# An Inexpensive Model of the Insulin Molecule

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The use of models to illustrate properties of various molecules is a widely established practice in the science classroom (Goodman, 1970). Models of the smaller organic molecules are readily available from commercial sources at reasonable prices or can be easily constructed from common household materials. However, good models of large biomolecules, such as nucleic acids and proteins, are more difficult to fabricate and those available from scientific supply companies are expensive.

The model of a protein, insulin, is described here. It is easily constructed, costs little, and can be assembled in less than an hour. The model is durable and versatile: it can be used to illustrate many characteristics of insulin as well as to demonstrate the major structural features of proteins and enzymes in general.

## Structure of the Molecule

Insulin was the first protein for which the molecular structure was elucidated. The fascinating story of how Frederick Sanger and his associates at the Cambridge University deduced the structure is retold in many textbooks of biology and biochemistry; for primary accounts see Sanger (1949), Sanger and Thompson (1953), Thompson (1955), and Sanger and Smith (1957).

Insulin is a relatively small protein found in the blood of most mammals. Produced by special cells in the pancreas, it is involved in the regulation and metabolism of glucose. Beef insulin is composed of 17 different amino acids. The total number of amino acid units in the molecule is 51. These are

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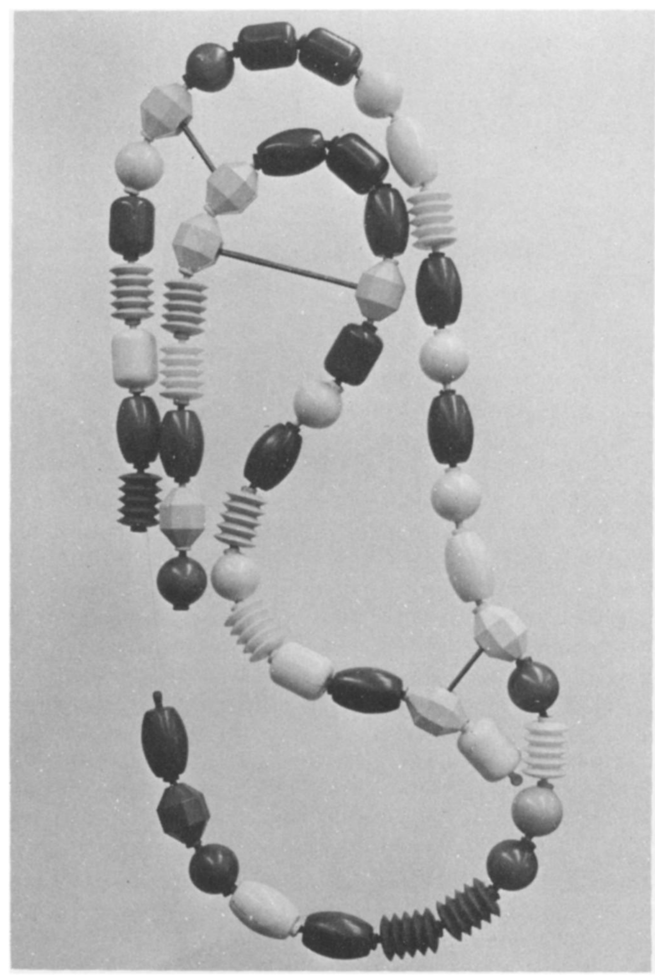

Fig. 1. Model of the beef insulin molecule. Each bead represents a different amino acid.

arranged in two chains or peptides of unequal length. The smaller chain, known as the glycl or A chain, is composed of 21 amino acid units. The larger chain, called the phenyalanyl or B chain, contains 30 amino acid units and is linked to the smaller peptide at two points by disulfide bonds.

The amino acid sequence of a protein is known as the primary structure. Insulin, like many other proteins, contains a large diversity of amino acids rather than a large number of one or two particular amino acids. Also, there are no obvious repeating amino acid sequences or other systematic arrangement of the amino acids—a characteristic that should stimulate considerable classroom speculation into evolutionary mechanisms at the molecular level.

The secondary structure of a protein is formed by disulfide bonds that cross-link peptides. The cross-links occur between the sulfur-containing amino acid, cystine. Insulin contains three disulfide bridges: two bind the A and B chains together and the third links two cystine units within the A chain. The latter bridge causes a loop in the A chain.

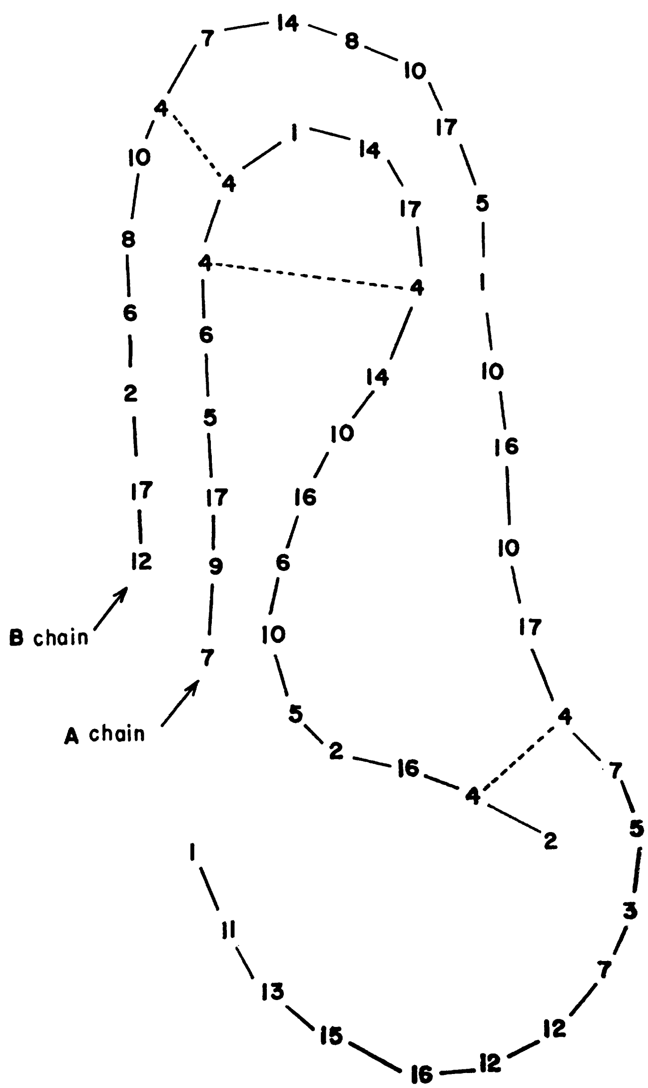


Fig. 2. Amino acid sequence of the beef insulin molecule. Numbers correspond to those in the listing of amino acids in the table. (Illustrations by the author.)

**Beads used to represent amino acids in the beef insulin molecule.**

| *Amino acid* | *Number required* | *Color* | *Shape* |
|---|---|---|---|
| 1. alanine | 3 | dark blue | football |
| 2. asparagine | 3 | pink | barrel |
| 3. arginine | 1 | orange | sphere |
| 4. cystine | 6 | yellow | 24 facets |
| 5. glutamic acid | 4 | yellow | accordian |
| 6. glutamine | 3 | light blue | accordian |
| 7. glycine | 4 | lavender | sphere |
| 8. histidine | 2 | dark blue | barrel |
| 9. isoleucine | 1 | light blue | 24 facets |
| 10. leucine | 6 | pink | sphere |
| 11. lysine | 1 | red | 24 facets |
| 12. phenyalanine | 3 | red | accordian |
| 13. proline | 1 | red | sphere |
| 14. serine | 3 | green | barrel |
| 15. threonine | 1 | pink | football |
| 16. tyrosine | 4 | green | football |
| 17. valine | 5 | red | football |

The tertiary structure of a protein is the three-dimensional configuration of the peptides. Because of a variety of possible interactions between amino acid side groups, peptides may be folded and twisted into a variety of forms and shapes. The three-dimensional structure of insulin was deduced from x-ray diffraction studies by Oxford professor and Nobel prizewinner Dorothy Hodgkin and a team of postdoctoral students. Their studies showed that the B chain is folded into a distorted U shape with the smaller A chain nesting inside.

## Features of the Model

It is difficult to model in detail all aspects of a large and complex molecule such as insulin. In the model shown (fig. 1), the primary, secondary, and tertiary structures are emphasized. The molecular structure of the amino acids is not shown. Components of the model are identified graphically in fig. 2.

The model is made from Giant Snap Lock Beads (Fisher Price Toys, Inc., East Aurora, N. Y.); however, similar beads from other manufacturers probably could be adapted for the same purpose. The Fisher Price beads are large plastic beads available in many different combinations of colors and shapes. The beads are hollow, with a small hole in one end and a knobbed prong on the other end. In the model, each bead represents an amino acid—the hole being the amino group and the prong the carboxyl group. The peptide linkage between amino acids is formed by simply snapping two beads together. Each amino acid is represented by a different bead. For example, in the model shown a spherical lavender bead always represents the amino acid glycine and a red accordion-shaped bead represents phenyalanine.

The table shows the kinds of beads, and the number of each, used to construct the model. Beads are frequently packaged in assortments that vary from carton to carton; if necessary, the code can be modified in accordance with the kinds of beads available.

The disulfide bridges are made from wooden tongue-depressors. A knob is carved on each end of the depressor and slits are cut into the sides of the appropriate (cystine) beads. The bridge, or cross-link, is formed by inserting the knobs of the tongue depressors into the slits in the beads and twisting the depressor 90 degrees to lock it in place. With this simple arrangement, the cleavage and the formation of the disulfide bridge can be demonstrated.

A number of refinements may be added to the model. For example, the molecular structure of each amino acid could be printed on cardboard and glued to the appropriate bead. Or only the side groups for each amino acid could be printed and fastened to the proper bead.

### Some Possible Uses

Because of the variety of brightly colored and distinctly shaped beads, the sequence and diversity of amino acids in insulin is readily apparent to a large class. The lack of repetitive patterns in the amino acids sequence is especially noticeable. The differences in amino acid composition between beef insulin and other mammalian insulin can be shown by substituting beads at the appropriate positions.

Since the model can be so quickly assembled and disassembled, denaturation of the protein can be demonstrated. Also, the variety of peptides resulting from various hydrolytic procedures and enzymatic digestions can be shown. Although little is known of the enzymatic mechanisms of insulin, the model can be used to demonstrate and speculate on "active site" theory as it applies to other enzymes.

### REFERENCES

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## AGRICULTURAL HALL OF FAME

The Agricultural Hall of Fame, chartered in 1960 by Congress, is located at Bonner Springs, Kan., 12 miles west of Kansas City. It is open to the public seven days a week.

## THE LITTLEST POLLUTER

The bacterium *Thiobacillus thiooxidans* is responsible for poisoning streams near hot springs, killing fish, disintegrating metal and concrete structures, destroying rocks, and stunting tree growth. During investigations of waters flowing out of regions of hot springs, such as Yellowstone National Park, scientists of the U.S. Geological Survey discovered that the bacteria turn hydrogen sulfide into sulfuric acid by consuming the gases boiling off the water underground. The sulfuric acid is carried away by rain, snow melt, and condensing steam to pollute streams. The bacteria are so efficient that they can produce about 1 kg of concentrated sulfuric acid daily per 100 $m^2$ of ground surface.

## SEARCH FOR ANTICANCER DRUGS

The National Cancer Institute's search of the plant and animal kingdoms for new sources of anticancer drugs has been extended to undersea plant life. Other organic materials currently being studied by the institute as possible drug sources include fungi, insects, and bacteria. One of the best-known cancer drugs, vincristine, was developed from an extract of the periwinkle plant, *Vinca rosea* Linn.

## WOLF IS RESOURCE SYMBOL

The timber wolf, long maligned as a creature of evil and destruction, has been chosen as the official symbol of the Manitoba Department of Mines and Natural Resources.

In announcing the new symbol to departmental staff, the department's deputy minister, W. Winston Mair, said: "The wolf best typifies much of Manitoba—wooded Precambrian Shield, strewn with lakes and laced with rivers. Manitoba without wolves would be a much poorer place in which to live because the wolf is inextricably bound up in the ecology of our province.

"By naming the wolf as our symbol, we are also undertaking to see that it gets the necessary protection to maintain a reasonably abundant population. I think this attitude toward the wolf, if it is carried on to all other forms of plant and animal life in Manitoba, is a good one for professional resource managers to take. It means we understand (or try to understand) the complex interrelationship of nature, we recognize the value of all life forms, and we are prepared to champion a worthy example of Manitoba wildlife despite the myths and legends that have made it an unpopular creature."