#7

THE CELLS OF LIFE

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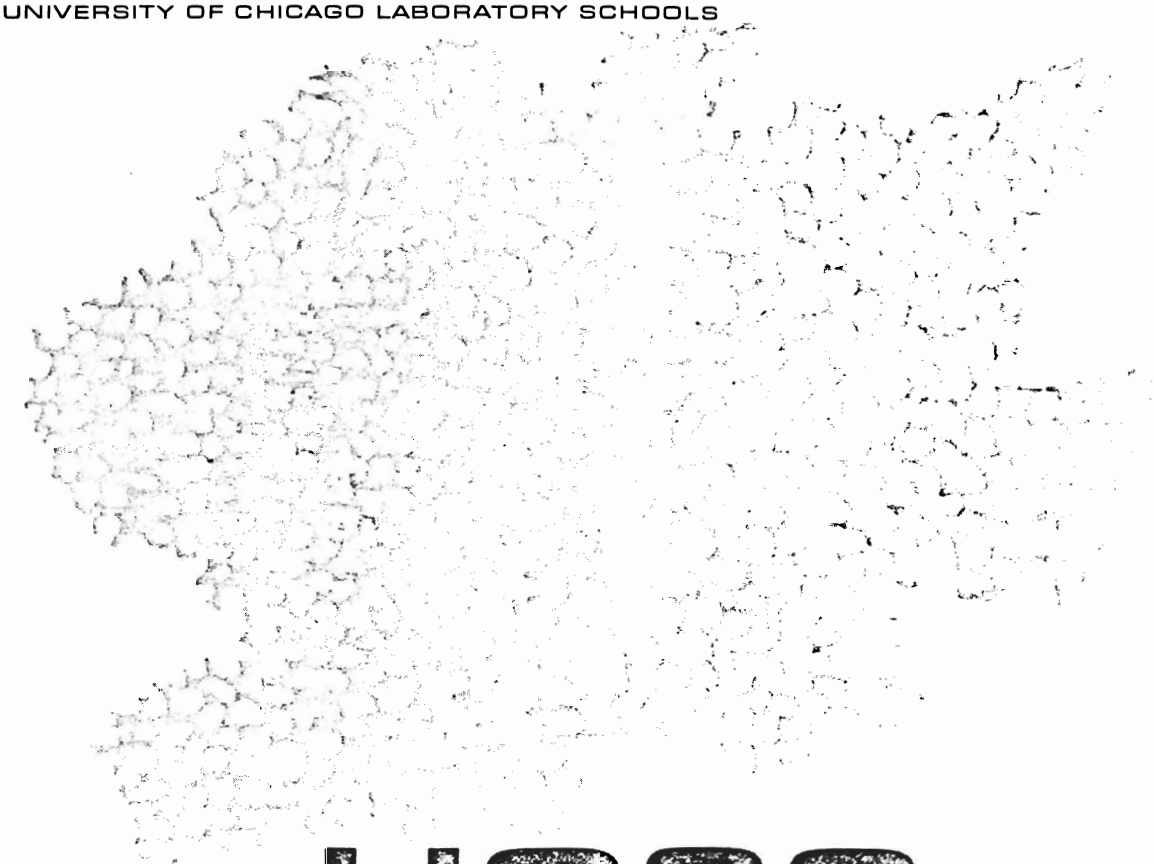

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HISTORY OF SCIENCE CASES

S R A SCIENCE RESEARCH ASSOCIATES, INC.

(Photo from The Bettmann Archive.)

Rudolf Virchow was one of the outstanding medical doctors of Germany in the nineteenth century. In addition to his medical, scientific, and public health work, Virchow was a liberal politician and statesman, often incurring the wrath of the powerful Prussian prime minister, Bismarck. Born on October 13, 1821, at Schivelbein in Pomerania, Virchow lived to see eighty years of exciting developments in the history of science, the history of medicine, and the history of Germany. He contributed to all three before his life ended in Berlin on September 5, 1902.

But the part that Virchow takes in our story of the cell theory was played out in his younger days, when he was in his thirties. It was then that Virchow proclaimed his doctrine of cellular pathology—the idea (no longer considered correct) that all diseases of the body are due to disturbances or diseases of the body's living cells. Before Virchow or anyone else could possibly develop such a doctrine, a rich background of ideas about cells had to be worked out by many other scientists. We will meet some of these scientists before we encounter Virchow again near the end of the story. They include:

ROBERT HOOKE, English physicist and chemist
Born July 18, 1635, on the Isle of Wight
Died March 3, 1703, in London

ANTON VAN LEEUWENHOEK, Dutch microscopist
Born October 24, 1632, in Delft
Died August 26, 1723, in Delft

ROBERT BROWN, Scottish botanist
Born December 21, 1773, in Montrose, Scotland
Died June 10, 1858, in London

MATTHIAS JAKOB SCHLEIDEN, German botanist
Born April 5, 1804, in Hamburg
Died June 23, 1881, in Frankfurt am Main

THEODOR SCHWANN, German physiologist
Born December 7, 1810, in Neuss, Prussia
Died January 11, 1882, in Koln (Cologne)

INTRODUCTION

In this HISTORY OF SCIENCE CASE we will make a critical study of a part of the development of a major scientific idea. Although we want to learn something about this idea, our chief interest in this case will be to find out as much as we can about

- the methods used by scientists
- the means by which science advances and the conditions under which it flourishes
- the personalities and human qualities of scientists
- the interplay of social, economic, technological, and psychological factors with the progress of science
- the importance to science of accurate and accessible records, constantly improved instruments, and free communication among scientists

To study this case effectively, you will need to do more than simply read the story that appears on the left-hand pages of the first section of this booklet. In the margins to the left of the narrative you will find numerous comments and questions. These marginal notes are intended to guide your thinking and to start the class discussions about the points illustrated by the case. On the right-hand pages, marginal questions are repeated in expanded form and spaces in which you may write your answers have been provided. These questions are different from those found in many workbooks. Often you will not find simple answers to the questions in this booklet. Many of the questions challenge you to think for yourself, to seek ideas or information from other books, to express your own opinions and to defend them.

Also included on the right-hand pages are a number of experiments which are a very important part of the study of this case. You should complete as many as possible, so that you may get a real feel for the situations faced by the scientists as they developed their ideas. Additional activities and exercises follow the narrative, and your teacher may suggest others that you can work on in connection with this case. On the last page of this booklet you will find a listing of some additional books and articles relating to the story of this particular case.

Some students may think that this case is out of date because the story is set in the scientific past. Nothing could be further from the truth. The points about science and scientists that are featured in this case are just as valid in the present as they were in the past. The methods of scientific investigations are much the same today as they have been for several hundred years; the nonscientific factors now interacting with the progress of science are similar to those that interacted with it in earlier times; the characteristics and personalities of scientists have always been important factors in the story of science; and, as in the past, the progress of science today continues to be dependent upon adequate recording of information, free communication of facts and ideas, and improved instrumentation. These aspects of science were the same yesterday as they are today, and they will remain the same tomorrow.

As you study this case and work through the various activities, you will learn a great deal about scientists and about what goes on in science.

L.E.K.

THE CELLS OF LIFE

Through their work, scientists try to find and to improve upon ideas that help us make sense out of what we see and otherwise experience in the natural world. The story that we will follow in this case is one example of how scientists attain ideas that help them interpret the natural world. This story is about living things—plants and animals. It deals with the idea that was gradually developed—over a period of many years and through the efforts of many workers—that cells are the basic units of all life.

Have you ever seen a cell? Can you identify the parts of a typical plant or animal cell? Because cells are very small, you cannot see them with your unaided eye. However, when your sense of sight is extended by means of a microscope, you can easily see both plant and animal cells, *provided* you have prepared your materials properly and know what you are looking for.

This last point is important: it is much easier to see something—a cell, for example—if we have an idea of what to look for. The world of nature presents many confusing impressions to our senses. The impressions are no less confusing when we can see smaller details by means of a microscope. But when we have an idea of what to look for in this maze of confusing impressions, we can begin to make some sense out of what we see.

Has seeing something under a microscope ever been a problem for you? (1)

Special instruments and equipment are needed in scientific work.

The idea of putting two lenses together to make distant objects appear nearer and small objects appear larger seems to have arisen among the lens makers of Holland early in the seventeenth century. However, scientific observations with both the telescope and microscope actually began in Italy, chiefly through the efforts of members of the Accademia dei Lincei (Academy of the Lynxlike) and Accademia del Cimento (Academy of Experiment), two of the earliest scientific societies. Still, no systematic investigations with the microscope were undertaken until after the middle of the seventeenth century.

The Lincei were as sharp-eyed as a lynx. "Scientific societies"??? What are they? (2)

In 1665 Robert Hooke, first curator of the Royal Society of London, published his *Micrographia.* This book contained, among a wealth of materials on a variety of topics, a collection of Hooke's careful observations with the microscope. In Observation XVIII, Hooke reported:

Careful observations are always important.

> I took a good clear piece of Cork, and with a Pen-knife sharpen'd as keen as a Razor, I cut a piece of it off, and thereby left the surface of it exceeding smooth, then examining it very diligently with a *Microscope,* me thought I could perceive it to appear a little porous; but I could not so plainly distinguish them, as to be sure that they were pores . . .

Hooke next tries to improve his observation:

> I with the same sharp Pen-knife, cut off from the former smooth surface an exceeding thin piece of it, and placing it on a black object Plate, because it was it self a white body, and casting the light on it . . . I could exceeding plainly perceive it to be all perforated and porous, much like a Honey-comb, but that the pores of it were not regular; yet it was not unlike a Honey-comb in these particulars.
>
> First, in that it had a very little solid substance, in comparison of the empty cavity that was contain'd between, . . . for the *Interstitia,* or walls (as I may so call them) . . . of those pores were neer as thin in proportion to their pores, as those thin films of Wax in a Honey-comb (which enclose and constitute the *sexangular cells)* are to theirs.

Note the importance of good techniques. How does a scientist learn them? (3)

"In proportion to" is a mathematical expression. What does it mean? (4)

(Use these right-hand pages to write your answers to the questions raised in the story of the case and to make notes on the experiments.)

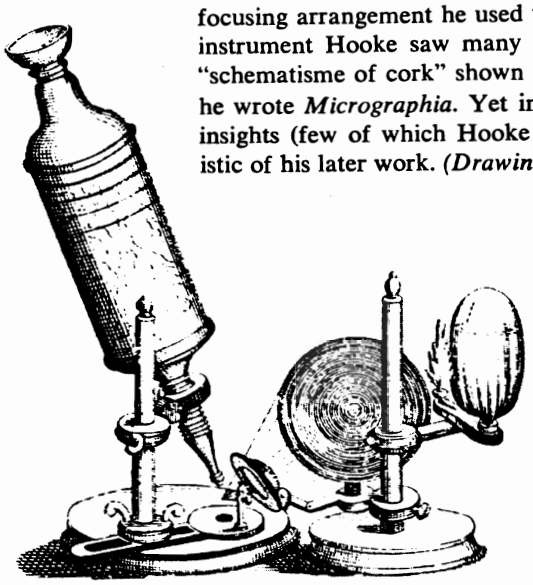
1. Have you ever had the problem of being unable to see something through a microscope because you didn't know what to look for? Is there any connection between what we expect to see and what we can see? Explain.

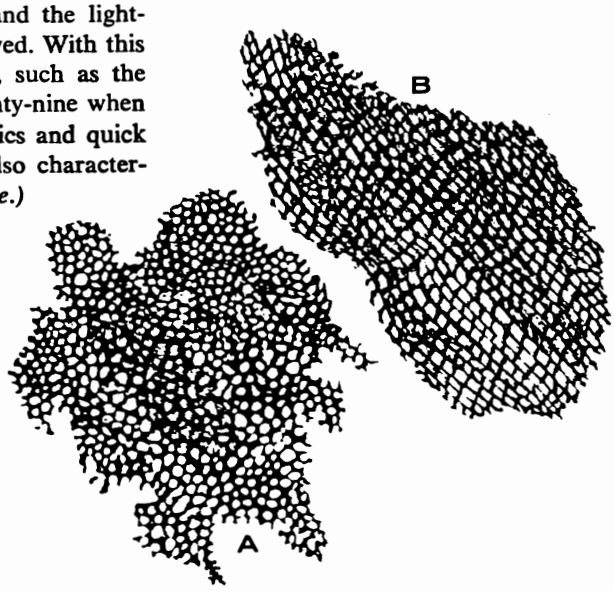
2. What are scientific societies? What purposes do they have? Do you know any present-day scientific societies?

3. How does a scientist learn good techniques? Name two or more ways. Do good techniques come more easily to some people than to others? Do some people have a special scientific aptitude? Explain and defend your point of view.

4. What does Hooke mean by the mathematical expression "in proportion to"?

Here are two drawings by Robert Hooke from his *Micrographia.* At left are the microscope that Hooke designed and constructed and the light-focusing arrangement he used to illuminate objects he observed. With this instrument Hooke saw many things never recorded before, such as the "schematisme of cork" shown at right. Hooke was only twenty-nine when he wrote *Micrographia.* Yet in it are the wide range of topics and quick insights (few of which Hooke ever followed up) that are also characteristic of his later work. *(Drawings from The Bettmann Archive.)*





Hooke recognizes the three-dimensional nature of cells.

Next, in that these pores, or cells, were not very deep, but consisted of a great many little Boxes, separated out of one continued long pore, by certain *Diaphragms,* as is visible by the Figure B [in the above illustration] which represents a sight of those pores split the long-ways.

A scientist must know the work of those who have gone before. How does he find out? (5)

I no sooner discern'd these (which were indeed the first *microscopical* pores I ever saw, and perhaps, that were ever seen, for I had not met with any Writer or Person, that had made any mention of them before this) but me thought I had with the discovery of them, presently hinted to me the true and intelligible reason of all the *Phaenomena* of Cork . . . [See Experiment 1 on page 7.]

Can you account for these characteristics of cork as Hooke did? (6)

Hooke proceeds to use his discovery of the cork cells to explain the "phaenomena" or characteristics of cork—namely, its lightness compared with other woods, its ability to float on water, and its compressibility. He then turns his attention to the size of the cork cells:

Numbers help to make scientific work more exact.

Are Hooke's calculations correct? (7)

I [counted] several lines of these pores, and found that there were usually about threescore of these small Cells placed end-ways in the eighteenth part of an Inch in length, whence I concluded there must be neer eleven hundred of them, or somewhat more than a thousand in the length of an Inch, and therefore in a square Inch above a Million, or 1166400. and in a Cubick Inch, above twelve hundred Millions, or 1259712000. a thing almost incredible, did not our *Microscope* assure us of it by ocular demonstration . . .

Further observations led Hooke to a description of the general structure of cork in its natural state:

. . . Cork seems to be by the transverse constitution of the pores, a kind of *Fungus* or Mushrome, for the pores lie like so many Rays tending from the center, or pith of the tree, outwards; so that if you cut off a piece from a

EXPERIMENT 1. Hooke's Experiment

In this and most of the experiments that follow, you will be making observations with a compound microscope. If you are not yet familiar with the use of this instrument, ask your teacher for instructions. For direction in making the wet mounts required in this and later experiments, see, for example, pages 28–30 of *Exploring Biology,* by Ella Thea Smith (5th ed.; New York: Harcourt, Brace, 1959).

Obtain a clean piece of cork and, with a razor, cut off as thin a slice as you can. Then cut off a piece of this thin section and place it on a microscope slide. Examine the cork under the low-power lens of the microscope. Do you see the cells that make the cork "not unlike a Honey-comb"?

Add a drop of water to the cork section on the slide and place a cover slip over it. Examine the cork again, still using the low-power lens of the microscope. Do you get a better view than you did the first time? In the space below, explain why viewing did or did not improve. Then, at the right, make a drawing of what you see through the microscope.

Cut a thin section of pith from an elder tree or one of the rushes. Make a wet mount and observe under low power. Can you see any more under the high-power lens (which Hooke did not have)? Compare what you observe here with your drawing of cork cells.

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5. How does a scientist find out about the work of those who have gone before? Suggest at least five different ways.

6. You can account for these characteristics of cork as Hooke did. Use the idea that cork has cells containing air to explain why (A) cork is light compared with other woods, (B) cork floats on water, (C) cork is compressible.

Would you call what you have just done an example of applying a scientific theory? Back up your answer.

7. Are Hooke's calculations correct? Check them to find out.

board of Cork transversly, to the flat of it, you will, as it were, split the pores, and they will appear just as they are express'd in the Figure B [in the illustration on page 6]. But if you shave off a very thin piece from this board, parallel to the plain of it, you will cut all the pores transversly, and they will appear almost as they are express'd in the Figure A [on page 6], save onely the solid *Interstitia* will not appear so thick as they are there represented.

Since the characteristics of cork are so nicely explained by his generalization about cork, Hooke wonders whether other substances with similar characteristics have similar structures.

Can the characteristics of piths be explained by Hooke's generalization? (8)

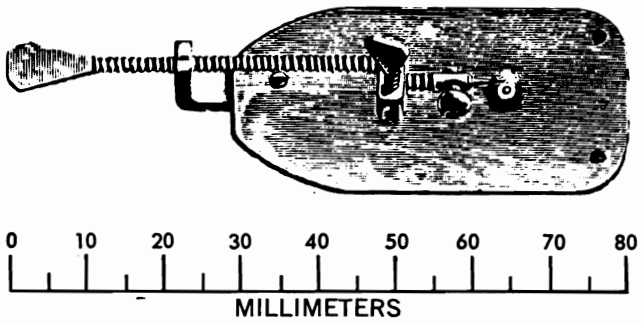
Nor is this kind of Texture peculiar to Cork onely; for upon examination with my *Microscope,* I have found that the pith of an Elder, or almost any other Tree, the inner pulp or pith of the Cany hollow stalks of several other Vegetables: as of Fennel, Carrets, Daucus, Bur-dock, Teasels, Fearn, some kinds of Reeds, *etc.* have much such a kind of *Schematisme* [arrangement], as I have lately shewn that of Cork . . .

Following Hooke's work, other seventeenth century scientists became interested in making microscopic observations. Among these, the most notable were Nehemiah Grew in England, Marcello Malpighi in Italy, and Anton van Leeuwenhoek in Holland. (See Activity 1, page 28.) Grew and Malpighi, who together founded the science of plant anatomy, observed cells in many plant structures and published good drawings of them in their books and papers. Leeuwenhoek devised a remarkable small microscope with only a single tiny lens. He used this instrument to make countless observations that he reported to the Royal Society of London in a series of about two hundred letters over a period of fifty years. In 1675 Leeuwenhoek observed protozoa (one-celled animals) and bacteria (one-celled plants) for the first time. From that time on, many of his letters described the sizes, shapes, and activities of what Leeuwenhoek called animalcules (little animals), as he saw them in his microscope. (You can see these animalcules yourself by doing Experiment 2.)

Why do scientists publish books and papers about their work? (9)

How is it possible to make a microscope with only a single lens? See Activity 2, page 28.

Unlike Hooke, who flirted with many different scientific problems, Anton van Leeuwenhoek gave all his energies to microscopy. A draper and chamberlain in the Dutch town of Delft, Leeuwenhoek constructed hundreds of tiny microscopes similar to the one shown below. With his inexhaustible patience and keen eyesight, Leeuwenhoek succeeded in making a vast number of microscopical discoveries. Yet, making observations and recording them was all he did; the interpretations and explanations of his discoveries were left to others. *(Pictures from The Bettmann Archive.)*



8. Piths are light and compressible. They float on water. Use Hooke's generalization to explain these characteristics of piths. By the way, what is Hooke's generalization now?

9. Why do scientists publish books and papers about their work? (This is a double-barreled question. As regards the advance of science, the reasons are quite clear, but scientists also have personal reasons for publishing books and papers. Your answer should include both kinds of reasons.)

EXPERIMENT 2. Leeuwenhoek's Animalcules

With your microscope you can readily observe some of the animalcules that Leeuwenhoek saw. (To learn how to build a simple microscope, see Activity 2 on page 28.) If no cultures of protozoa are available, you can make your own cultures by following the directions given below.

Obtain some water from a quiet pond and pour it into three pint bottles until they are each half full. In the first bottle, place some dry grass that has begun to decay. In the second, place some green scum from the pond. In the third, place a water plant such as elodea and a little soil from the bottom of the pond. Set the bottles aside in a warm place for a few days to let the cultures develop.

Now, with a medicine dropper, take a drop of water from one of the cultures and place it on a clean microscope slide. Examine the drop under high power. If you do not see living forms dashing about in the drop, try a drop of water from another part of the same bottle or from one of the other cultures. You can slow down the organisms by adding a drop of a 3 percent solution of gelatin to your drop of culture. In the right-hand margin, make sketches of as many different forms of protozoa as you can see.

You will find that bacteria are harder to see than protozoa, even under the high power of your microscope. In looking for them, first examine a drop of sauerkraut juice mounted on a microscope slide. The bacteria should appear as small specks. Next take a drop of sour milk and dilute it with a drop of water. Examine under high power. In the space below, make sketches of any bacteria that you see.

Unless an idea guides them to it, scientists may not use an instrument which is readily available.

After the death of Leeuwenhoek in 1723, few microscopic observations of any importance were reported until the beginning of the nineteenth century. As we have already seen, adequate instruments for making microscopic observations were readily available during this long interval. Their lack of use was due to several factors.

Is the scientist's choice of problems to be studied often influenced by events outside science? (10)

First, in the eighteenth century the attention of biologists was directed to matters other than the investigation of "animalcules" and cells. For instance, the 1700s were years of great exploration throughout the world. Thousands of specimens of new kinds of plants and animals from America and other newly explored places poured into the collecting centers of Europe Biologists wanted to make some order out of this chaos of new material. The newly discovered plants and animals also raised doubts about existing systems of classifications. Thus biologists in the eighteenth century gave much attention to devising better, more inclusive systems for classifying plants and animals.

Then, too, when Hooke, Grew, Malpighi, Leeuwenhoek, and their contemporaries made observations and investigations with the microscope, they never associated their discoveries with any clear ideas about the nature of living things. Nor in the hundred years following this pioneering period of microscopic investigations did other scientists recognize such a connection.

After 1800, biologists again became interested in the microscope as a tool of research. New techniques of preparing materials for viewing were worked out, and many new observations were reported. Among these, the observations of Robert Brown, a Scottish botanist, are important to the development of our story. Brown's paper "The Organs and Mode of Fecundation in Orchideae and Asclepiadeae," published in the *Transactions of the Linnean Society* in 1833, announced the discovery of the nucleus of the plant cell. (You will have a much better understanding of Brown's discovery if at this point you study some typical plant cells under the microscope. See Experiment 3.)

What do all the big words mean? (11)

Accurate, detailed observation and classification of plants were Robert Brown's great strengths as a scientist. His most important studies dealt with the Australian flora. One of the Australian plant families that he studied intensively was the Asclepiadaceae; the illustration below is from his paper of 1833 and shows *Asclepias purpurascens. (Picture of Robert Brown from Historical Pictures Service—Chicago)*

10. Is a scientist's choice of problems to be investigated often influenced by events quite outside science, or are scientists working pretty much in an ivory tower that is quite isolated from the rest of society? Do you know of any present-day examples to back up your opinion?

11. What do all the big words mean? Define: mode of fecundation; Orchideae; Asclepiadeae. (Note that Brown uses the ending "-eae" for plant families, whereas today we usually use the ending "-aceae.")

EXPERIMENT 3. Brown's Discovery

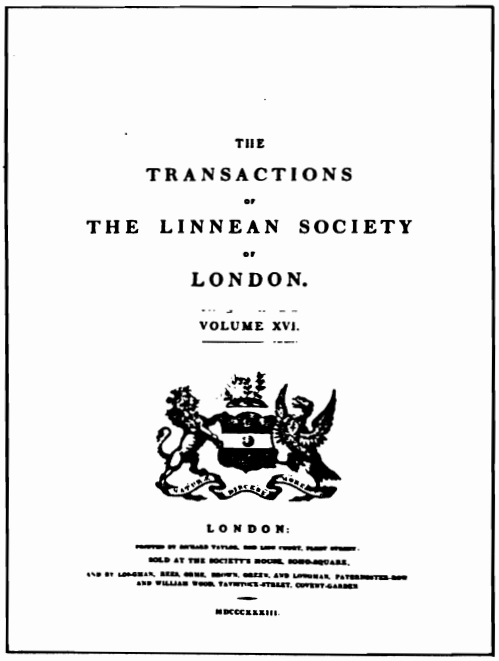
If some tissues from orchids are available, you can use them, as Brown did. Otherwise, the skin of an onion will work very well to begin with, for an onion has clearly visible cells.

Cut a wedge about one-quarter inch square out of an onion. With tweezers, peel off the skin on one side. Place this small piece of onionskin in a drop of water on a clean microscope slide. Cover with a cover slip, and examine the mount under low power.

To see the cells more clearly, stain the onionskin as follows: To five drops of 2 percent iodine solution, add ten drops of water. Place a drop of this dilute iodine solution at the edge of the cover slip of your onionskin mount. The iodine will run under the cover slip and stain the onionskin. Now observe again, still using low power. Can you see the cells more clearly than before? What is the importance of proper technique?

Make a drawing of one of the cells that you can see clearly. Label the cell wall, nucleus, and cytoplasm.

EXPERIMENT 3 continued on page 13



THE
TRANSACTIONS
OF
THE LINNEAN SOCIETY
OF
LONDON.

VOLUME XVI.

LONDON:

MDCCCXXXIII.

This is the title page of Volume 16 of the *Transactions of the Linnean Society*, in which Brown's paper was published in 1833. Scientific journals like this one make it possible for scientists to share new ideas and information with other investigators who may be very far away. Today scientific journals have become the principal means of communication between scientists; hundreds of different scientific journals are now being published regularly throughout the world. Most of these journals are sponsored by scientific societies like the Linnean Society of London. These societies are the professional organizations to which scientists belong.

To be effective in his work, a scientist must learn a great deal.

In his famous paper of 1833, Brown displays some of the special knowledge and skills that he learned through a lifelong study of many species of plants. Near the end of the first part of his paper, Brown reveals the new discovery he has made about plant cells:

> I shall conclude my observations on Orchideae with a notice of some points of their general structure, which chiefly relate to the cellular tissue.
>
> In each cell of the epidermis [the outer layer of cells] of a great part of this family . . . a single circular areola [small area], generally somewhat more opake than the membrane of the cell, is observable. This areola, which is more or less distinctly granular, is slightly convex, and although it seems to be on the surface is in reality covered by the outer lamina [layer] of the cell. There is no regularity as to its place in the cell; it is not unfrequently however central or nearly so . . .

Brown gives a name to his discovery.

> This areola, or nucleus of the cell as perhaps it might be termed, is not confined to the epidermis, being found not only in the [covering of soft, short hairs] of the surface . . . but in many cases in the parenchyma or internal cells of the tissue . . .
>
> In the compressed cells of the epidermis the nucleus is in a corresponding degree flattened; but in the internal tissue it is often nearly spherical, more or less firmly adhering to one of the walls, and projecting into the cavity of the cell. In this state it may not unfrequently be found in the substance of the column [the united stamens and styles of the orchid], and in that of the [floral envelope].
>
> The nucleus is manifest also in the tissue of the stigma, where, in accordance with the compression of the [contents of the cell], it has an intermediate form, being neither so much flattened as in the epidermis, nor so convex as it is in the internal tissue of the column. . . .
>
> The nucleus of the cell is not confined to Orchideae, but is easily manifest in many other Monocotyledonous families; and I have even found it, hitherto however in very few cases, in the epidermis of Dicotyledonous plants . . . Among the Monocotyledones the [families] in which it is most remarkable are Liliaceae, Hermocalideae, Asphodeleae, Irideae, and Cinnelineae.

Where are the various flower parts to which Brown refers? (12)

Do you think Brown was a careful observer? (13)

How are monocotyledons different from dicotyledons? (14)

EXPERIMENT 3 (continued)

Prepare several other plant tissues in the same way that you did the onion-skin. Observe them under the microscope and make drawings. Do all the plant cells you've examined have a cell wall?

Do they all have nuclei?

What generalizations, if any, can you make on the basis of your observations? Was Brown correct in believing that the cells of seed plants always contain nuclei? What about the cells of plants that are not seed plants?

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12. Where are the various parts of the flower to which Brown refers? On a diagram or model of a flower locate epidermis, stamens, styles, floral envelope, stigma.

13. Do you think Brown was a careful observer? In your opinion, was he born with this skill? What makes you answer as you do? Back up your opinion with facts.

14. In what ways are the monocotyledons and dicotyledons similar? How do they differ?

Observations do not speak for themselves; they must be interpreted.

Notice that all the plants in which Brown saw a cell nucleus are seed plants. Thus, Brown's observations might be interpreted to imply that the cells of seed plants always contain a nucleus. Brown believed this to be so. Brown is therefore duly recognized as the discoverer of the plant cell nucleus. However, he did not realize the importance of his discovery and he made no use of it. This was done five years later by Matthias Jakob Schleiden, a German botanist. Improved compound microscopes, which came into wider use in the 1830s, helped Schleiden to see more and to "see" more than Brown had.

What is the meaning of this last sentence? (15)

Schleiden has been called "one of the strangest scientific personalities of his age." (See Activity 3, page 29.) As we shall see, in making his contribution to our understanding of cells, he developed concepts that combined correct basic ideas with completely wrong details. In 1838 he published a memorable essay in the *Archiv für Anatomie, Physiologie, und wissenschaftliches Medizin* (Archive for Anatomy, Physiology, and Scientific Medicine) in which he stated:

Scientists, being human, sometimes make mistakes.

What kind of publication was this "Archiv"? (16)

> Each cell leads a double life, an independent one as a cell-individual, another as a dependent integral part of the plant. It is obvious that the understanding of the life process of the individual cells is the primary, indispensable base for the understanding of plant—as well as of comparative—physiology. Hence the importance of the question: What is the origin of this peculiar small organism, the Cell?

Scientists must ask the right questions.

Schleiden seized on the cell nucleus, which Brown had discovered, to account for the origin of the cell. Schleiden was the first to appreciate the importance of the nucleus, although the details of the process by which, according to Schleiden, the nucleus arises and grows in the cells were later found to be quite incorrect. Schleiden thought that the plant cell was formed from the cell nucleus, which he accordingly named the "cytoblast" (or cell bud). He chose to study the formation of cells in two of the reproductive parts of plants, the embryo sac and the end of the pollen tube.

Note the materials Schleiden chooses. Why is this important? (17)

> At these two places, small slime bodies within the gum soon originate and cause the hitherto clear and homogeneous gum-solution to become opaque and to increase the quantity of its granulation. Then, a few larger and sharper granules [the nucleoli] stand out in this mass, and soon afterwards the cytoblasts emerge and arrange themselves . . . [around the nucleoli]. The cytoblasts grow considerably in this free state, thus I observed an increase in *Fritilaria pyrenaica* from 0.0032 to 0.027 cm. in diameter.

Of what use are these numbers? (18)

Thus Schleiden thinks of the nucleoli and cytoblasts as crystallizing out of the surrounding gum solution. This is a remarkable idea, and it seems likely that Schleiden hit on this notion by watching the formation of crystals from their surrounding solutions. (See Experiment 4, page 17.) From the cytoblasts that have crystallized out, Schleiden believes, come the cells.

> As soon as the cytoblasts have reached their full size a transparent vesicle [small bladder] rises upon their surface. This is the young cell which begins as a very flat globular segment; the cytoblasts as the plane and the young cell on the convex side resemble a watch glass sitting upon the watch . . . The vesicles slowly extend and grow to be of greater consistency. The wall is now formed . . . In this stage the entire cell grows beyond the margin of the cytoblast, increases rapidly in size and the cytoblast remains only as a small part included within one of the cell walls.

How could Schleiden make all these observations? (19)

15. Explain the meaning of the awkward sentence, "Improved compound microscopes . . . helped Schleiden to see more and to 'see' more than Brown had." (Some of the remarks made on previous pages should help you figure out the meaning.) Could you say the same thing in another way?

16. What kind of publication was this "Archiv"? List at least three different functions such publications serve.

17. What is important about the choice of material that Schleiden makes? (You may not be able to answer this question until you've read on for a few pages. But it's an important question, so be sure to come back to it.)

18. Of what use are these numbers? In general, of what use are numbers and mathematics in science?

19. How could Schleiden make all these observations? (His description sounds like something you might see on motion picture film, but Schleiden certainly did not take movies of cell growth in 1838.) What techniques did he use? What part did Schleiden's imagination play in his description?

Matthias Jakob Schleiden had little patience for lengthy, painstaking observations and plant classification. He irreverently referred to the valuable plant collections of the systematic botanists as "hay." To Schleiden, what was important in the study of botany was not the arranging of plants in neat groupings but rather the organizing of the science on the basis of a few fundamental principles. He plunged into this task with the zeal of a pioneer. For this reason, it is hardly surprising that he soon convinced himself that two of the fundamental principles he was seeking were found in his definition of the cell and his law of cell formation. *(Photo from The Bettmann Archive.)*

Again, observations do not speak for themselves.

As Schleiden continues his description of the growth of cells, we can see that he adds his own interpretations to the observations on almost every line. (There are at least three examples of this in the following paragraph. Can you spot them?)

> At the same time the young cell often shows very irregular extrusions [bulges] which is evidence that the growth is not effected from one point only. With further growth, however, the circumference becomes more regular, obviously due to internal pressure. The cytoblast is still included in the cell wall, in which place it remains throughout life. Only in those cells which are determined for higher development is it either dissolved in its place or expelled into the cell cavity as an organ without further use.

Schleiden formulates a law. What is a scientific law? (20)

Having made his observations, Schleiden generalized them into a law. In summary, he says:

> It is an absolute law that every cell takes its origin as a very small vesicle and grows only slowly to its defined size. The process of cell formation which I have just described . . . is that process which I was able to follow in most of the plants which I have studied. Yet many modifications of this development can be observed. In some plants the observation is difficult in parts or in all cells. Neverthless, the general law remains incontestable since analogy requires it, and since we fully understand the causes which sometimes prevent complete observation.

What does Schleiden mean by "analogy requires it"? (21)

Schleiden's work helped greatly to establish in the minds of botanists the idea that all plants are composed of cells. His notions concerning the formation of cells, which have just been described, were erroneous, as we shall see later. However, even in the imperfect form in which Schleiden presented it, the idea of the cellular structure of plants had an immediate and significant effect.

Is an incorrect idea of any value in science? (22)

EXPERIMENT 4. Crystallization

You can see for yourself the crystallization process that Schleiden thought explained the formation of cells. One good way to do this is to observe crystals grow when a hot, saturated solution of sodium chlorate cools. Add twelve grams of sodium chlorate to ten milliliters of water in a test tube. Heat the water until all of the sodium chlorate is dissolved. Using a medicine dropper, place a few drops of the hot, clear solution on a microscope slide and observe under low power. Crystals will begin to form as the solution cools. Why? (If crystals do not begin to form, add a grain of the sodium chlorate solid to the drops on the slide to start crystallization.) What shape and color do the crystals of sodium chlorate have? Are you watching a living or a nonliving process? Explain.

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20. What is a scientific law? How can laws in science be established? Do you think Schleiden established his "general law" of cell origin and growth on a firm basis?

21. What does Schleiden mean by "analogy requires it"? Is this a good argument? Why?

22. Is an incorrect idea of any value in science? How can an idea be shown to be incorrect?

Scientists gather a great deal of information, but that is not their main interest. (23)

So far in this case we have been primarily concerned with microscopic observations made on parts of plants. However, in the 1830s many workers also turned their microscopes on the structure of a variety of animals. Much new information was accumulated through these studies; but it was not meaningfully organized until Theodor Schwann, a German zoologist, made his historic contribution to the cell theory. In 1839 Schwann published his *Mikroskopische Untersuchungen über die Übereinstimmung in der Struktur und dem Wachsthum der Thiere und Pflanzen* (Microscopic Investigations on the Concord in the Structure and Growth of Animals and Plants). In this careful and thoughtful book, he says:

It's a complicated world we live in, isn't it?

> Animals present a much greater variation in external form than is to be found in the vegetable kingdom and, particularly in the higher more perfectly developed classes, exhibit also a much more complex structure in their individual tissues. How far exactly does the distinction go between muscle and nerve tissue . . . or between flexible and horny tissue, and so on? When we look into the question of development of these tissues, however, it becomes evident that all their manifold forms likewise originate from cells in fact which are absolutely similar to plant-cells . . . The object of the present work is to prove this thesis by a series of observed facts.

Schwann wants to "prove" a thesis. How will he do this? (24)

Observations and ideas go hand in hand.

Here Schwann sets himself a major problem, for, without careful observations and clear insight, it is far from evident that animal cells are similar to plant cells. The cells of animals differ greatly in shape and size, much more than plant cells. Moreover, most animal cells do not have the cell wall which is clearly visible in plant cells. (See Experiment 5.) How does Schwann attack this problem?

The personality of Theodor Schwann was in sharp contrast to Schleiden's outspoken, impulsive nature. Schwann was gentle and amiable and willing to devote himself to slow, careful research work. He had already completed several important studies when, at the age of twenty-nine, he published his book on the cell theory. It was Schwann's work that effectively established the cell theory even though, because of his modesty and Schleiden's bragging, Schwann is sometimes given less credit than he deserves. Strangely enough, for the remaining forty years of his life, Schwann made no further important contributions to the cell theory or to biological research. *(Photo from The Bettmann Archive.)*

23. Explain the comment: "Scientists gather a great deal of information, but that is not their main interest." What is the main interest of scientists?

24. How will Schwann prove his thesis? (This is a tough question, but it's an important one. To begin finding an answer, think about these questions: How do we prove a theorem in geometry? How do we "prove" an idea in science?)

EXPERIMENT 5. Animal Cells

You can appreciate the difficulties Schwann faced if you examine a variety of animal cells under a microscope. Prepared, stained slides are best for this, but you can make your own wet mounts of several different kinds of animal cells. Here is one suggestion for preparing animal cells for microscopic viewing:

Place a frog in a jar containing one inch of water and allow it to stand for about four hours. The water will become cloudy with thin flakes from the outer layers of the frog's skin. With a needle, lift out a small piece of this material and place it in a drop of water on a clean microscope slide. Try to straighten out the material into a thin sheet, and stain it with fountain-pen ink or methylene blue. Add a cover slip and observe the material under low power, then under high power. Can you see a cell wall, nucleus, and cytoplasm? In the right-hand margin, make a labeled drawing of one of the cells.

Other convenient sources of animal cells are the inner lining of your cheek, a drop of frog's blood, and a drop of your own blood. Make wet mounts, and observe at least two kinds of these animal cells with a microscope. Make drawings at the right of what you see. In what ways are animal cells and plant cells alike? How are they different? Write your answers below.

In setting down his experimental approach, Schwann points out how he will seek to "prove" his theory:

What does Schwann mean by "logically correct"? (25)

> The similarity between certain individual animal tissues with those of plants has already been mentioned . . . Nevertheless, as is logically correct, no inference has been made from such individual similarities. Every cell is not necessarily analogous in structure to some plant cells . . . We can only draw an analogy between the cells of animal tissues with plant structures of similar elementary identity on the following grounds—
>
> **1.** By demonstrating that a large part of the animal tissues originates from or consists of cells, each having its own particular wall [and a nucleus, whence] it becomes probable that such cells do correspond to the cellular elementary structure present in all plants; or
>
> **2.** By proving, in connection with any particular animal tissue made up of cells, that . . . growth proceeds in them in a way similar or identical to that which occurs in plant cells.

1 and 2 might be called Schwann's hypotheses. What is a hypothesis? (26)

Let's interrupt our story for a moment to consider the line of reasoning Schwann might have used to get to these two hypotheses. This kind of analysis is important in helping us to understand how scientists work, for a broad conceptual scheme in science, such as Schwann's theory about cells, can never be tested directly by experiment. Therefore, when a scientist wants to find out whether or not his broad conceptual scheme is correct (or, as Schwann would say, wants to "prove the thesis"), he must first reason by logical steps from a statement of his theory to working hypotheses, which *can* be checked by experiments and observations.

If after completing his observations the scientist finds that the results indicate his working hypothesis is correct, he begins to have confidence in the conceptual scheme or theory from which he derived this hypothesis by reasoning. As the results of further experiments and observations show that other working hypotheses connected with the theory are also correct, the scientist places more and more confidence in the theory that has yielded these successful hypotheses. However, the reasoning that originally connects the scientist's theory with a testable working hypothesis can be quite a tricky business. It almost always involves a number of assumptions, which are often not stated, and these assumptions themselves may or may not be correct, as we shall see.

What is an assumption? (27)

To begin our analysis of Schwann's reasoning, we can write out a statement of his theory or conceptual scheme in this way:

- **CONCEPTUAL SCHEME: Cells are the basic unit of all life.**

Next we note that Schwann makes an assumption, which he does not state. Nevertheless this assumption—as given below—is an important link in his reasoning.

- **ASSUMPTION A:** All life consists of plants and animals.

From this point in the line of reasoning it is a simple matter to move to the following:

- **DEDUCTION:** Plants and animals are composed of cells.

And then another key assumption appears as one of the steps that connects Schwann's theory with his working hypotheses.

- **ASSUMPTION B:** Cells are defined (1) by their structure—cell walls plus cell nuclei, and (2) by their manner of growth—as described by Schleiden in plants.

25. What does Schwann mean by "logically correct"? (As a hint, try this example: Almost all cars are similar in many characteristics. All have metal bodies, rubber tires, glass windows, steering wheels, and so forth. Is it therefore logically correct to say that all cars are made of the same parts? Explain your answer.)

26. What is a hypothesis in science?

27. What is an assumption? Consider Assumption A and Assumption B in our analysis of Schwann's reasoning at the bottom of page 20. Are they both correct? Is either one correct? If not, why not?

From the above deduction and from Part 1 of Assumption B, Schwann arrives logically at

- **HYPOTHESIS I:** If the elementary parts of a sufficient number of animal tissues have nuclei and cell walls, then animal tissues are composed of cells.

Similarly, from the deduction and from Part 2 of Assumption B, the reasoning leads to

- **HYPOTHESIS II:** If the elementary parts of any animal tissue grow in the same manner as plant cells (as described by Schleiden), then the tissue is composed of cells.

Our analysis demonstrates how Schwann's thinking moved from a broad conceptual scheme that he could not test directly to two working hypotheses that could be tested. We can have little quarrel with the logical soundness of Schwann's reasoning. Therefore the testing of his two hypotheses will also serve as good tests of his conceptual scheme, providing his assumptions were correct. We may wonder about the correctness of his assumptions. Schwann, of course, did not, as we can see from the fact that he went ahead to the testing of his working hypotheses.

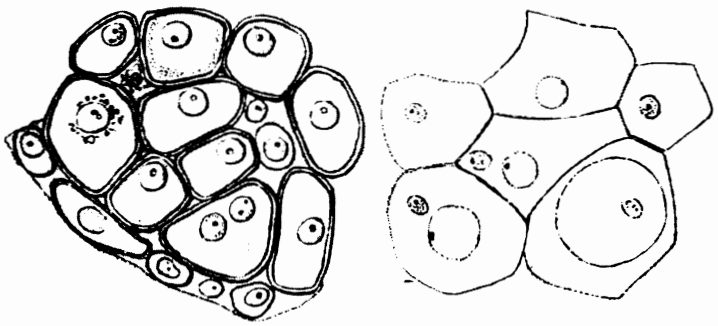
Schwann needed to make a large number of observations on a variety of animal tissues to gather evidence to back up his hypotheses. He examined under the microscope preparations taken from frogs, calves, foetal pigs, chick embryos, carp, pike, insect larvae, feathers of birds, and many others. He also collected the relevant observations of other workers, and, for an extensive study of his own, he selected the notochord of tadpoles. (See Experiment 6.)

Did you lose your notochord? (28)

In the course of my experiment on nerve-endings in the tails of frog larvae [tadpoles], I not only saw for myself the beautiful cellular formation of the dorsal cord in these larvae, but also discovered the nuclei in the cells. J. Müller has already proved that the dorsal cord in fishes is composed of separate cells provided with definite walls and packed closely together . . . The nuclei, so similar in form to the usual flat nuclei of plant cells, might well be mistaken for these, and thus supplied a further point of similarity . . .

Müller had proved, in connection with the cartilage corpuscles discovered by Purkinje and Deutsch, that because of their gradual change into larger cells they must be hollow and therefore *cells* in the wider meaning of the term: Miescher also points out a special class of spongy cartilages of cellular structure. Similarly, nuclei were observable in the cartilage corpuscles . . . I next succeeded in actually seeing the true wall of these corpuscles, first in the branchial [gill] cartilages of frog larvae and later also in fish, and the concordance between all of them thus proved that all cartilages possessed a cellular structure in the restricted sense of the word.

Schwann has "proved" his first hypothesis. How did he do it? (29)



Reproduced here are two of Schwann's drawings from his *Mikroskopische Untersuchungen.* Note the nuclei and cell walls and, as Schwann believed, new cells without walls growing between the older cells. At the left are cells from the branchial cartilage of *Rana esculenta* (frog); at the right the cells from the notochord of *Cyprinus erythrophthalmus* (carp), as Schwann reported he saw them.

28. What is a "notochord"? Do you have one, or did you lose it?

EXPERIMENT 6. Cartilage Cells

In this experiment we select a particular kind of material for observation. The animal cartilage cells that we shall look at are similar to the material that Schwann selected for his principal study.

Obtain a prepared slide of animal cartilage cells and observe under low power. Can you see a cell wall? nucleus? cytoplasm? Make a drawing of one of these cells. Is there a cell wall in this particular kind of animal cell? How was this important to Schwann?

29. How did Schwann "prove" his first hypothesis? Describe his way of testing Hypothesis I and give examples of the materials he used.

Scientists exchange ideas through publications and meetings and on a personal basis.

At about this point in Schwann's investigation, Schleiden entered the picture. The two men met informally, as Schwann tells us:

> One day, when I was dining with M. Schleiden, this illustrious botanist pointed out to me the important role that the nucleus plays in the development of plant cells. I at once recalled having seen a similar organ in the cells of the notochord, and in the same instant I grasped the extreme importance that my discovery would have if I succeeded in showing that this nucleus plays the same role in the cells of the notochord as does the nucleus of plants in the development of plant cells.

Aha!

With this clue, Schwann busied himself amassing evidence to support his second hypothesis. He applied Schleiden's notion about the growth of plant cells to the animal cells he had observed:

> The previously baffling contents of the cells in the branchial cartilages of frog larvae [I now recognized as] infant cells provided with a nucleus . . . As, soon after this, I succeeded in ascertaining the origin of young cells from nuclei . . . in the branchial cartilages, the matter was settled. Cells in the animal body showed themselves with a nucleus whose position with regard to the rest of the cell, shape, and modification were similar to the plant cytoblasts. Thickening of the cell wall took place and infant cells were formed . . . from a similar cytoblast [as in the plant cell] . . . This concordance was still further shown by many other details, and in this way, so far as concerns these individual tissues, the necessary evidence was obtained to show that these cells did indeed correspond to the elementary cells of plants.

Compare this description with Schleiden's account of plant cells. (30)

How does Schwann test his second hypothesis? (31)

Were the cells of other tissues formed in the same way? Schwann took steps to find out and then reported:

> Many cells, some with nuclei, were already within our knowledge; for instance, in the ovum, epithelium, blood corpuscles, pigment, and so on . . . Many points of similarity in the development of such cells were already known. C. H. Schultz had already demonstrated the pre-existence of nuclei in blood corpuscles, the formation of a vesicle around them, and the gradual expansion of this vesicle. Henle had observed the gradual expansion of epidermal cells from the lower layers of the epidermis towards the upper layers . . .
>
> On still further investigation, I continually found this principle of cellular formation coming into its own . . . Cell nuclei and later on cells themselves were discovered to be at the origin of all tissues in the animal body, whence all tissues consist of cells or are formed from cells by various means. The alternate proof of the analogy between animal and vegetable cells was thus supplied.

Every scientist builds on the work of others.

Has Schwann proved his point satisfactorily? (32)

Schwann's conception, which he so painstakingly demonstrated, of the cell as the basic structural unit of life and as a basis for the vital processes in both the plant and the animal kingdoms was immediately accepted by the biologists of his time. The cell concept still underlies most of our biological knowledge and research. But the cell that biologists now work with and think about is vastly different from the cell that Schleiden and Schwann imagined. Their notions about the cell have been replaced because of later, more accurate observations.

Are scientific ideas replaced very often? (33)

Schleiden and Schwann made no further important contributions to our understanding of the cell. Still, their ideas had opened a floodgate, and many

30. Compare Schwann's description of various animal cells with Schleiden's account of plant cells given on pages 14 and 16. Does Schwann see something similar to what Schleiden saw?

31. How does Schwann test his second hypothesis? Compare his way of testing Hypothesis II with his way of testing Hypothesis I. Are there any differences?

32. Do you think Schwann proved his point satisfactorily? Did he really show that cells are the basic unit of all life? What more, if anything, could he have done?

33. It often happens in science that earlier ideas are replaced. What other examples do you know of? Since scientific ideas may have to be revised at some future time, does this mean that they are not very dependable? Defend your answer.

Through further research, scientists can correct errors.

workers rushed in to explore further. In the ensuing decades, much effort was expended in correcting two erroneous notions that Schleiden had introduced and Schwann had accepted. Much was learned about cells through this effort.

How can a scientist know if he has selected a typical material for study? (34)

Schleiden believed that new nuclei appeared between cells, having crystallized out of the surrounding "gum solution." New cells were formed by a kind of budding from these nuclei. Schwann strengthened this belief by formulating a detailed analysis of the crystallization process. Now it happens that the particular cells in the embryo sac that Schleiden selected for study are different from almost all other plant and animal cells in the way they grow and reproduce. Later investigators gradually learned that the typical means of cell reproduction is division of each cell into two daughter cells.

Are scientists concerned with health problems? (35)

The death knell for the notion of cellular crystallization was sounded by Rudolf Virchow, professor of pathology at the University of Berlin. Virchow, whose investigations dealt with the causes of diseases, believed that a person's health depended upon the health or sickness of the individual cells. In a lecture series, "Cellular Pathology," which began in 1858, Virchow declared:

> We can now . . . reject the theory of spontaneous generation just as much in the history of the development of individual parts as we do in that of entire organisms. Just as little as we can now admit . . . that out of the residue of the decomposition of animal or vegetable matter an animalcule, a fungus, or an alga, can be formed, equally little are we disposed to concede . . . that a new cell can build itself up out of any non-cellular substance. *Where a cell arises, there a cell must have previously existed,* just as an animal can spring only from an animal, a plant only from a plant.

Virchow's generalization, *Omnis cellula e cellula,* was correct, but details of the process by which cells arise from previously existing cells were not fully worked out until more than twenty years after Virchow's declaration. (In Activity 4, page 29, a key part of these developments—the recognition of the phases in the division of the cell and nucleus—is presented.)

Twenty years is a long time. Why the delay? (36)

The second erroneous notion about the cell, passed on by Schleiden and Schwann, was that the cell wall is an integral part of the living cell. Of course, the cell wall is usually the most conspicuous part of a plant cell, and this is what Hooke had originally observed in cork. But most animal cells do not possess a rigid cell wall. One exception is in the cells of cartilaginous tissue, the particular animal cells that Schwann had studied. Later workers established that the cell wall consists of nonliving material that is secreted by the cell's living material through the cell membrane. The cell membrane is the outer living boundary of both plants and animal cells, and it provides them with mechanical support. More or less filling the space between the cell membrane and the cell nucleus is the living cytoplasm, which Schleiden had regarded simply as a gum solution.

Schwann's selection of cartilaginous tissue helped him. How? (37)

What does a scientist "see" through his instruments? (38)

In this case we followed the formulation of a major biological idea, an idea that scientists were able to use fruitfully in their efforts to understand the natural world. Yet our story is not complete. Many questions have not been answered. For instance: (1) What materials are different parts of the cell made of? (2) If *Omnis cellula e cellula* is correct, how was the first cell formed? (3) What mechanism produces daughter cells that are exactly like the parent cell? (4) How can cells change? Some answers to such questions have been found in the 125 years since the work of Schleiden and Schwann. Other answers are being obtained by scientists today or will continue to be sought tomorrow.

34. How can a scientist know if he has selected a typical material for study? Is there any way, or must he take a chance? What may happen if the material he studies and observes is not typical?

35. Are scientists concerned with health problems? What kinds of scientists are particularly concerned? What kinds are not?

36. What might have been some reasons for the delay in learning about the details of the process of cell division? Suggest three or more different reasons.

37. How did the selection of cartilaginous tissue help Schwann?

38. What does a scientist "see" through his instruments? (This question refers to the same problem that was mentioned in questions 1 and 15. Now that we are near the end of this case, can you discuss the problem more fully?)

ADDITIONAL ACTIVITIES

ACTIVITY 1: Scientists and Nations

Here, listed by the countries in which they lived, are the men who made contributions to our understanding of cells from the time of Hooke, who begins our study of this case, to the time of Virchow, who comes near the end of it.

Czechoslovakia—Johannes Evangelista Purkinje

England—Nehemiah Grew, Robert Hooke

France—Félix Dujardin, René Joachim Dutrochet, Charles François Mirbel

Germany—Christian Gottfried Ehrenberg, Jacob Henle, Franz Leydig, Hugo von Mohl, Johannes Peter Müller, Karl von Nägeli, Lorenz Oken, Robert Remak, Matthias Jakob Schleiden, Max Johann Schultze, Theodor Schwann, Karl Theodor Ernst von Siebold, Ludolf Christian Treviranus, Gabriel Gustav Valentin, Rudolf Ludwig Carl Virchow

Holland—Anton van Leeuwenhoek

Italy—Marcello Malpighi

Scotland—Robert Brown (1773–1858)

Switzerland—Rudolf Albert von Kölliker

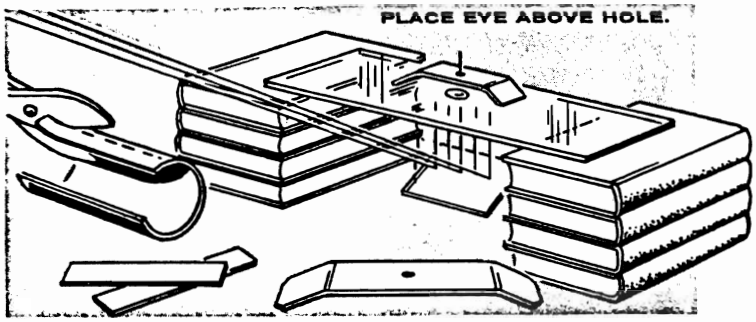
Members of the class may wish to use this list as a takeoff point for special reports. In your library research and your report about one of these men, you will want to find and discuss the answers to the following questions: Who was the man? What did he contribute to our understanding of cells? What other contributions to science did he make? What did he do in other fields?

From the above list of countries, you can see that science is an international activity. This fact suggests other subjects from which you might choose a topic for a written report. How did these men, some living great distances from one another and speaking different languages, learn of one another's work? How do American scientists today learn of the work of foreign scientists? Are there barriers, other than language, to efficient international communication between scientists? Write an essay discussing these problems.

Finally, isn't there something peculiar about the above list? Although there are representatives of eight countries on the list, there were certainly many more countries than this in the world between 1665 and 1860. Why aren't there scientists listed from these many other countries? (The list is a fairly complete one for the period, so incompleteness isn't the answer.) With the help of the library card file and your school librarian, you may be able to locate books discussing the social, cultural, and intellectual histories of such countries as England, France, and Germany during the period in question. See whether you can discover from these books what factors operating in a particular country at a particular time are likely to produce a large number of scientists and scientific discoveries. Write an essay discussing your personal generalizations on the subject and any evidence you have to back up these generalizations. Why is it important to us today to know what factors help nations produce scientists and scientific ideas?

ACTIVITY 2: Make Your Own Microscope!

Leeuwenhoek made remarkable observations of microorganisms, using a microscope with only a single tiny lens. You can easily construct a microscope that will magnify up to 100 times by using a tiny drop of water as a lens. The following directions for doing so are adapted from the New York State *General Science Handbook*, Part 3 (1956), pages 7–11.



The chief item you need is a small tin can (the kind that frozen juices come in). Remove the crimped ends of the empty can with a rotary can opener. Cut through the can lengthwise with scissors or tin snips. Flatten out the sheet and cut out a strip one inch wide. Cut off the four corners of the strip. Drive a small finishing nail through the center of the metal strip. Turn the strip over and file off the ragged points of metal around the hole made by the nail. Insert the nail in the hole again to make the hole perfectly round. Bend down the ends of the metal strip slightly. This is the body of your microscope, and it holds the water-drop lens.

The stage of your microscope is made by supporting a glass windowpane between two piles of books, each about one foot high. Place the body in the middle of the stage. The light source for your microscope is a rectangular pocket mirror set at an angle on an Artgum eraser or a small piece of wood under the stage.

To use your water-drop microscope, place the stage on a desk or table and adjust the light source so that the mirror reflects light from the sky directly up-

ward through the pane of glass. Dip a sharpened pencil into a glass of water and shake off any large drops. Place the point of the pencil in the hole of the body so that a fairly large drop is deposited directly over the hole. Several trials may be needed before the water drop is round and perfectly centered. Place a drop of the material to be observed on the stage and spread it slightly. Slide the body into position so that the water-drop lens is directly over the material. Place one eye very near the water drop and press down on the metal strip with one finger until the object comes into focus.

Hints: One of the secrets for getting a high magnification is to have the water drop as round as possible. If your drop flattens out or evaporates, restore its roundness by adding more water with the point of a pencil. You may also wipe the body with a dry cloth and add a new drop of water. Performance of the water-drop microscope can be improved by polishing the metal strip with a silicone automobile polish.

With practice, you can make almost all the observations with your water-drop microscope that can be made with the low power of a compound microscope.

ACTIVITY 3: Matthias Jakob Schleiden

The following account of the colorful life of Schleiden is given by Erik Nordenskiöld in *The History of Biology* (New York: Knopf, 1928), page 392:

"He was born in Hamburg in 1804, the son of an eminent doctor. He began by studying jurisprudence, became a doctor of law, and took up a practice as barrister in his native town. He had, however, little success as a pleader, a fact that increased his naturally melancholy disposition. Finally, in a fit of despondency he shot himself in the forehead, but without the result he intended; he recovered and then resolved to devote himself to natural science. He became both doctor of philosophy and medicine, gained a great reputation by his writings, and in 1850 became professor of botany at Jena. After twelve years, however, he resigned . . . and after that led a life of wandering, with brief sojourns in various German towns, which lasted till his death, in 1881."

Does this sound like the sort of career that scientists usually have? Is it usual for scientists to have a "naturally melancholy disposition"? If not, what kind of disposition do scientists usually have? Do you think it would be possible for a scientist to be successful today with the kind of training that Schleiden had?

In any encyclopedia, quickly read the life stories of three of the scientists listed in Activity 1. Then read the life stories of several modern scientists. After doing these things, write a short essay giving and defending your answers to the above questions.

ACTIVITY 4: Division of the Cell and Nucleus

One of the major contributors to the clarification of the process of cell and nuclear division was the German biologist, Walther Flemming (1843–1915). How well this process was understood by scientists in the late 1870s is well represented in a paper by Flemming from which excerpts are given in this activity.

As you read this paper, you should look in Flemming's remarks for illustrations of how scientists work and think—the same sorts of ideas we looked for in the main story of this case. Some of the ideas you will find illustrated are:

A. The importance of developing new techniques for preparing and observing cellular tissue.

B. Interweaving of interpretations into the description of observations.

C. The use of assumptions in reasoning.

D. The use of analogies in giving descriptions (recall Hooke's honeycomb analogy).

When you find an example of one of these ideas in Flemming's paper, mark an **A, B, C,** or **D** beside it to show which of the above ideas the example illustrates. Try to find other ideas about scientific work illustrated in Flemming's paper.

Flemming published his paper under the title "Beiträge zur Kenntniss der Zelle und ihrer Lebenserscheinungen" (Contributions to the Knowledge of the Cell and Its Life Phenomena) in the *Archiv für mikroskopische Anatomie,* 16: 302–406 (1879). You will quickly see that the present-day names for the various phases of cell division had not been invented when this paper was written. Modern terms have been added, printed in boldface type and enclosed in square brackets, to the excerpts from the original text that appear below.

Contributions to the Knowledge of the Cell and its Life Phenomena*

In the larva of the salamander the unpigmented regions of the tail fin are the best object for observation of the living cell-divisions in the epithelium [surface layer of cells]. The wonderfully transparent gill filaments do not show the living epithelium, and although they show the dividing nuclei, these are, however, too pale to be sufficiently visible. . . .

On the other hand, the gill filaments are as though made to order for obtaining fixed and stained

*Mordecai L. Gabriel & Seymour Fogel, *Great Experiments in Biology.*

preparations of cell divisions, since no further sectioning or preparation is required. As fixatives I have tried out a number of reagents, but have always come back to the same three which give the best results: picric acid, chromic acid, and less satisfactory, gold chloride.

A chief advantage of the picric acid treatment is that it subsequently provides very beautiful nuclear staining with haematoxylin or (less good) carmine. The acid must be well washed out before the staining; the haematoxylin solution is best when much diluted.

DESCRIPTION OF CELL DIVISION IN SALAMANDRA (AFTER THE LIVING OBJECTS) IN COMPARISON WITH STAINED PREPARATIONS

In the description I shall restrict myself chiefly to the epithelium of the fins and the gill filaments.

In a well-fed larva one need not search long to find various stages of division, which one encounters in the superficial cell layers as well as in the deep layers, among the resting nuclei of the tail fin. The earliest stages that can be recognized in the living tissue show the following:

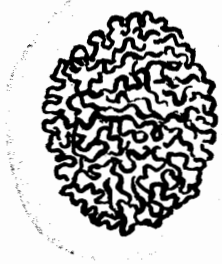
1st Phase: Appearance of a fine basketwork of tightly wound threads

Instead of the pale but sharply marked-off resting nucleus, the middle of the epithelial cell is occupied by a pale body, not sharply delimited, which is often slightly or markedly larger than a resting nucleus, and which in the living condition appears to be densely and finely granular. This granulation is, however, only apparent: stained preparations of this phase show with great clarity that this is a coherent, dense, and regular framework of delicately spiraled threads, which in the living condition are too pale to be entirely visible, so that the optical cross and oblique sections of their gyres [spirals] give the impression of granulations. In lightly stained preparations one can ascertain that the nucleolus is no longer present. On the other hand there still exists a sharp differentiation of the nuclear figure from the plasma visible in stained objects as a fine but sharp contour. . . .

In its resting condition the ground substance is stainable like the network and the nucleoli, but in lesser degree. In the well-marked coil stage [**prophase**], on the other hand, a stainable ground substance is no longer present. We now assume that this substance is taken over into the formed part of the nucleus, into the network, in preparation for the division (in connection with which the nucleoli at this time lose their form and disappear and presumably divide). Where this transition of the stainable substance into the network has not yet been completely accomplished, the ground substance takes a pale stain and unchanged remnants of it may be present. The reagents show these up as granules just as in the resting nucleus. Later these two remnants disappear also, and there is no longer present in the nucleus any substance which can coagulate as granules; everything stainable has been taken up into the structural elements. The latter have therefore grown in size and simultaneously divided into nearly equal spirals through the nucleus. All this occurs first at the periphery of the nucleus.

That an actual transformation of this kind of the substance in the nucleus must take place is immediately evident. It is only necessary to recall that the ground substance of the reticulum was stainable in the resting stage, whereas the stainability disappears during the division. It is on the face of it impossible that the coiled thread of the developing nucleus is only a morphological rearrangement of the resting network including the nucleoli. This is obvious from the fact that the mass of the coiled thread is clearly larger than that of the resting nuclear structure, and that—if I may thus express it—the quantity of stain which the basket accumulates may be estimated to be as large as that which the entire nucleus including the ground substance takes up in the resting condition . . .

2nd Phase: Loose coil or basket form of the mother nucleus



If one observes a metamorphosed nucleus for some time, the visible granules gradually become thicker and more isolated, and soon one clearly recognizes coiled threads which, however, on account of their paleness cannot clearly be seen to be connected. The staining of such an object shows plainly that this connection is actually present. The nucleus has the form of a very delicate extensively interconnected basketwork of winding threads of uniform thickness which are distinctly stainable. The ground substance, on the other

hand, no longer takes up any trace of stain, and there are no longer present in the nucleus any finely granular masses (coagulations). The nucleoli have already disappeared prior to this. The threads loosen out more and more, and their direction becomes for the most part perpendicular or nearly so to the long axis of the nucleus, a condition that quite typically recurs (even more markedly) at the formation of the young nuclei after division. . . .

3rd Phase: Astral form of the mother nucleus

In living divisions during the transition to this phase, the thread network is seen to become somewhat looser, and loops spread out peripherally to the clear space. The center remains indistinct. Stained preparations of the transition to this condition show a stratification of the threads in which the order is often difficult to discern; soon, however, there follow groupings in which a typical stratification of the threads is apparent, although it is not equally distinct in all cases. That is to say, there occur central and peripheral bendings of the threads—I will briefly call them loops . . .

Up to now I have passed over another very remarkable phenomenon: *the threads divide themselves in half length-wise.* This process can already occur at the end of the coiled stage, or in the course of the third phase now being described: accordingly one encounters both single and double threads in all these conditions. The threads may remain single during the stage of the transformation of the star. But that the length-wise splitting of the threads is a typical process is proven without any doubt in *Salamandra* by the great number of such figures.

The thread halves lie almost exactly parallel in epithelial nuclei and red blood-cell nuclei, slightly diverging in endothelial cells, and often are turned back in the same direction for a short distance in connective tissue cells.

Later the threads move apart from one another along their entire length, and in this way there arises a fine threaded star, the rays of which are double in number and half as thick as previously.

That this longitudinal division of the threads (in *Salamandra,* at least) is an essential and constant stage, is indicated by the simple fact that also in the following stage (equatorial plate) the threads are always of approximately half the thickness as compared with the single-threaded star.

No investigator of nuclear division has hitherto reported anything of such a splitting of the threads; I therefore immediately asked myself whether the action of the reagents might perhaps be involved, unlikely as this might appear, since the phenomenon was always encountered in a similar manner in picric acid and chromic acid preparations. I can rule out every such idea, since I have been fortunate enough in several cases to see the double threads in the living condition as well. . . .

4th Phase: Equatorial plate [metaphase]

This stage sets in quickly and passes quickly, and is therefore fixed by reagents relatively infrequently; in the investigation of every living epithelial cell division, however, one sees it typically recurring, and because of its characteristic form it deserved to be denoted as a separate phase.

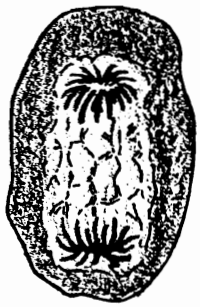
Instead of the flattened star extending toward the poles in the form of two cones, as is characteristic of the previous stage, a grouping of the threads occurs in such a way that all the elements, at first somewhat coiled, but later stretched out more and more parallel to the division axis, fill up the space of a thick plate comprising about one-fifth to one-fourth and sometimes as much as one-third of the entire cell length. The plate always lies in the equator and is oriented at right angles to the division axis . . .

5th Phase: Separation of the nuclear figure [anaphase]

This expression is meant to signify only the moving apart of the two halves since the actual separation of the two nuclear halves has already taken place.

Each half of the figure has somewhat the form of a broad fish-basket but with outwardly slightly convex rods. If this stage is seen in polar view, it has the appearance of a star. This, however, is not very distinctly observed in the epithelium since the cells, as mentioned, always divide in the horizontal plane. . . .

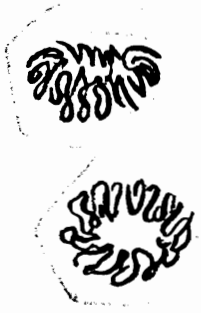
6th Phase: Star form of the daughter nuclei



The threads of the two nuclear halves* up to now having their free ends directed opposite those of the other side, move further and further apart so that some of those situated in the periphery often attain an orientation towards the poles of the cell. In this way the figure acquires the form of a flattened star, sometimes very regular and sometimes less so. . . .

At this time the constriction furrow frequently makes its appearance in one side of the cell body.

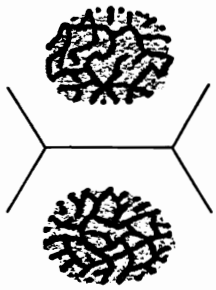
7th Phase: Wreath and coil form of the daughter nuclei [telophase]



In the living cell each daughter nucleus has somewhat the appearance that the mother nucleus had earlier in the second phase. A characteristic feature is the constant deepening of the polar side, so that the two baskets, each with the shape of a convex-concave plate, turn their convex sides to one another. In the later course of this phase the windings move so close together that the living young nucleus gives the impression of a lumpy, internally homogeneous clump; staining shows very clearly, however, that this is a false impression and that an entirely homogeneous phase does not at all occur here. It is only necessary to add acetic acid to the apparently homogeneous form to see immediately a clear picture of a structure of irregular rods.

In this phase the cell divides. The first sign of this was already present in the previous phase; the furrow gradually affects also the other side, the equator becomes progressively narrower, and the cell body constricts in two; in the epithelial cells this happens quite gradually without interruptions and pauses (in other cells I was not able to observe this directly). No differentiation is noticeable in the equatorial plane in the interior of the cell . . .

8th Phase (if one wishes to distinguish this as such): Reticular form of the daughter nuclei, reversion to resting condition



Pairs of young nuclei in all stages of transition from the seventh phase to the resting form are everywhere abundantly found; hence this transition lasts a fairly long time. It is quite clear that after the division of the cell the threads are at first coiled, and then become so arranged that the majority lie extended transversely to the longitudinal axis of the nucleus. As a result, such young, transversely barred nuclear pairs are at first glance like resting stages, except for the fact that they are smaller. From this condition the filamentous structure passes into the condition of a uniform reticulum; however, the threads are no longer coiled. The reticulum becomes progressively more dense but ever paler, while the nucleus slowly enlarges. Simultaneously, the nucleus has acquired a sharp demarcation from the cell body, and the interstitial substance between the threads is now stainable. But an actual, substantial membrane cannot yet be demonstrated in nuclei. In the following, still paler stage, a more distinct contour appears, whereupon the form reverts to that of the resting stage. . . .

From all this it is clear that the daughter nuclei at first have the form of a flattened star. This transforms into a star or wreath having coiled threads, which become peripheral, and central loops from which a convoluted skein arises. From this a reticulum with interstitial substance is formed. It is likewise clear that this whole process, with the exception of the double-stranded stars, is a reversed sequence of the changes which the mother nucleus underwent.

*I use the expression nuclear halves for convenience; it remains an open question whether during or before the separation any part of the old nucleus might remain in the plasma or whether anything might be acquired from the plasma.

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