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ACKNOWLEDGEMENTS

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DEDICATION

This book is dedicated to Toby and Davis and all children who remind us that the smallest things can be the most important.
Imagine you could build something from scratch atom by atom. What would you build? Would you build a robot that would move through your body gobbling up diseased cells or create a new molecule that when sprinkled on an oil spill would break down the oil, eliminating any risk to the environment? For the first time in human history we have the ability to manipulate and build materials from the atom up. New tools such as the atomic force microscope allow us to not only image atoms, but also move atoms into new arrangements that have never been attempted before. What makes all this particularly remarkable is that all this takes place at the nanoscale—one-billionth of the size of a meter. Futurists predict that nanotechnology will be the next major scientific revolution and will have greater impact on our lives than the industrial revolution or the great advances that have been made in genomics.

This book examines nanoscale science with an eye toward understanding nanotechnology. Geared toward middle and high school teachers, these investigations are designed to teach students about the unique properties and behaviors of materials at the nanoscale. The investigations were developed as a result of three National Science Foundation grants given to the authors for research examining effective ways to teach and learn nanoscale science. The investigations are designed as guided inquiry with open-ended exploration where possible. The goal of the book is to introduce the essential concepts that students need to understand nanoscale science while maintaining a broad inquiry approach. The activities of this introductory book may serve to whet the students’ appetites to know more. The book is organized around five themes: scale, tools and techniques, unique properties and behaviors, nanotechnology applications, and societal implications (see key concepts listed in Table 1).
Table 1: Key NanoScience and Engineering Concepts.

<table>
<thead>
<tr>
<th>Size and Scale</th>
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<tbody>
<tr>
<td>Nanoscale</td>
<td>The unique placement of the nanoworld between atomic and micro/macro scales allows exploration of the regime where properties transition from atomic behavior to familiar macro behavior.</td>
</tr>
<tr>
<td>Relative Scale</td>
<td>How large objects are in relation to each other. (Which is bigger an atom, molecule, or a virus?)</td>
</tr>
<tr>
<td>Powers of Ten</td>
<td>What is a nanometer? How much smaller is a nanometer than a micrometer?</td>
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<table>
<thead>
<tr>
<th>Tools and Techniques</th>
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<tbody>
<tr>
<td>Atomic Force Microscopy</td>
<td>Probing microscopes use a scanning tip to detect physical properties of materials.</td>
</tr>
<tr>
<td>Nanoimaging</td>
<td>The ability to detect the arrangement of matter at the nanoscale allows for the design of new materials.</td>
</tr>
<tr>
<td>Nanomanipulation</td>
<td>Manipulating matter at the nanoscale opens up whole new possibilities building new objects.</td>
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<table>
<thead>
<tr>
<th>Unique Properties and Behavior</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Stickiness</td>
<td>Intermolecular forces dominate familiar forces such as gravity (van der Waals bonding, hydrogen bonding…) at this scale.</td>
</tr>
<tr>
<td>Shakiness</td>
<td>Thermal energy produces strong effects (Brownian motion, thermally activated processes).</td>
</tr>
<tr>
<td>Bumpiness</td>
<td>Graininess of matter (atoms/molecules) and properties (quantization, quantum confinement) makes working at this scale bumpy.</td>
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</table>

<table>
<thead>
<tr>
<th>Nanotechnology Applications</th>
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</thead>
<tbody>
<tr>
<td>Nanomaterials</td>
<td>The ability to synthesize small materials means new functionality, improved materials properties, and revolutionary technology.</td>
</tr>
<tr>
<td>Textiles</td>
<td>Nano construction allows for the creation of new fabrics that resist staining or have antibacterial properties.</td>
</tr>
<tr>
<td>Building Materials</td>
<td>The ability to mimic nature at the nanoscale allows the lotus effect to be applied to objects such as windows.</td>
</tr>
<tr>
<td>Medicine</td>
<td>Medical applications include nanoshells that target cancers and tumors for detection and treatment.</td>
</tr>
<tr>
<td>Water Quality</td>
<td>Nanoparticles that can detect and combine with pollutants may provide more efficient ways to clean water.</td>
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<table>
<thead>
<tr>
<th>Societal Implications</th>
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<tbody>
<tr>
<td>Environmental</td>
<td>What are the unknown dangers of generating new nanoparticles that may be released in the environment?</td>
</tr>
<tr>
<td>Ethical</td>
<td>What are the ethics of creating new materials and rearranging matter?</td>
</tr>
<tr>
<td>Social</td>
<td>How will society change as a result of using nanolabels to track the movement of people, animals, and materials throughout the globe?</td>
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</tbody>
</table>

Nanoscale science uniquely ties together all the science domains because it focuses on the raw materials—atoms and molecules—that are the building blocks of physics, chemistry, biology, and Earth and space sciences (Table 2). In unprecedented ways, scientists from different departments are collaborating in nanoscale research to explore science from multiple perspectives. For example, physicists are interested in the unusual properties of gold nanoshells. These tiny nanoparticles begin as glass beads that are then covered with gold. The nanoshell behaves differently depending on the size of the gold shell. Different-sized shells have different melting temperatures, different electrical conductivity behaviors, and are even different colors. These properties make it an ideal tool for use in medical testing and treatment.
### Table 2: Nano Investigations and the Science Domains

<table>
<thead>
<tr>
<th>Investigations</th>
<th>Biology</th>
<th>Physics</th>
<th>Chemistry</th>
<th>Mathematics</th>
<th>Environment</th>
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<tr>
<td><strong>Introduction</strong></td>
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<td><strong>Tools and Techniques</strong></td>
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<td><strong>Unique Properties of Nano Materials</strong></td>
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<td>It’s a Small World After All: Nanofabric</td>
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<td>How Nature Builds Itself: Self-Assembly</td>
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<td>Physics Changes With Scale</td>
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<td>Limits to Size: Could King Kong Exist?</td>
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<td>Promise or Peril: Nanotechnology and the Environment</td>
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The gold that coats the nanoshell is an inert metal that easily absorbs light and the rate of absorption and reflection depends on the thickness of the gold layer. This differential rate of absorption means the nanoshell can be used for locating and treating cancer. When nanoshells are coated with antibodies and injected into the body, they are delivered by the body to a specific cancer where antibodies on the nanoshell attach to antigens on cancer cells. When a laser is shown on the cancerous area, the gold nanoshells heat up—essentially cooking the cancer while the surrounding healthy cells are unharmed. In addition to treating the cancer, a similar process is used to attach fluorescent dyes to nanoshells. When the fluorescent dyes...
are injected into the body the nanoshells glow in areas where there are cancer cells, which makes the nanoshells a remarkable tool that allows doctors to very specifically locate cancers and target specific areas for treatment. Not only is nanotechnology being innovatively used in medicine but also in environmental science. Scientists are exploring the use of nanoshells as a way to target and filter specific pollutants in water. The goal is to have a highly efficient way to provide clean water to countries around the Earth. As this example shows, a single application such as a nanoshell can be used in chemistry, physics, biology, and Earth and space sciences. By exploring science at the tiniest of scales, students can begin to understand the building blocks of materials and the properties of atoms and molecules that make up our world.

This book begins the study of nanotechnology for students by getting them to think about the very small size of a nanometer. Understanding size and scale at this very tiny level is difficult because we cannot easily experience things this small. Most students have trouble understanding the small sizes of things like cells or bacteria, and even more difficulty understanding the size of atoms, molecules, or viruses. The investigation of scale begins with a focus on relative size (understanding which is bigger, a virus or a cell) and moves to investigating the powers of ten, which are the foundation of the metric system. Students explore just how tiny one part in a billion really is through a series of investigations with dilutions (One in a Billion). Students explore the size and geometry of nanomaterials such as buckyballs, carbon nanotubes, and even viruses (Nano Shapes: Tiny Geometry). Next students take a look at viruses as self-assembling nanomachines (Biological Nanomachines: Viruses). These activities lay the foundation for later concepts that focus on molecular self-assembly and the introduction of unique properties of nanotubes.

**Tools and Techniques**

Just as the microscope and the telescope opened up new worlds that had never been seen before, the atomic force microscope and other new nanoscale tools have enabled significant advancements in nanoscale science. But unlike the telescope and microscope, the nanoscale world is too small to be seen and can only be detected through other more indirect means. Students explore what it is like to try to detect unknown materials bound inside a black bag (What’s in Your Bag: Investigating the Unknown). They must think like scientists to detect the properties and shape of their unknown materials. Next, students explore how an atomic force microscope (AFM) works to probe these tiny materials. Using a pen flashlight they model how an AFM scans back and forth to detect shape (Scanning Probe Microscopy). Next, students use magnets to shape ferrofluid into new forms and explore how magnetism can be a tool for detection and manipulation (NanoMagnets: Fun With Ferrofluid).

**Unique Properties and Behaviors**

The section on unique properties and behaviors of nanoscale materials introduces students to the structure of these materials. They begin their investigations exploring how nanofabrics are able to repel a range of stains and liquids (It’s a Small World After All: Nanofabric). This effect is explored further with living materials as students explore biomimicry of the lotus effect using plant leaves. This remarkable activity shows how the structure of some leaves makes them highly resistant to dirt, giving them a self-cleaning mechanism. Using magnifying glasses, students can see water bead up on leaves like cabbage and then watch as water droplets pick up other solid materials and as it rolls off the leaf (Biomimicry: The Mystery of the Lotus Effect). This macroscale investigation models the behavior of new self-cleaning glass that is used in skyscraper windows.
Materials behave very differently at the nanoscale than they do at the macroscale that we usually experience. The investigations Physics Changes With Scale, How Nature Builds Itself, and Shrinking Cups are designed to explore the shaky, bumpy, and sticky nanoworld. At this tiny scale materials are very bumpy and are highly influenced by changes in thermal energy. Students model this behavior through a self-assembly activity using Legos and magnets. After placing pieces of magnets and Legos into a box and shaking the box repeatedly, uniform structures form. This investigation models self-assembly that occurs with structures such as virus capsids at the nanoscale. The magnets in this activity model the intermolecular forces that dominate other forces such as gravity. Students explore how different scales influence each other by looking at the relationships of surface area to volume (Limits to Size: Could King Kong Exist?). By measuring different sized cubes and examining how the volume differs when surface area decreases, students are encouraged to think about why friction and heat play major roles in nanoscale manipulation.

**Nanotechnology Applications**

An examination of new applications in nanotechnology challenges students to think about the tremendous potential nanoscale engineering may offer to our society. Students conduct investigations with memory wire (NanoMaterials: Memory Wire) and nanofabricated socks that are antibacterial (NanoTech, Inc.). Using gelatin and gel, students explore how gold nanocapsids are able to kill tumors without damaging the surrounding healthy tissue (Nano Medicine). This section ends by challenging students to think of their own inventions that could be created with nanotechnology. Students imagine a world where nanobots can reshape their eyes so they don’t need glasses or a world where nanomachines move around their mouths mopping up bacteria. This futuristic writing activity places them in the shoes of modern engineers who apply nanoscale science to human problems (Building Small: Nano Inventions).

**Societal Implications**

One of the greatest changes that nanotechnology may bring is the use of tiny labels and tracking devices that will allow us to monitor the movement of most materials around the globe. The changes in our privacy may be dramatic, from diamond rings that can have nanosized names and addresses tagged in them, to explosive materials that are embedded with distinctive markers (Too Little Privacy). What are the ethical implications of engineering new and totally different materials that are released into the environment? Should we build self-assembling robots just because the technology is available? Furthermore, what are the potential problems that can occur from this type of invisible engineering (Promise or Peril)? The last section of this book examines the ethical and societal implications of nanotechnology. Students consider how this remarkable technology could alter the way we live and imagine a new world where we can build nearly anything from the bottom up.
Chapter 5

Biological Nanomachines: Viruses

Overview

Although nanotechnology is a new and emerging field, nanoscale structures are not new. Small molecules such as water, large molecules such as proteins, and larger, more complex objects such as viruses and nanotubes are naturally occurring and exist all around us. Viruses are particularly interesting nanoscale objects because of their precise geometrical shape, their self-assembling capability, and their fascinating ability to invade cells and alter their function. Nanoscale science researchers are studying virus properties with the aim of developing new treatments for human disease. The virus is also being studied as a model for how to make materials and engineer products at the nanoscale through a process called “self-assembly.” In this investigation, students create an icosahedral virus model and consider how virus structure and behavior could be mimicked in nanotechnology applications.

Objectives

- To be able to describe the morphology of a virus.
- To be able to describe how viruses function as nanomachines.
- To be able to describe how viruses self-replicate.

Process Skills

- Observing
- Predicting

Activity Duration

30 minutes

Background

Viruses are natural nanomachines. They are exquisitely well designed to enter the body, travel through the bloodstream, and then attach, invade, and infect cells. They accomplish this complex task through the use of a host of protein machines that act at each stage of the infection process. Scientists are very interested in viruses both for their efficient biological function, as well as their beautiful architecture and assembling behavior.

The typical virus is 20 to 250 nanometers in length. This is incredibly tiny. A single nanometer is 0.00000004 inches. If a cell were the size of a classroom, then an average virus would be the size of a softball. Research has shown that most students think a virus is much larger than a bacterium since they hear about serious viral diseases. But in reality, most bacteria are a few micrometers (a millionth of a meter) long whereas viruses are nanometer-sized (a billionth of a meter).

As biological machines, viruses are interesting because they are able to perform complex targeted tasks at the molecular scale where the environment is so very different. At this scale thermal energy makes the world very shaky, gravity has almost no effect, there are huge frictional effects, and tiny attractive forces (van der Waals forces) make things stick together. But even with these adverse environmental conditions, viruses exist and find ways to locate their specific target receptors on cells, invade them, and multiply. Given that viruses lack a brain, sensory receptors, a reproductive system, or independent movement, it is clear that the virus is able to perform these tasks purely through its architectural and biochemical design. Unraveling the mysteries of virus design and function provides scientists clues as to how we might design artificial machines that could function at this tiny scale.

Are Viruses Living or Nonliving?

This is a difficult question to answer because we have yet to define what it means to be living. Does having genetic material mean that it is living? Does having the ability to reproduce mean that it is living? Does needing food and metabolizing mean that it is living?
Clearly, viruses are more complicated than simple molecules or even complex proteins. Yet, they are much simpler than the most basic single-celled organism. Similar to organisms, viruses are made up of proteins and nucleic acids, which are organic compounds. Some viruses have a lipid membrane. They evolve and mutate. A virus has the potential to reproduce with the aid of their host cell, but it does not require food to exist. So it has the ability to reproduce but has no metabolism, which many biologists hold as one of the requirements for being defined as living.

So, depending on how you define living, a virus can be either living or nonliving.

Viruses are essentially nucleic acids packed in a “box” made of proteins. The nucleic acid can be either ribonucleic acid (RNA) or single-stranded deoxyribonucleic acid (DNA) or double-stranded DNA. The protein coat (or capsid) is typically an assembly of one to several protein subunits.

**Why Are Some Viruses Harmful?**

Viruses can infect many living organisms, from bacteria to plants to animals. However, a single type of virus cannot infect all cell types. Your dog cannot catch a cold from you, for example. Viruses invade cells and force the host cells to produce multiple copies of the virus. In some cases, so many viruses are made in the cell that the cell eventually explodes and dies. Other viruses incorporate their genetic material into the host’s chromosomes and stay dormant and then multiply with the cell. Often the host cells are eventually destroyed. When you are infected with a virus, your body’s immune system kicks in to start destroying the virus. Many of the symptoms that those who are infected with mild viral infections suffer are actually caused by the body’s immune response. For example, fever is one of the body’s quick responses to help slow down virus multiplication. The higher the temperature in the body, the more difficult it is for viruses. Eventually, enough antibodies are produced to overwhelm the viruses and the infection and illness subside.

**Are Viruses Dangerous or Not?**

Viral infections vary in severity from those that cause warts to those that are very serious (such as Ebola). Surprisingly, viruses can be used to help cure diseases rather than causing them. Scientists have found ways to modify the virus so that it acts as a gene vector rather than a parasite. They remove the viral genome so that the virus can no longer replicate and replace it with human genes that direct proper cell functioning. A vector is an object that can be injected into the bloodstream and get into target cells. A gene vector is then a carrier for a gene that arrives at a target cell, invades it, and alters the cell’s nucleus by inserting the gene into the cell’s genetic material. This is what is known as “gene therapy” and is still very much in the developmental stage as a therapy for human disease. One example of proposed gene therapy uses the viral vector to insert a gene into a diabetic patient’s cells that produces insulin.

**Defining Properties of Viruses**

What makes something a virus? There are common characteristics that viruses share. Viruses are parasites that invade cells. Without the cell the virus cannot survive. Viruses have either DNA or RNA that are gene codes for reproduction of the virus and other reprogramming of the host cell viral characteristics and behavior. As parasites, viruses direct the synthesis of new viruses within the host cell. Newly made viruses infect other cells. This infection process is highly specific and critical for the virus to keep the replication process going.

**Virus Structure**

Viruses are covered by a protein coat known as a capsid. Viruses are usually shaped somewhat like rods or spheres. A closer look at viruses reveals that there is a remarkable geometry to each virus shape. Furthermore, viruses utilize a highly efficient shape to ensure replication within a cell.

In 1956, Francis Crick and James Watson noticed that the genetic material in small viruses was probably insufficient to code for more than a few protein molecules of limited size. They speculated that the only way a virus could build a protein coat was to use the same type of molecule over and over again. They called this theory the theory of identical subunits. Crick and Watson noticed that the only way to provide each component of a virus with an identical environment was by packing them to fit some form of cubic symmetry. We now know that Crick and Watson were right and that viruses are composed of repeated, identical subunits. Furthermore, scientists have found there are only a very few shapes of viruses, that differ externally only slightly. There are two primary shapes that make up most viruses: helical capsids (rod shaped) and icosahedral (spherical shaped).
Helical Capsids
Helical capsids are filament-shaped structures with the RNA in the center of an outer helix. The helix is made by stacking repeating protein subunits in a spiral of RNA. Tobacco Mosaic Virus (TMV) is an example of a virus with a helical capsid.

Icosahedral Capsids
The icosahedron is the most common virus structure, with 20 triangular faces and 2-fold, 3-fold and 5-fold symmetry axes. These are the axes about which the virus may be rotated to give a number of identical appearances. The icosahedral geometry is found in a number of unrelated viruses, suggesting that the shape is highly functional for virus replication. DNA or RNA is found in the center or the core of the capsid. Examples of icosahedral viruses include the adenoviruses that cause diseases like pinkeye or the common cold. The bacteriophage (phage) is a virus that infects bacteria and has an icosahedral head and a rigid tail. This “space ship” looking virus injects DNA or RNA into the bacterium and hijacks its internal operation. The stages of the process include:

1. Viruses attach to the bacterium.
2. Tail penetrates inside the bacterium.
3. The virus protein coat is lost.
4. The virus tricks the bacterium into making more DNA.
5. The bacterium makes proteins for new phage capsids.
6. New phages are released outside of the bacterium.

Enveloped Viruses
Enveloped viruses are viruses that have a lipid bilayer membrane coat surrounding the protein coat. These viruses are common in animal viruses, but are uncommon in plant viruses. The membrane comes from the host cell, either from the plasma membrane, golgi membrane, or nuclear membrane. Herpes and HIV are examples of envelope viruses.

Life Revised
Are viruses living or not? The answer depends on how life is defined. Viruses do not breathe, metabolize, or grow. However, they do reproduce. Not only do they reproduce but they self-assemble (see How Nature Builds Itself: Self Assembly in Chapter 11). Researchers have found that virus capsids spontaneously form when given a solution that includes...
proteins, the right temperature, pH, and salinity. Using traditional criteria for life, such as breathing, metabolism, or growth, viruses are not living. But if one defines life from the bottom up—that is, from the simplest forms capable of displaying the most essential attributes of a living thing—the criteria for life rest on the ability to reproduce. As engineers learn to create machines that can self-assemble and replicate themselves, we might ask again, are these living or not?

**Viruses as Nano Trucks**

Like the buckyball, scientists are exploring ways to use viruses as tiny trucks to deliver drugs, repair DNA, or act as tiny sensors. Each virus has specific bonding site requirements, which means that viruses are highly specific in the type of host they will invade. Already viruses are being used in gene therapy as vehicles that can carry and deliver DNA to a host cell. The host takes in the virus and assimilates the viral DNA into its own genetic code. The goal is to use this form of gene therapy to repair mutated DNA or replace a faulty code with a functioning gene sequence. The hope is that through gene therapy, diseases like diabetes, cystic fibrosis, or Parkinson’s disease could be eradicated.
**Build a Virus**

**Materials**

- Each individual will need:
  - Virus capsid template
  - 10 meters of yarn
  - Tape

- Optional materials
  - 3 pipe cleaners
  - 1 pencil

**Note:** Copy virus capsid pattern on card stock for best results

**Engage**

Ask students to work with a partner to brainstorm as many names of different types of viruses as possible. Ask them, What viral diseases have you heard of?

Show the class a series of photographs of different types of viruses. Ask them to describe the shapes of the different viruses. A great source for images of viruses is the The Big Picture Book of Viruses available online at [www.virology.net/BVHomePage.html](http://www.virology.net/BVHomePage.html). Viruses are not only beautiful to look at but they have amazing details and configurations.

**Explore**

Explain to the students that they will create a model of an icosahedral virus—a biological nanomachine. The icosahedral shape is very common and includes viruses such as the polio virus, adenovirus (common cold) and the virus that causes hepatitis A. Review the characteristics of viruses and the morphology of viruses. Point out the 20 triangular faces and 2-fold, 3-fold and 5-fold symmetry axes found on the icosahedral virus. Note that DNA or RNA is found in the center or the core of the virus capsid.

**Instructions for Building an Icosahedral Virus**

1. Make a copy of the virus pattern (page 37).
2. Cut along the outer edge of the pattern.
3. Fold and crease the bold lines.
4. Tape the edges together, leaving one side open.
5. Cut 10 meters of yarn to represent the DNA and place it inside your virus.
6. Tape the virus model closed.

**Explain**

Review the components of the virus. Describe the different shapes of viruses and the process viruses use to infect a host cell, replicate, and infect new viruses. Discuss theories about why viruses are symmetrical and have repeated faces composed of regular subunits.

**Extend**

Invite your students to find the most unusual virus they can locate on the internet. What is the shape of the virus? What is the host cell for this new virus?

Encourage your students to add to their virus model to more accurately represent specific viruses. What would it take to make the model look like HIV or herpes simplex?

Ask students to decide if a virus is living or nonliving. What defines life in this context? If a human engineered nanomachine could self-assemble and self-replicate, would it be considered living or not?

Research how viruses recognize and attach to specific types of host cells. How does a virus know when to penetrate a cell?

**Evaluate**

Show students a series of different virus images and ask them to identify whether or not it is an icosahedral or helical capsid virus type.

Check for understanding:

1. What is the shape of the virus model that you made?
   - **Answer:** icosahedral
2. How many faces are there on the virus model?
   - **Answer:** 20
3. What is the protein shell called?
   - **Answer:** capsid
4. Why do most viruses take the form of one or two basic shapes? Why would two very unrelated viruses have the same shape?
   - **Answer:** Given the small size of the virus and the limited amounts of DNA or RNA, scientists speculate that using repeated faces and a regular symmetry allows the virus to replicate with the fewest number of unique parts.
5. How is a virus like a machine? If you could alter a virus to benefit humans, what would you engineer the virus to do?
   - **Answer:** This question allows students to think creatively about how viruses might deliver drugs, clean out plaque from arteries, gobble up fat cells, or provide extra calcium for bone repair or growth.
Make a Virus Model
Using the pattern on the next page, you can make an icosahedral virus like the adenovirus.

Instructions for Building an Icosahedral Virus

1. Print the virus pattern.

2. Cut along the outer edge of the pattern. Students may want to color the capsid.

3. Fold and crease the bold lines.

4. Tape the edges together, leaving one side open.

5. Cut 10 meters of yarn to represent the DNA and place it inside your virus.

6. Tape the virus model closed.

Optional
To add the tail to the capsid, insert a pencil into the bottom of the capsid and tape the paper “capsid” to the paper “tail.” Use pipe cleaners or paper clips for tail fibers.
Build a Virus

Capsid template
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