** (T). The first two (A, G) are examples of a **purine** which contains a six atom ring and five atom ring sharing two atoms. The second two (C, T) are examples of a **pyrimidine** which is composed of a single six atom ring. A **base pair** is one of the pairs A-T or C-G. Notice that each base pair consists of a purine and a pyrimidine. The nucleotides in a base pair are **complementary** which means their shape allows them to bond together with **hydrogen bonds**. The A-T pair forms two hydrogen bonds. The C-G pair forms three. The hydrogen bonding between complementary bases holds the two strands of DNA together. Hydrogen bonds are not chemical bonds. They can be easily disrupted. This permits the DNA strands to separate for **transcription** (copying DNA to RNA) and **replication** (copying DNA to DNA). In our simple model, the entire base pair structure is represented by the single blue rod. Various more elaborate models can be constructed to represent base pairs, including the one above which shows individual atoms and bonds.

Helix Flexibility

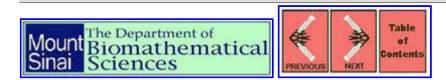


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Helix Flexibility



Both the model and real DNA helices can be deformed from their linear shape into curves and bends. Real DNA does this as a result of normal thermal motion and under the influence of certain proteins which bind to DNA. The **nucleosome** which is a DNA packing structure is one example where DNA is held in a non-linear form. Each nucleosome consists of a core of **histone** proteins around which the DNA double helix is wrapped some 1.6 turns. Other proteins such as DNA **transcription factors** also alter the geometry of DNA and thereby modify its ability to be transcriped into RNA. Above is a model of DNA deformed into a circle. This requires just over 8 helical turns (50 base pairs). If you build this model, be sure to attach the same strand to itself when closing the circle.



http://c3.biomath.mssm.edu/knex/helix.flexibility.knex.html

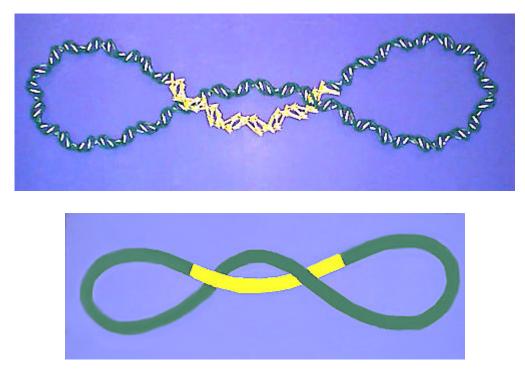
Supercoiling



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Supercoiling

When the DNA helix has the normal number of base pairs per helical turn it is in the **relaxed** state. Changing this normal amount of twist can be demonstrated by grasping both ends of a short linear model (one to two complete turns) and twisting the ends in opposite directions. If the helix is overtwisted so that it becomes tighter, the edges of the narrow groove move closer together. If the helix is undertwisted, the edges of the narrow groove move further apart. Notice that changing the twist from the relaxed state requires adding energy and increases the stress along the molecule.



If DNA is in the form of a circular molecule, or if the ends are rigidly held so that it forms a loop, then overtwisting or undertwisting leads to the supercoiled state. **Supercoiling** occurs when the molecule relieves the helical stress by twisting around itself. Overtwisting leads to **postive supercoiling**, while undertwisting leads to **negative supercoiling**. Twist can be altered in a circular model by breaking the circle, over or undertwisting and then reconnecting the ends. In the illustration above of a negatively supercoiled molecule, part of the helix is yellow to show how the molecule twists around itself. If you attempt to unwind this **molecular twist**, the helix will become further undertwisted.

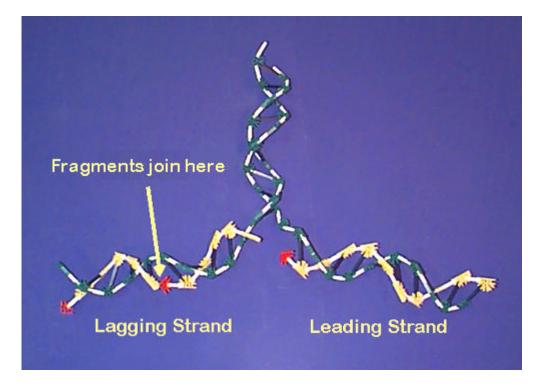
Although supercoiling relieves some stress in the molecule, when there is negative supercoiling, further stress can be relieved by partial **strand separation**. The hydrogen bonds (holding together complementary bases) break and part of the double helix separates. Strand separation is required for transcription (copying DNA to RNA) and replication (copying DNA to DNA). In the figure below, the yellow strands have separated allowing the molecule to relax and assume a circular configuration.

Replication

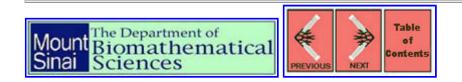


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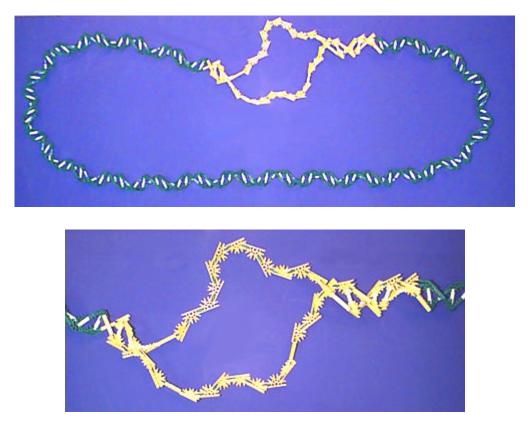
Replication



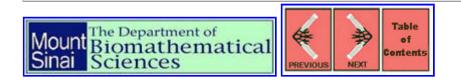
The figure shows DNA in the process of replication (the production of two DNA molecules from one). The original (template) strands have green and white backbones. The new strands have yellow and white backbones. New nucleotides are added on the 3' ends which are shown with red arrowheads. The **leading strand** (shown on the right) is the new strand which grows towards the **replication fork**. The **lagging strand** (left) grows away from the fork. Periodically, the lagging strand is joined (ligated) with the previous lagging strand to make one long piece. The joining occurs where the red arrowhead on the 3' end abuts the yellow connector on the 5' end. As the original DNA unwinds, a new lagging strand will grow and join with this one. Replication requires the action of many proteins which are not shown.



Supercoiling



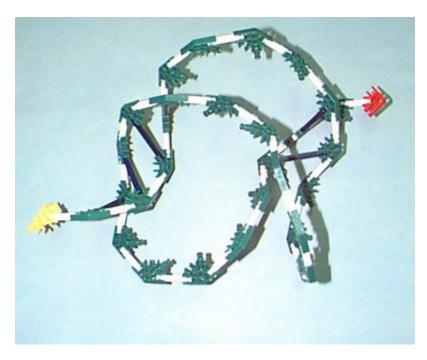
The models above were built with white rods for the base pairs and small green rods for the phosphodiester bonds. Yellow 180 degree connectors were used for the separating strands. The models contain approximately 26 helical turns or 160 base pairs.





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RNA



RNA is very similar to DNA. The differences are 1) the sugar is **ribose** rather than deoxyribose, 2) the nucleotide **Uracil** (U) is used instead of Thymine, and 3) RNA is **single stranded** rather than double stranded. But, the nucleotides in RNA are able to form complementary base pairs A-U (rather than A-T) and C-G which allows the single strand of RNA to form **short double stranded regions** by looping back on itself.

