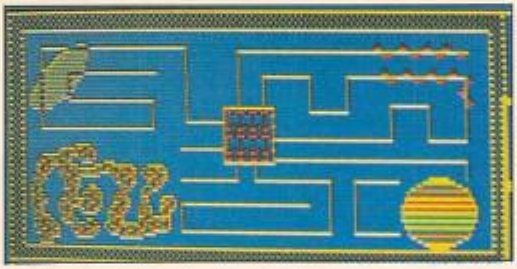

CELL MATES

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How complex is a living cell? Is it a static structure—or a dynamic system? How do symbiotic organisms make all cellular life possible? Find some answers with this fascinating bio-simulation.

There is more going on inside a living cell than meets the eye. Even the most powerful microscopes have not yet revealed the entire story—the secret life of the cell. Ask most people what they know about this basic life unit, and their reply, if any, may invoke a static picture of the cell and its interior: the cell wall, the nucleus, and "a bunch of little floaty things." But when biologists look closer at these little floaty things, they see participants in an incredibly complex, wonderfully cooperative, and dynamic *ecosystem*; for the metabolism of a living cell involves some strange and alien participants who apparently learned to live together millions of years ago. Directing this metabolic dance, communicating with each cell part through encoded molecules, is the nucleus. Some of the participants—called *organelles*—possess their own DNA (deoxyribonucleic acid) and reproduce themselves independently from the nucleus. Together, they are all *Cell Mates*.

What if you could place yourself at the center of this dance—consciously balancing the entire system moment by moment? There may be no better way to appreciate just how dynamic and basically cooperative this system is. We can't literally perform such a miracle, but we *can* give you *Cell Mates*, a simplified computer simulation that places you in the role of the nucleus, the cell's "choreographer."

The Major Performers And You

Plant and animal cells each have a somewhat different cast of dancers. But in both cases, each kind of organelle has a specific role to perform. In animal cells, some organelles, called *ribosomes*, manufacture various proteins. Another group, the *Golgi apparatus*, "packages" these proteins for internal use or secretion (export). *Lysosomes* are the garbage collectors. And tiny mobile chemical plants, called *mitochondria*, supply energy for all of these activities.

Special thanks for technical advice goes to W.R. Sistrom, University of Oregon Department of Biology.

Although these organelles perform the cell's main functions, there are many other participants performing minor, but essential parts. Because of the difficulty in portraying all of the cell's diverse components, these minor players are beyond the scope of *Cell Mates*.

In *Cell Mates*, you direct the show, allocating energy to these 4 essential functions: protein production, waste disposal, ribosome production, and protein export. Your goal is to direct these functions in such a manner that the cell is able to divide—effectively producing two new cells in its place. When the cell divides, you receive a total score. The less time you take to reach cell division, the higher is your score.

You must meet certain requirements before the cell can divide: You must double the supply of protein as well as the number of several internal components (such as the ribosomes); and you must support the larger family of surrounding cells by exporting protein.

After displaying the title, the program presents the actual playing screen. This screen contains a graphics representation of the cell (in the upper-left corner), and 12 indicators that show the status of the various processes in the cell. You can gauge your progress by viewing these indicators. Some of the indicators contain areas highlighted against the background color. To maintain and eventually reproduce the cell, you must manipulate the cell's life processes so that the pointers remain in these "safe" areas. Indicators that contain no distinguished area show the actual level of energy going to specific activities.

THE SECRET LIFE OF ORGANELLES

Millions of years ago, life wasn't what it is today. In the still waters of land-locked lakes and ponds, primitive single-celled creatures without true nuclei learned to obtain energy and reorganize materials through ingenious chemical processes. These were the ancestors of the organelles; for as life became more and more organized, such specialized organisms became permanent fixtures within higher lifeforms. Some—such as the *chloroplasts*—integrated themselves into the first true plants, capturing energy from the sun for use by the entire organism. Others—such as the *mitochondria*—took oxygen from the atmosphere (mostly produced by the activity of the chloroplasts) and used it to "burn" complex molecules as an energy source for animal life. Even today, these organelles possess their own DNA, and reproduce themselves independently of the organisms they support. (For example, mitochondria in a fertilized egg cell come partly from the mother cell and partly from the sperm—and as this cell divides, each new cell starts off with half the mitochondria of a mature cell.)

Why Life chose to organize itself in this way is a question that has preoccupied many people—not just the biologists who discovered these facts. For whatever reasons, the organizing process was primarily *cooperative*, rather than competitive. It is still an open question whether organelles live for the sake of the higher organisms—or whether we are living for them. What is apparent is that all the players in this game have a total stake in the system. Neither the organelles nor the organisms in which they reside could live without each other. The fact that each maintains a separate genetic indentity actually serves to dramatize the cooperative nature of their relationship. Of all life's mysteries, this may be one of the most curious and wonderful.

[For more on this subject, read *The Lives of A Cell* by Lewis Thomas.—Ed.]

We have incorporated a delay factor into the simulation, representing the real-world lag between the initiation of an action and its effect. This delay is not constant—it varies with internal and external conditions. Because of this built-in lag, any action that you take does not immediately show up on the screen indicators.

Dividing Energy

This simulation focuses on the 5 most important cell components: the mitochondria, the nucleus, the lysosome, the ribosome, and the Golgi apparatus.

> *". . . when biologists look closer at these little floaty things, they see participants in an incredibly complex, wonderfully cooperative, and dynamic ecosystem."*

Mitochondria—In animal cells, mitochondria produce ATP (adenosine triphosphate)—life's most available source of chemical energy. Similar organelles in plant cells—the *chloroplasts*—actually perform photosynthesis (the conversion of light into energy). All of the cell components, including the mitochondria themselves, use ATP as their energy source. Without this substance, the cell would not be able to carry out any activity. Mitochondria manufacture ATP by combining products of available nutrients with oxygen (and emitting carbon dioxide as a waste product). Thus, when cellular biologists talk about *respiration*, they are talking about a process that occurs inside the mitochondria. The amount and quality of available nutrients directly affect the amount of ATP that the mitochondria can produce.

Mitochondria are mobile, and can move to the areas of the cell where energy is most needed. Most animal cells contain anywhere from one to hundreds of thousands of mitochondria. For the sake of simplicity, our cell representation contains only one. To increase the energy allocation to any of the cell's components, simply move the mitochondrion to the corresponding organelle symbol by pressing the appropriate key (see the Control Capsule). Once the mitochondrion reaches the designated organelle, it automatically starts producing ATP. The mitochondrion does not manufacture ATP while it is in transit between cell parts.

Nucleus—The nucleus is the cell's control center—the "central computer." It sends signals in the form of encoded molecules to each part of the cell, telling it to carry out various operations. (In addition, the nucleus carries genetic information in its DNA that determines the form of new cells resulting from cell division, or "mitosis.") Again for simplicity, we have symbolized the message-sending activity of the nucleus with one example: the message to increase production of ribosomes. Of course, the nucleus requires energy each time it sends a message.

To allocate more energy to the production of ribosomes, press N. The mitochondrion responds by migrating to the nucleus. Once the mitochondrion reaches the nucleus, it begins producing ATP. The increase in energy shows up on the screen indicator labeled RIB.ENERGY (energy for the ribosome-production message).

As you allocate this energy, the RIBOSOMES pointer shows an increase by moving to the right. If you direct the mitochondrion away from the nucleus, the RIB.ENERGY indicator shows a decline, and the RIBOSOMES indicator ceases to increase.

Ribosomes do not live forever. They die occasionally, and become part of the cell's waste. You need to replenish your supply of ribosomes occasionally to maintain their numbers.

Ribosomes—Ribosomes produce protein. These tiny organelles are attached to the *endoplasmic reticulum*—a convoluted membrane extending out from the nucleus. The ribosomes assemble various proteins according to patterns supplied by the nucleus. Although we symbolize the ribosomes in a discrete corner of our cell, in reality they are more evenly distributed.

Protein is the cell's prime material. Before a cell can reproduce, it must double its original supply of protein. The speed at which ribosomes produce protein depends on the total ribosome quantity. If you need to produce protein at a faster rate (to keep up with the protein exportation rate, for example), you must increase this quantity. (See the Nucleus section above for directions on increasing the ribosome count.)

Press R for Ribosomes to allocate energy to the production of protein. This signals the mitochondrion to migrate toward the ribosomes (upper-right corner of the cell area). Once the mitochondrion reaches the ribosomes, the PRO.ENERGY indicator shows an increase as the protein energy level ascends. This increase in

Photo 1
Cell display from IBM version at top left shows (clockwise from display's upper-right): protein-producing ribosomes; waste-eliminating lysosome; and the convoluted Golgi apparatus where the mitochondrion (green) is supplying ATP energy for protein export. Nucleus is at center with extending endoplasmic reticulum membrane.

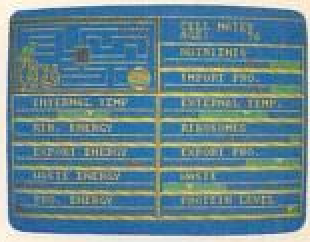
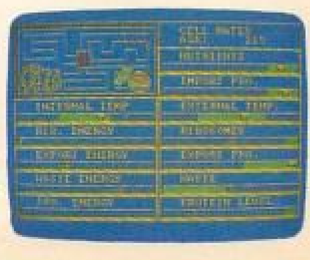


Photo 2
As the waste level continues to increase (as shown by waste indicator), the mitochondrion produces no ATP while traveling from the Golgi apparatus to the waste-eliminating lysosome at lower-right.

Photo 3
Now at the lysosome, the mitochondrion's ATP energy goes toward eliminating cell waste products—and in the nick of time, waste levels begin to decrease.



energy shows up in the PROTEIN indicator. But, as we stated, to achieve the desired increase in protein, you may need to increase the number of ribosomes first.

Lysosomes—The lysosomes are the cell's housekeepers. They carry degradative enzymes and travel around inside the cell collecting and digesting larger chunks of waste composed mostly of worn-out cell parts. This waste is always accumulating, so you must frequently budget energy for lysosome activity.

As the amount of waste in the cell increases, the WASTE pointer moves to the right. The only way to reduce the level of waste is to increase the amount of energy allocated to waste disposal. To do this, press L for Lysosome. In response, the mitochondrion moves to the lysosome symbol at lower-right corner of the cell. Once the mitochondrion arrives, the energy level shown by the WASTE ENERGY indicator increases. After the energy reaches a sufficient level, the amount of waste starts to decrease as the lysosomes do their job.

Golgi Apparatus—Your cell is also in the import/export business. Few cells can survive without the aid of other cells, so you must not only support your own cell, but those cells surrounding you. You must supply these cells with the protein they need for their existence, and in return you will receive protein from them—some of the nutrients vital to the production of ATP. The Golgi apparatus is responsible for exporting protein to other cells. As a secondary role, the Golgi apparatus spends a small percentage of its total energy packaging up waste and sending it out of the cell. If you fail to export sufficient protein, both the level of imported protein (IMPORT PRO.) and the nutrient level (NUTRIENTS) decline.

> *"Tiny mobile chemical plants, called mitochondria, supply energy for all of these activities."*

To increase the amount of protein that you export, press G for Golgi apparatus. The mitochondrion responds by moving towards the lower-left corner of the cell area to the Golgi apparatus symbol. Once the mitochondrion reaches the Golgi apparatus, EXPORT ENERGY begins to show an increase. If you have a supply of protein, EXPORT PRO. also shows an increase.

The rate at which you can export depends entirely on how much protein is available. As you export protein, PROTEIN LEVEL declines. As the protein level decreases, EXPORT PRO. starts to decrease. All of the protein you export must come from the protein you have produced (shown on the PROTEIN LEVEL indicator).

Additional Factors—The AGE display indicates the passage of a relative amount of time. The AGE counter does not represent any real time frame—to make the simulation playable, we have accelerated certain aspects of the cell's metabolic system, while slowing down others.

The older the cell gets, the harder it must work to produce protein (or ribosomes). You may also notice that the average amount of nutrients and imported protein also drops off with age. Many factors affect an individual cell's lifespan—too many to explain here. But every living cell has a built-in "time limit": The cell must reproduce within a specific period of time, or it will die. Our model reflects this basic fact.

The NUTRIENTS indicator shows the cell's current food supply. The mitochondria use these nutrients to manufacture ATP. In order for the cell to reproduce, the pointer must be in the highlighted portion of the display.

The IMPORT PROTEIN indicator shows how much protein is available from the surrounding cells. This protein contributes to the cell's protein level. In order to reproduce the cell, you must move the pointer to the the highlighted area.

The INTERNAL TEMP indicator shows the cell's current temperature. The optimum temperature is directly at the center of the indicator. The highlighted area is the safe zone for the cell. If the pointer leaves this area, the cell dies. Even if the pointer remains in the safe zone, high and low temperatures (relative to center) affect the efficiency of every metabolic operation.

Most individual cells have little control over internal temperature when the external temperature goes outside a life-supporting range. Therefore, the "generic" animal cell that we depict in this simulation depends on the temperature of the tissue of which it is a part. If the cell doesn't adequately perform its part in this tissue structure—neither maintaining itself, nor supplying needed protein to the surrounding cells—its external environment tends to degrade. This can cause a drop in external temperature, as well as a shrinking nutrient supply. Normal cell activity usually maintains a safe internal temperature. If the energy levels for ribosomes, export, waste, or protein increase, the internal temperature also increases slightly. But it is more important to ensure a steady external temperature by exporting enough protein to maintain the health of the entire tissue. If the external temperature does become excessive due to high mitochondrion activity, you can press M to send the Mitochondrion to its neutral, inactive corner.

Of course, the external temperature sometimes goes outside a safe range, no matter what an individual cell does. If it remains outside this range, the cell will die—which, as they say, is Life.

Life Goes On

A BASIC computer program can only "scratch the surface" of a living cell's complex nature. While being purely fun to operate, *Cell Mates* should also serve to awaken your curiosity about this fascinating subject. Perhaps just knowing that your very life depends on the activity of microscopic creatures with their own separate genetic identities will contribute to your curiosity. As biologists continue to unravel the mysteries of cells in general, and organelles in particular, you may be in a better position to understand and appreciate this new knowledge. Here's to a lifetime of learning about life itself!

CONTROL CAPSULE
Cell Mates

Key	Function
M	Move mitochondrion to home position—upper-left corner of cell area
G	Move mitochondrion to Golgi apparatus—lower-left corner of cell area
L	Move mitochondrion to lysosome—lower-right corner of cell area
R	Move mitochondria to ribosomes—upper-right corner of cell area
N	Move mitochondria to nucleus—center of cell area
Q	Quit option—exit simulation

HCM Glossary terms: ATP, DNA, ecosystem, endoplasmic reticulum, enzyme, Golgi apparatus, lysosome, organelle, metabolism, mitochondrion, nucleus, protein, respiration, ribosome, symbiotic.

For your type-in listings, see HCM PROGRAM LISTINGS CONTENTS.

HCM

Cell Mates

REMARKS

The Atari version of *Cell Mates* uses the Atari computer's ability to place machine-language routines in a string variable. Although many machine-language routines are written for a particular section of memory (because they access particular addresses within the routine), routines that use the string variable method *must* be relocatable.

The routine that moves the mitochondrion vertically is located in the string **ML2$** in line 330. This line initializes the length of the string to 30 characters, then places 30 characters in the string. The ASCII values of these characters actually make up the code for the machine-language routine. The Design Focus demonstrates how these ASCII characters correspond to the machine-language instructions.

To branch to such a routine, we need to know the memory address of the string. Atari BASIC offers a convenient way to retrieve the address of the string—the **ADR** function. In line 1120, **ADR (ML2$)** returns the address of the string **ML2$**. In this way, the **USR** function transfers program control to the machine-language routine:

H = USR(ADR(ML2$),256 + SGN(MY-DY))

The variable **H** is a dummy variable required for BASIC syntax—any variable name could be used in place of **H**. The first parameter in the **USR** function is the address of the string **ML2$** returned from the **ADR** function. The second parameter is a numeric expression passed to the machine-language routine for it to determine the direction that the mitochondrion moves. The low byte of this value is either a 1 or a 255. The machine-language routine interprets these values as positive or negative, respectively. A negative value moves the mitochondrion down; a non-negative value moves it up.

The **USR** function passes this value to the machine language routine by placing it on the stack along with the number of parameters being passed and the return address of the BASIC program.

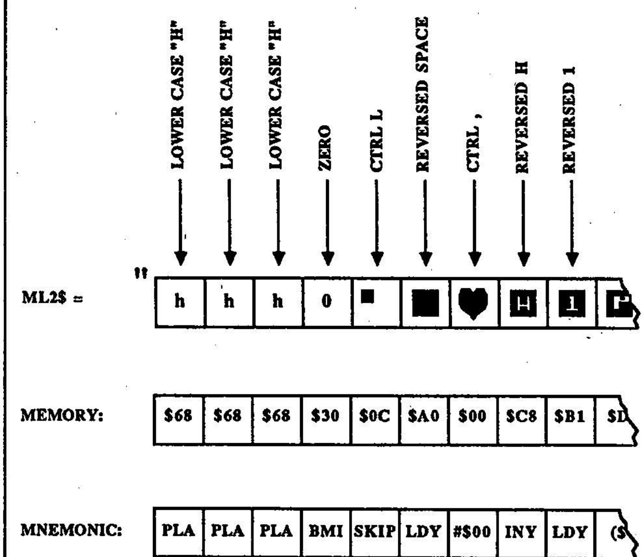
HCM Glossary terms: parameter, stack.

LISTING ANNOTATIONS

Line Nos.	
100-200	Program header.
210-250	Title screen
260-400	Program initialization
410-470	Main control loop
480-530	End of program—branch to appropriate message routine
540-770	Vital statistics calculations
780-840	Check for an end-of-program condition
850-1050	End-of-game messages, option to play again
1060-1090	Meters update
1100-1130	Mitochondrion movement
1140-1210	ATP administration
1220-1370	Character graphics data
1380-1430	Cell data
1440-1460	Data for initial values of C( ) array
1470-1760	Playing screen graphics
1770-1780	C( ) array initialization
1790-1840	Limit values to minimum and maximum
1850-1920	Death-of-cell special effects routines

DESIGN FOCUS

Atari
Machine Language Strings



DIRECTORY OF VARIABLES

Variables	Functions
C( )	Values for indicators
A$	Utility string for inputs etc.
ML$	Routine to move the character set
ML2$	Routine to move the mitochondrion
A	Utility variable
AGE	Age of the cell
ATP	Amount of ATP administered
CH	Rebuilds the character set
D	Flag indicating when game is over
DST	Destination of mitochondrion
DX	X coordinate of mitochondrion destination
DY	Y coordinate of mitochondrion destination
H	Starts the ML2$ Routine
I	Utility loop counter
J, K	Indicates element in C( ) array for limit checking
MF	Mitochondrion movement flag
MX	Mitochondrion X axis movement
MY	Mitochondrion Y axis movement
P	Key pressed
PM	Utility variable
RN	Random multiplier affecting nutrient supply
RT	Random multiplier affecting the internal temperature
TA	Effect that the internal temperature deviation has on other cell parts
X	Used in waste calculation
Y	Used to read data
Z	Utility — loop counter

PROGRAMMER'S WINDOW