The Game of "Metabolism"

By RICHARD E. GOODMAN

Intermediary metabolism is important in biology but often is a tedious and difficult subject for the student. We instructors are reluctant to come right out and tell our students to memorize the glycolytic pathway or the citric acid cycle, yet we want our students to "understand" these pathways. We want them to know in which reactions ATP is generated and in which it is used. We would like the students to learn where compounds are oxidized and reduced and which reactions require oxygen.

I have created a board game designed for students of biology and biochemistry as a means of learning aspects of intermediary metabolism enjoyably. Each player is a living cell faced with the problem of acquiring chemical potential energy (ATP) from carbon compounds. His playing tokens are the carbon atoms; these are moved on the board as he carries out various enzymatic reactions.

Object, Equipment, Preparation

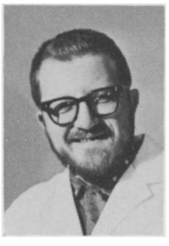
The object of the game is to accumulate 50 molecules of adenosine triphosphate (ATP). The first player to do so wins the game. (If time is limiting, the object can be changed to accumulation of the most ATP in a given time.)

The equipment is as follows:

1. A *playing board* showing several interconnected biochemical pathways (fig. 1: next page).

List 1. Enzyme cards for "Metabolism." Three of each are needed.

Glycolysis (color-coded green)	*Krebs cycle (color-coded yellow)*	*Wild*
Invertase	Citrate condensing enzyme	Wild enzyme card
Hexokinase	Aconitase	
Phosphoglucose isomerase	Isocitrate dehydrogenase	
Phosphofructokinase	α-ketoglutarate dehydrogenase	
Aldolase	Succinate thiokinase	
Glycerokinase	Succinate dehydrogenase	
Glycerophosphate dehydrogenase	Fumarase	
Triose phosphate isomerase	Malate dehydrogenase	
Glyceraldehyde-3-phosphate dehydrogenase		
Phosphoglycerate kinase		
Phosphoglyceromutase		
Enolase		
Pyruvate kinase		
Pyruvate carboxylase		
Pyruvate dehydrogenase		



Richard E. Goodman is associate professor of biology, California State College, 5500 State College Parkway, San Bernardino 92407; he has taught there since 1967. His A.B., in bacteriology, and Ph.D., in microbiology, were awarded by the University of California at Los Angeles, where he held U.S. Public Health Service predoctoral fellowships. He has pursued postdoctoral studies at the University of Washington. Goodman has published technical papers in journals of microbiology; his article "Molecular Models in Biology" appeared in *ABT* in 1970 (32 [1]: 34-38).

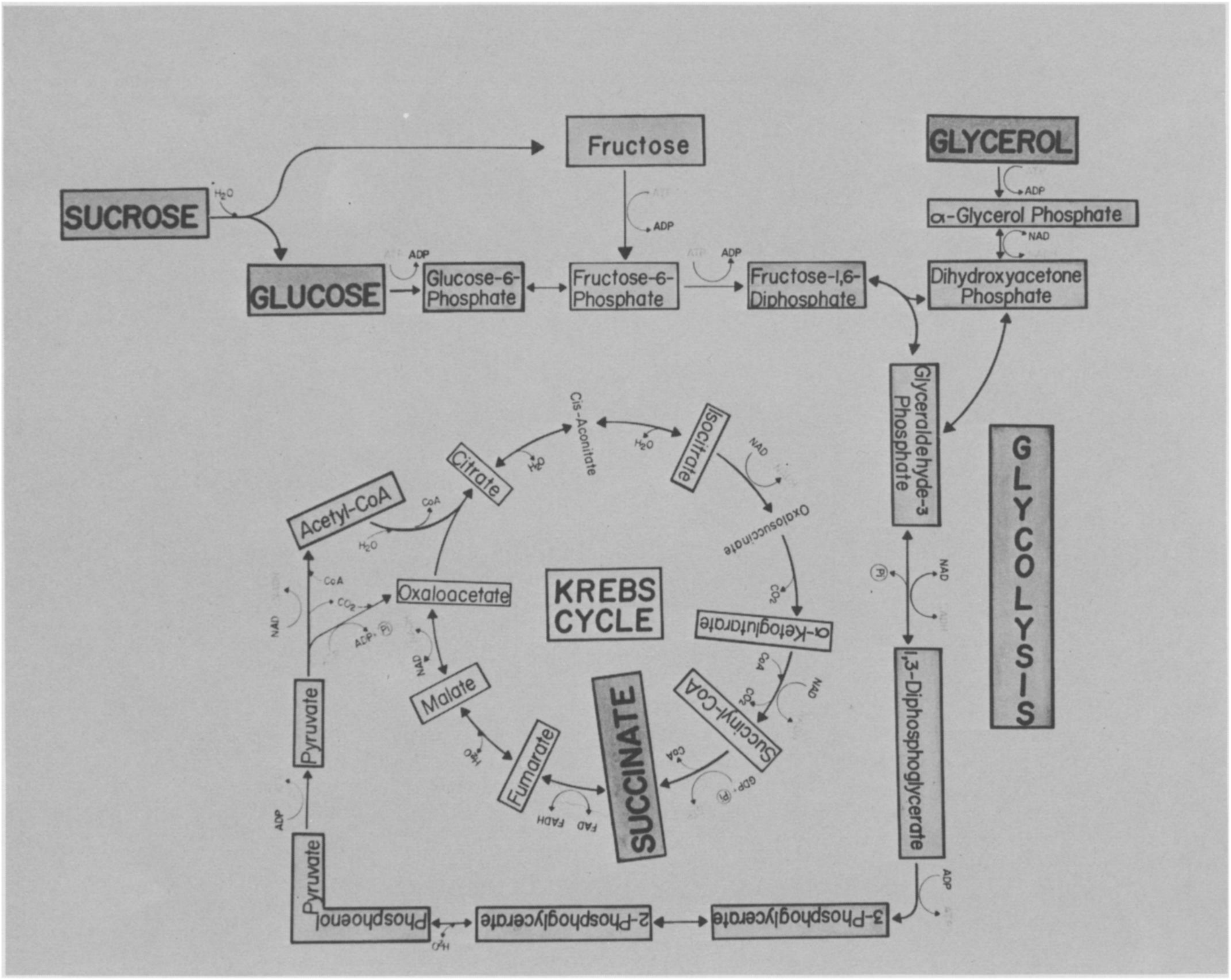


Fig. 1. "Metabolism" playing board. Symbols not well reproduced here (color in original) are ATP, NADH, and GTP, in the expectable places.

2. One deck of *enzyme cards,* each with the name of an enzyme and the chemical reaction it catalyzes. There are three of each kind of enzyme card (list 1; fig. 2.)

The two major pathways are color-coded on the playing board and on the cards, as follows: glycolytic pathway, green; Krebs cycle, yellow.

3. Ten *oxygen cards* (fig. 2.)

4. Four sets of disc-shaped playing tokens representing *carbon atoms,* with 18 atoms per set and each set of a different color.

5. *ATP tokens* of three sizes representing one, three, and 10 ATP molecules.

6. *NADH tokens* (color-coded).

7. *FADH tokens* (color-coded).

"Metabolism" is designed for two to four players. Each player starts with 18 carbon atoms of one color and two ATP molecules. The oxygen cards are pooled with the enzyme cards and the deck is thoroughly shuffled. Each player is then dealt nine cards. The remaining cards are placed face-down and serve as a draw pile.

The first player is chosen by any convenient means and the play proceeds clockwise.

Rules of Play

There are three kinds of play: (i) *carbon entry* (ii) *enzymatic reaction,* and (iii) *oxidative phosphorylation.* All plays start with a draw from either the draw pile or the discard pile and end with a discard, face up, onto the discard pile. A player may carry out a play with a card he has picked from the draw pile or with a card he has had in his hand since his last turn; but he may not carry out a play with a card picked from the discard pile, nor with an identical one from his hand. A card drawn from the discard pile may be played on any subsequent turn but not during the turn in which it is drawn. A player may draw any *enzyme* card from the top of the discard pile but may *not* draw an oxygen card.

If a player is unable to make any play, he simply discards a card that he believes is of no immediate value. A player's hand always contains nine cards at the end of his turn.

Carbon Entry

For his turn, a player may enter carbon atoms on any one (and only one per turn) of the four carbon sources: sucrose, glucose, succinate, or glycerol. He does so by placing the correct number of carbon atoms on the board in the correct space. The carbon sources are color-coded brown on the playing board. The number of carbon atoms varies for each of the compounds as follows: sucrose, 12; glucose, 6; succinate, 4; glycerol, 3.

A carbon-entry play begins with a draw from the draw pile as usual, but no card is used in the play. Therefore, the player must discard a card he believes to be without immediate value. Neither an *enzymatic reaction* or *oxidative phosphorylation* may be carried out during a carbon-entry turn.

A carbon-entry play may be made during any turn, provided the player has at his disposal a sufficient number of carbon atoms. A player may have up to 18 carbon atoms on the board.

A player may wish to refrain from entering carbon atoms at first until he has in his hand some of the initial enzymes in a given pathway.

Enzyme Reaction

When a player has in his hand an enzyme card that will catalyze a reaction for which he has a substrate as represented by his carbon atoms on the board, he may place the card face up in the discard pile and move his carbon atoms to the space (or spaces) on the board representing the product (or products) of that reaction. If ATP is required in that reaction, he must discard one molecule of ATP. If

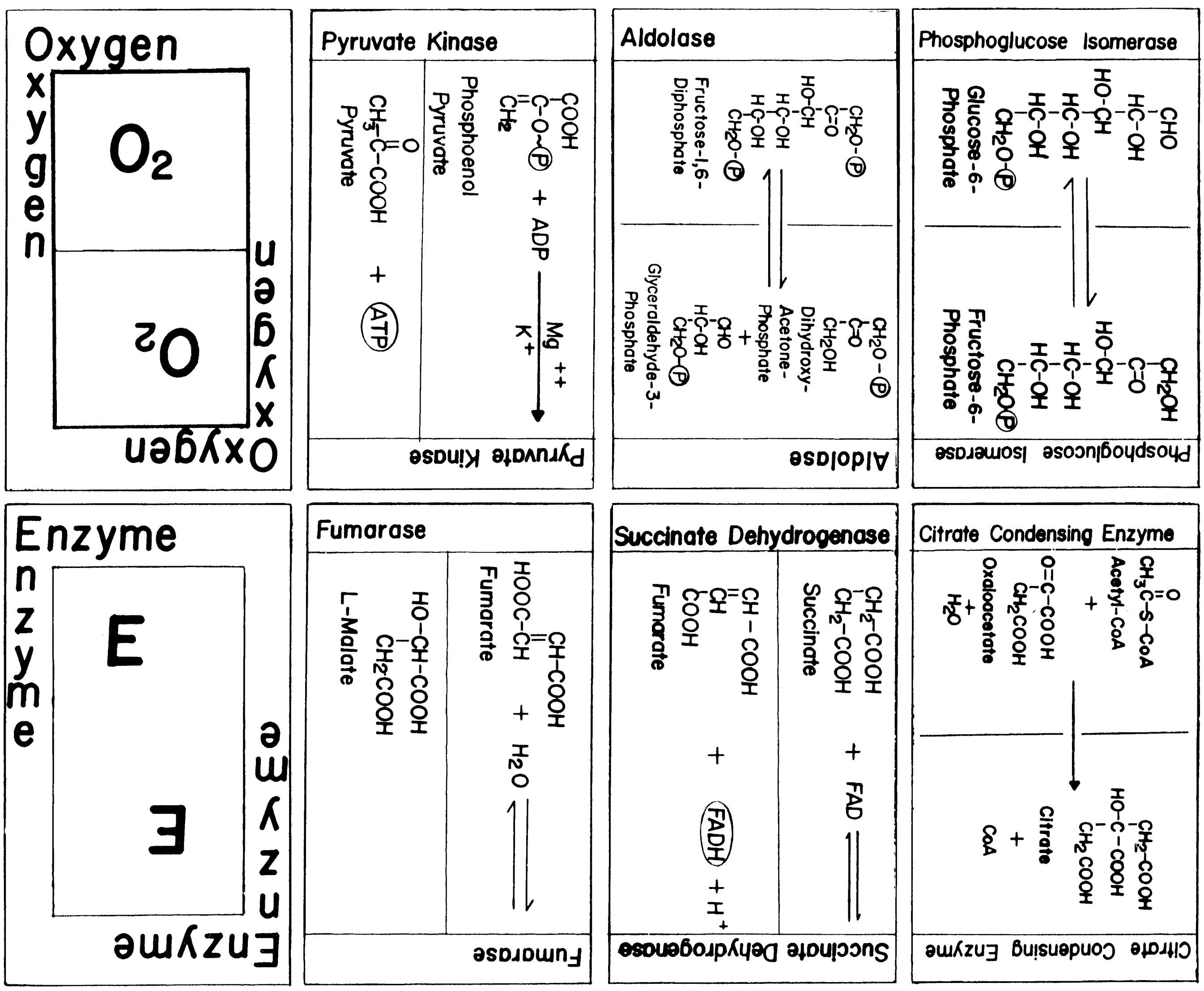


Fig. 2. Examples of cards for "Metabolism."

List 2. Abbreviations used in "Metabolism."

ADP	Adenosine diphosphate
ATP	Adenosine triphosphate
CoA	Coenzyme A
FAD	Flavin adenine dinucleotine (oxidized)
FADH	Flavin adenine dinucleotide (reduced)
GDP	Guanosine diphosphate
GTP	Guanosine triphosphate
NAD	Nicotinamide adenine dinucleotide (oxidized)
NADH	Nicotinamide adenine dinucleotide (reduced)
Pi	Inorganic phosphate
TPP	Thiamine pyrophosphate

ATP is generated in the reaction, he receives one. Likewise, if either NADH or FADH is required or produced, he discards or receives the proper token.

Examples

1. A player has 12 carbon atoms on the space labeled "sucrose" and has an invertase card in his hand. He places the invertase card face up on the discard pile and moves six carbon atoms to "glucose" and six to "fructose."
2. A player has three carbon atoms on the space labeled "1,3-diphosphoglycerate" and has a phosphoglycerate kinase card in his hand. He places the enzyme card face up on the discard pile and moves three carbon atoms to "3-phosphoglycerate." He receives one ATP molecule, because ATP is generated in this reaction.

If the player is able to make more than one play, he should try to choose the best; only one play is allowed per turn. If the player cannot (or chooses not to) make any play, he discards a card; he always ends his turn with nine cards in his hand.

There are three *wild* enzyme cards in the deck. These may be used to catalyze *any* reaction but may not be used as oxygen cards.

Fig. 3. Students playing "Metabolism" in a lower-division cell-biology course.

Some of the reactions are reversible; others are not. The former are indicated on the board by two-headed arrows. Any enzyme for a reversible reaction may catalyze that reaction in either direction.

Oxidative Phosphorylation

Molecules of NADH and FADH are said to have "reducing power" because, with the right enzymes, they can be used to reduce oxidized carbon compounds, or by oxidative phosphorylation they may be used to generate ATP. NADH gives rise to three molecules of ATP; FADH gives rise to two. A player may, at his option, use his turn to exchange one molecule of either FADH or NADH along with one oxygen card for two or three molecules of ATP, respectively. This constitutes *oxidative phosphorylation*. The oxygen card is placed on the discard pile as usual.

Any player with two molecules of unexpended reducing power is in a state of anaerobiasis, or "oxygen debt." He may not carry out an enzymatic reaction during his turn unless that reaction allows him to dispose of a molecule of reducing power. Nor may he draw from the discard pile or make carbon entry.

Additional Rules and Notes

1. For reasons of strategy, it is to a player's advantage to keep his hand concealed. However, when first learning the game the players may find it expedient to observe each other's cards.
2. The GTP generated by the succinate thiokinase reaction in the Krebs cycle is energetically equivalent to ATP. A player carrying out this reaction therefore receives one ATP token.
3. Whenever carbon dioxide (CO_2) is a product of a reaction the player discards one carbon atom from the substrate, and whenever CO_2 is a substrate he adds one carbon atom (of his color). Carbon atoms removed from play as CO_2 are returned to the player's pool of atoms and may be used for further carbon entry.
4. Any reaction represented by an enzyme card placed on the discard pile *must* be carried out if the player has his carbon atoms in the proper spaces on the board (even if such a reaction is contrary to the wishes of the player). The only exception to this rule is the situation in which a player has two molecules of reducing power and the reaction in question does not allow him to dispose of one of them. In any case, a player not wishing to carry out a reaction must choose his discard wisely.
5. The enzyme hexokinase catalyzes two reactions; namely, the phosphorylation of glucose to give glucose-6-phosphate and the phosphorylation of fructose to give fructose-6-phosphate.
6. When the draw pile is exhausted, the discard pile is thoroughly shuffled and becomes the draw pile.

(Concluded on p. 83)

the chemical change is minimal and not limiting upon the fauna.

Undoubtedly, dissolved oxygen plays a role in limiting sensitive benthic macroinvertebrates in certain polluted streams; however, no relationship was demonstrated in this study, because all sampling was done during daylight hours, when photosynthesis exceeded the respiratory demand.

It is hoped that the relationship established between the biotic index, the diversity index, and specific conductance in Chester County streams will stimulate further efforts in this direction. The physiologic tolerances of species to their environment, in comparison with the tolerances of higher taxa, are a vast unknown.

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"SCIENCE FOR SOCIETY" READINGS

The Commission on Science Education of the American Association for the Advancement of Science (AAAS) has published a 96-page survey of environmental literature, *Science for Society: a Bibliography.* It contains about 4,000 references, many of them annotated, to books and articles dealing with environmental subjects. The publication is designed primarily for use in physical-science and social-studies courses in high schools and colleges but would, of course, have interdisciplinary uses. Copies are available at $1 a copy, or 75¢ a copy for 10 or more, from Education Dept., AAAS, 1515 Massachusetts Ave., N.W., Washington, D.C. 20005.

Metabolism Game . . . . . . from p. 78

7. Beginners commonly misunderstand the reaction catalyzed by the citrate-condensing enzyme. In order to carry out this reaction, the player must have *two* carbon atoms on "acetyl-CoA" and *four* on "citrate." On condensation, these become the *six* carbon atoms of citrate.

Uses in Teaching

The rules may seem complicated on first reading, but I have found that students learn them rapidly. I recommend supervision by the instructor while the students are learning "Metabolism."

I have used the game in two courses: a lower-division course in cell biology and an upper division course in molecular biology (fig. 3). In both, the game was enthusiastically received by the students. (I am indebted to my students for their many constructive suggestions.) I believe the game is a suitable learning device from high school through advanced-biochemistry courses. The instructor can emphasize the aspects he considers important; for example, in a high school class the names of the enzymes and the structures of substrates and products probably would not be emphasized, but in advanced courses they would be. I have found that if the game is placed in a conspicuous place in the laboratory or classroom, students will come in and play even when class is not in session.

Obviously "Metabolism" could be expanded to cover additional pathways, including biosynthetic ones. I would appreciate learning of successful modifications of the game.

Acknowledgments.—Fig. 1 and 2 photos are by Wayne Wilbanks; fig. 3 photo is by Edna Steinman.

STOPPING THE STREAM-BRUISERS

Utah's newly passed law requiring a permit before heavy equipment is allowed to muck about in state streams has been termed a landmark in fish and wildlife legislation by conservationists and legislators alike. Before any applicant can obtain a permit he must convince the state engineer in Utah's Department of Natural Resources that the project "will not unreasonably affect the natural stream environment, or recreational uses thereof."

It's hoped that the law, which one former legislator termed the most "notable achievement in environmental legislation in the past century in Utah," may spark new respect among those who have nonchalantly torn up state streams in the past.

The Utah Fish & Game Division and the Utah Wildlife Federation are credited with the successful launching of an aggressive educational drive, which spelled out why the bill was needed and what it was all about.

Conservation News