

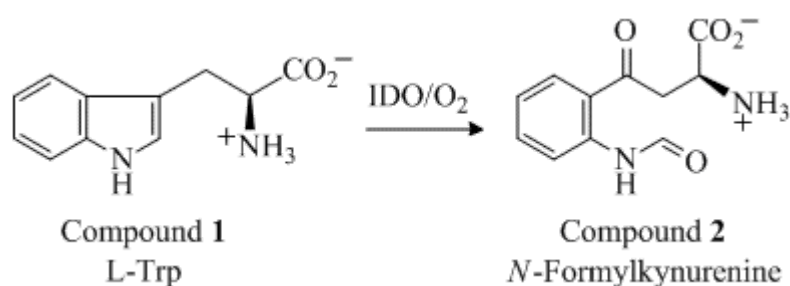
Chemical and Physical Foundations of Biological Systems

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New section

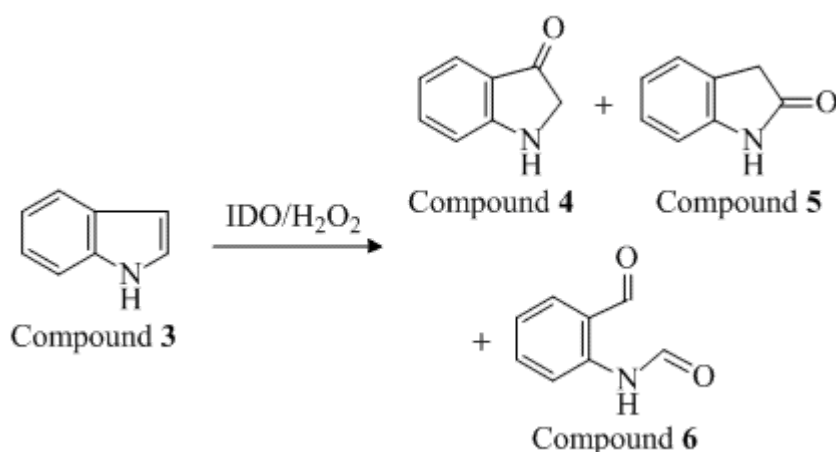
Passage

The heme enzyme indoleamine 2,3 dioxygenase (IDO) catalyzes Reaction 1, the first and rate-determining step of L-tryptophan (Compound 1) metabolism, and is an important enzyme of the human immune system.



Reaction 1

The IDO-catalyzed oxidation of Compound 1 by H_2O_2 does not occur. However, researchers have recently discovered that IDO-catalyzed oxidation of indole (Compound 3) by H_2O_2 (Reaction 2) does occur.



Reaction 2

Under the conditions employed, the number of catalytic turnovers appeared to stop at roughly 100, on average. A plot of the concentration of Compound 3 that was oxidized versus the concentration of H_2O_2 employed, at two different initial concentrations of IDO, gave the results shown in Figure 1.

Aerobic oxidation of Compound **3** in the presence of ^{18}O -labeled $\text{H}_2^{18}\text{O}_2$ resulted in the formation of ^{18}O -labeled oxidation products (Table 1).

The formation of Compound **6** does not appear to be the result of a sequential oxidation process. Isotopically labeled Compound **4** does not exchange ^{18}O for ^{16}O in water over 3 hours, but Compound **6** completely loses its ^{18}O label in unlabeled water over the same time period.

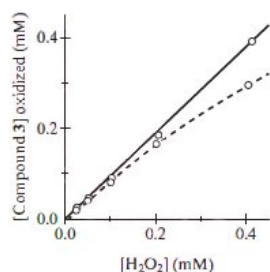


Figure 1 Stoichiometry of IDO-catalyzed oxidation of Compound **3** by H_2O_2 at $1\ \mu\text{M}$ (dashed line) and $10\ \mu\text{M}$ (solid line) IDO

Table 1 Isotopic Composition of Compound **3** Oxidation Products Using $\text{H}_2^{18}\text{O}_2$

Product	Percentage of ^{18}O incorporated (%)	
	Mono- ^{18}O	Di- ^{18}O
Compound 4	100	—
Compound 5	100	—
Compound 6	60	40

Adapted from: Kuo HH, Mauk AG. Indole peroxygenase activity of indoleamine 2,3-dioxygenase. *Proceedings of the National Academy of Sciences of the United States of America*. 2012;109(35):13966–71.

Questions

1. The progress of Reaction 2 can be monitored by observing what change to the IR spectrum of the product mixture?

- A) Appearance of a broad peak at $3400\ \text{cm}^{-1}$
- B) Disappearance of a broad peak at $3400\ \text{cm}^{-1}$
- C) Appearance of a sharp peak at $1700\text{--}1750\ \text{cm}^{-1}$
- D) Disappearance of a sharp peak at $1700\text{--}1750\ \text{cm}^{-1}$

Answer

Correct Answer is C) Appearance of a sharp peak at $1700\text{--}1750\ \text{cm}^{-1}$

Rationale: This question requires the test taker to combine knowledge about infrared spectroscopy with reasoning about the structural differences between the products and reactants of Reaction 2. The test taker must work with the scientific model of the differences in IR absorbance of various functional groups and apply this model to the experiment described in the passage. Recognition of the presence of additional carbonyl groups in the products of the reaction should lead the test taker to conclude that appearance of a peak between $1700\text{--}1750\ \text{cm}^{-1}$ in the IR spectrum would provide the most effective way to monitor product formation.

2. The following kinetic parameters were obtained for the IDO-catalyzed oxidation of Compound 3 by H₂O₂ in the presence of L-Trp.

Based on this data, what effect does L-Trp have on the reaction?

- A) L-Trp oxidizes Compound 3 directly.
- B) L-Trp is oxidized instead of Compound 3.
- C) L-Trp does not interact with the enzyme.
- D) L-Trp inhibits the enzyme.

[L-Trp], μM	k_{cat} , s^{-1}
0	1.3
2	0.34
5	~0

Answer

Correct Answer is D) L-Trp inhibits the enzyme.

Rationale: This question requires the test taker to combine knowledge of enzyme kinetics with interpretation of data. The test taker must understand what the decreasing values of k_{cat} in the presence of higher concentrations of L-Trp mean with respect to the kinetics of IDO-catalyzed indole oxidation. The k_{cat} is representative of the rate of product turnover, which means that the enzyme produces less product in the presence of L-Trp. Combining this trend in the data with a knowledge of enzyme kinetics, it can be concluded that L-Trp is inhibiting the reaction.

3. Which experiment can be used to show that Compound 6 is not formed sequentially from either Compound 4 or Compound 5?

- A) Conduct the reaction of Compound 4 with Compound 5, and identify the products.
- B) Oxidize Compound 4 and Compound 5 with IDO/H₂O₂, and identify the products.
- C) Reduce pure Compound 6 without added catalyst, and identify the products.
- D) Conduct the reaction of Compound 2 with H₂O₂ without added catalyst, and identify the products.

Answer

Correct Answer is B) Oxidize Compound 4 and Compound 5 with IDO/H₂O₂, and identify the products.

Rationale: This question requires the test taker to apply knowledge about how enzymes catalyze reactions to the design of an experiment. The question asks how researchers can be sure that Compound 6 is not formed from either Compound 4 or Compound 5 in a sequential enzyme mechanism. Enzymes are not used up during catalysis, so any experiment that includes just Compound 4 or just Compound 5 would determine if either is also a substrate for IDO-catalyzed conversion to Compound 6. Having both

compounds in solution with IDO adds unnecessary complexity to the interpretation of the experimental results. Examining the products of IDO-catalyzed reduction of Compound **6** would not give the necessary direct evidence, as Compound **6** could be sequentially reduced to Compound **3**.

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Critical Analysis and Reasoning Skills

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Passage

The Wealth of Nations (1776) popularized “the invisible hand,” the idea that an individual who intends only personal gain is, as it were, led by an invisible hand to promote the public interest. Adam Smith did not assert that this principle was invariably true, but it contributed to a tendency of thought that has since remained dominant, preventing action based on rational analysis: the assumption that decisions reached individually will collectively be the best decisions for society as a whole. If this assumption is correct, it justifies the continuance of the U.S. policy of laissez-faire in many issues affecting business, the environment, and the family. If it is not correct, U.S. citizens need to re-examine their individual freedoms to see which are defensible.

The rebuttal to the invisible hand theory could be called “the tragedy of the commons.” Picture a pasture open to all. It can be expected that each herder will try to keep as many cattle as possible on this commons. Such an arrangement may work reasonably well for centuries because tribal wars, poaching, and disease keep the numbers of both human and beast far below the carrying capacity of the land. Finally, however, comes the day of reckoning—that is, the day on which the long-desired goal of social stability becomes a reality. At this point, the inherent logic of the commons remorselessly generates tragedy.

As a rational being, each herder seeks to maximize personal gain. More or less consciously, the individual asks, “What is the utility to me of adding one more animal to my herd?” Since the herder would receive all the proceeds from the sale of the additional animal, the positive component of this utility is nearly +1. The negative component is a function of the overgrazing caused by an additional animal. Since the effects of overgrazing are shared by all the herders, the negative utility for any particular decision-maker is some fraction of -1.

Adding the component utilities, the rational herder concludes that the only sensible course is to add another animal to his or her herd—and another, and another. . . . This conclusion is reached by every rational herder who shares the commons. All are locked into a system that compels each to increase his or her gain without limit in a world that is limited. Ruin is the destination toward which all rush, each pursuing the right to use a public resource. The problem is that a commons, if justifiable at all, is justifiable only under conditions of low population density. As the human population has increased, the commons concept has had to be abandoned in one aspect after another.

The social arrangements that would produce responsibility in this scenario create coercion. The only kind of coercion I recommend is mutual coercion, agreed to by a majority of those affected. Compulsory taxes are acceptable because a system of voluntary contributions would favor the conscienceless. A society institutes and (grumblingly) supports taxes and other coercive devices to escape the horror of the commons.

Every new enclosure of the commons involves the infringement of somebody's personal freedom. But what does "freedom" mean? Those subject to the logic of the commons are free only to bring on universal ruin. Once they acknowledge the logic of mutual coercion, they become free to pursue other goals. We must now recognize the necessity of abandoning the commons assumption in our reproduction. Failure to do so will bring ruin on us all.

Material used in this test passage has been adapted from the following source:

G. Hardin, The tragedy of the commons. ©1968 by American Association for the Advancement of Science.

Questions

1. According to the passage, the decisive factor in determining whether someone's actions should be subject to coercion is whether the actions:

- A) are determined solely by self-interest.
- B) affect collectively held resources.
- C) degrade the natural environment.
- D) are commonly considered immoral.

Answer

Correct Answer is B) affect collectively held resources.

Rationale: The passage argument is not that all actions determined by self-interest should be regulated—only those actions in which the gain of one represents a loss to all and voluntary restraint is unlikely. Thus, option A is incorrect. Implicitly, coercion is needed to "produce responsibility" in circumstances to which the parable of the commons applies—i.e., resources are held collectively, so that self-interest "compels each to increase his or her gain without limit in a world that is limited." Thus, option B is correct. The author implicitly favors coercion rather than "the U.S. policy of laissez-faire in many issues affecting business, the environment, and the family." Therefore, degradation of the natural environment, although among the issues affecting "the public interest," would not be a relevant criterion for every

decision about the need for coercion. Thus, option C is incorrect. The passage questions the “assumption that decisions reached individually will collectively be the best decisions for society as a whole.” This is a question of economic philosophy, not of personal morality. Thus, option D is incorrect.

2. The passage argument suggests that national parks might benefit from:

- I. the restriction of recreational use by means of fees.
- II. the selling of the facilities to private investors.
- III. the opening of additional facilities to the public.

- A) I only
- B) III only
- C) I and II only
- D) II and III only

Answer

Correct Answer is A) I only

Rationale: Since everyone has “the right to use a public resource,” pressure on the terrain and ecosystems of national parks increases as population increases. Therefore, these lands would benefit by the imposition of fees that reduced their use by the public (option I). Thus, option A is correct. The opening of additional parklands to the public (option III) might delay “the day of reckoning,” but only by exposing even more resources to the tragedy of the commons. According to the passage, the solution to the problem of overuse is not to enlarge the commons but to abandon the commons concept. If resources to which the commons analogy currently applied became concessions for private investors (option II), charges in their use by the public might result. However, since the passage provides no analysis of the decision-making process involved in the wish of private owners “to maximize personal gain,” it does not justify a conclusion about the effect on parklands of privatization.

3. Some communities with expanding populations have for centuries successfully managed commonly held land. An appropriate clarification of the passage would be the stipulation that the author’s argument applies only to:

- A) the future.
- B) unregulated resources.

- C) conditions of social instability.
- D) resources that are not managed locally.

Answer

Correct Answer is B) unregulated resources.

Rationale: The past perfect tense of “the commons concept has had to be abandoned” indicates that the abandonment, even if continuing, occurred over an indefinite period in the past. Thus, option A is incorrect. Communities that managed commonly held land so that it was preserved despite an increasing population would necessarily have infringed on “somebody’s personal freedom,” probably through some form of coercion. To accommodate these cases, the author might appropriately qualify the statement that “as the human population increased, the commons concept has had to be abandoned in one aspect after another” with the stipulation that it applies only to unregulated resources. Thus, option B is correct. Although the premise of the question suggests social stability, it does not imply that such stability is necessary to the successful management of commonly held land or that only unstable communities are subject to “the inherent logic of the commons.” Thus, option C is incorrect. The passage author opposes assumptions about publicly held resources that are used to defend “the U.S. policy of laissez-faire.” That is, the problem addressed in the passage is a failure to manage these resources effectively, whether on a local or a national level. Thus, option D is incorrect.

Biological and Biochemical Foundations of Living Systems

students-residents.aamc.org/prepare-mcat-exam/biological-and-biochemical-foundations-living-systems

Passage

The myocellular transmembrane Na^+ gradient is important for proper cellular function. During septic shock, disruption of Na^+ homeostasis often occurs and leads to decreased membrane potential and increased intracellular Na^+ . It has been found that failure of cellular energy metabolism is a common symptom in septic patients who do not respond to therapeutics. Because normal intracellular levels of Na^+ are maintained by the Na^+K^+ ATPase, it is important to understand how metabolic energy production is linked to cation transport.

Researchers are interested in whether the energy used for ion transport is derived from glycolysis or oxidative phosphorylation. This information would provide a better understanding of myocellular damage that occurs during critical illness. Experiments were conducted to evaluate the effects of glycolytic inhibition on cellular Na^+ and K^+ concentrations and lactate production in rat skeletal myocytes.

Rat skeletal muscle fibers were extracted and incubated in normal media (control), glucose-free media (G(-)), and glucose-free media with various concentrations of the glycolytic inhibitor iodoacetate (IAA). IAA directly prevents the formation of 1,3-bisphosphoglycerate. After one hour in the media, the muscle tissues were assayed for intracellular Na^+ and K^+ content and lactate production. Cellular viability was determined by measuring the amount of lactate dehydrogenase (LDH) released, as LDH release is an indicator of cell death. The results are displayed in Figure 1.

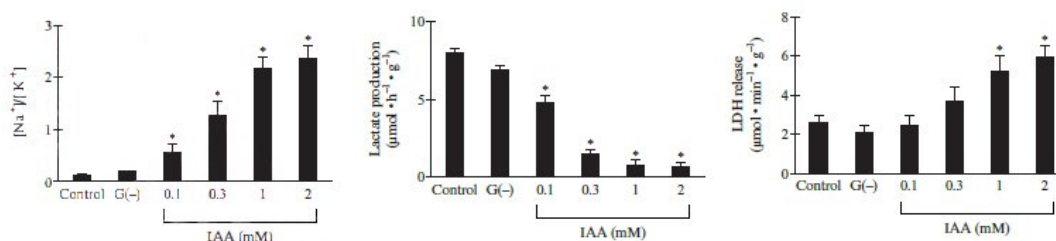


Figure 1 Effects of glycolytic inhibition on intracellular Na^+ and K^+ content and lactate production with cellular viability measured by LDH release. (Note: The * indicates $p < 0.05$ versus control.)

The researchers also examined the effect disruption of oxidative phosphorylation had on Na^+ and K^+ content. Inhibition of oxidative phosphorylation was caused by carbonyl-cyanide *m*-chlorophenylhydrazone (CCCP), an ionophore that allows protons to move

freely through membranes. No correlation between Na^+ and K^+ content and oxidative phosphorylation was found.

Adapted from: Okamoto K, Wang W, Rounds J, Chambers EA, Jacobs DO. ATP from glycolysis is required for normal sodium homeostasis in resting fast-twitch rodent skeletal muscle. *The American Journal of Physiology-Endocrinology and Metabolism*. 2001 Sept;281(3):E479-88.

Questions:

1. The researchers chose a concentration of 0.3 mM IAA as the working concentration for any additional studies instead of 1 mM or 2 mM. What is the likely reason for this?

- A) The lower concentration of IAA gave the largest Na^+ response.
- B) Higher concentrations induced significant cytotoxicity.
- C) The solubility of IAA was not high enough.
- D) The researchers were trying to mimic control conditions as closely as possible.

Answer

Correct Answer is B) Higher concentrations induced significant cytotoxicity.

Rationale: This question requires the test taker to apply knowledge about cytotoxicity and cell lysis to the design of an experiment described in the passage. In particular, the examinee should understand that conducting an experiment where the level of IAA was cytotoxic to the cells (when compared to control conditions) would not be desirable for understanding the role of glycolysis in establishing ion concentration gradients, as these cells would lose membrane integrity and undergo lysis. Therefore, the experimental design should not use an IAA concentration that results in significantly increased cell lysis.

2. The information in the passage suggests that glycolysis:

- A) is important for maintaining normal Na^+ and K^+ levels in skeletal muscle.
- B) facilitates membrane permeability in skeletal muscle.
- C) impedes the function of the Na^+ and K^+ ATPase in skeletal muscle.
- D) is regulated by the Na^+ and K^+ ATPase in skeletal muscle.

Answer

Correct Answer is A) is important for maintaining normal Na^+ and K^+ levels in skeletal muscle.

Rationale: This question requires the test taker to apply knowledge about glycolysis to the experimental data from Figure 1. In particular, the trend in the data that shows increasing concentration of IAA results in a higher ratio of the concentration of Na^+ to K^+ than observed in the control sample must be correlated with role of IAA in the disruption of glycolysis. This is further supported by the drop in lactate production shown in Figure 1 at higher concentrations of IAA, because IAA prevents the formation of NADH, which is used when pyruvate is reduced to lactate. The combination of the proposed role of IAA and the results from Figure 1 lead the test taker to the conclusion that glycolysis is important to the Na^+K^+ ATPase and, therefore, important to the maintenance of the concentration ratio of Na^+ to the K^+ .

3. If the effects of IAA treatment in nerve cells are the same as those observed in myocytes, which feature of an action potential would be most affected by IAA treatment?

- A) Initiation of depolarization
- B) Rising phase of depolarization
- C) Falling phase to undershoot
- D) Return to resting potential

Answer

Correct Answer is D) Return to resting potential

Rationale: This question requires the test taker to recall information about the role of the Na^+K^+ ATPase in the recovery of the nerve cell resting potential after an action potential. In addition, the test taker must reason about the effect of IAA treatment based on the information presented in the passage, and how the inhibition of glycolysis by IAA would affect the cellular concentration of ATP. Based on these two lines of reasoning, the test taker can propose a hypothesis about which portion of an action potential would be affected by IAA treatment.

Psychological, Social, and Biological Foundations of Behavior

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New section

New section

Passage

The illness experience shapes the way that people use health information. For patients with a rare health disorder, which is defined as a medical condition that affects fewer than 200,000 individuals living in the United States, online sources of information tend to be particularly important.

An example of a rare disorder is Amyotrophic Lateral Sclerosis (ALS), also known as “Lou Gehrig’s disease.” ALS results from the progressive loss of motor nerves and affects about 1 out of 100,000 people. About 10% of people with ALS have a familial form of the condition, which is caused by an inherited genetic mutation. Aside from the familial form, the cause of ALS is largely unknown, though it is believed that the disorder results from both genetic and environmental factors.

Having a rare medical condition, such as ALS, can make it difficult to meet and interact with others who have the same rare disorder. Despite great distances, online communication provides a form of social interaction for those facing an uncommon health problem. Virtual peer networks provide vital social support for those who are affected by a rare disorder.

Research has found that women with rare disorders are more likely to access online support networks than men with rare disorders. Relationships formed through online support networks often become a meaningful part of a person’s identity. Individuals with rare disorders report that relating to others who have the same condition is often easier than trying to relate to friends or family members who do not share their condition.

Questions:

1. Which statement best represents a threat to social identity? A young woman with a rare disorder:

A) believes that others treat her as less capable, and then she starts to see herself as deficient.

B) becomes discouraged when she hears that others with rare disorders are treated as less capable.

C) hides her disorder from others in order to project more confidence in social situations.

D) reveals her disorder to friends, who mistakenly assume that it is a social limitation.

Answer

Correct Answer is B) becomes discouraged when she hears that others with rare disorders are treated as less capable.

Rationale: This Psychology question assesses the “Knowledge of Scientific Concepts and Principles” skill with a concept that is part of the content category of “Self-identity.” Social identity addresses the feelings that individuals derive from, or that are associated with, their membership in a group. Self-esteem can be undermined by threats to social identity, which is represented in the correct answer, Option B. The incorrect options do not clearly identify the connection between an individual’s sense of self and their perceived membership in a group.

2. Over the course of ten years, a rare disorder increases in prevalence such that it eventually affects more than 200,000 people in the United States. Based on the passage and this scenario, which prediction is most consistent with the sociological paradigm of symbolic interactionism?

A) As the number of affected individuals increases, government research funding increases.

B) Affected individuals are less likely to conceal their condition as it becomes less stigmatized.

C) As more people with the condition are treated, it receives less attention as a health concern.

D) Insurance coverage for the condition becomes more likely as more people require treatment.

Answer

Correct Answer is B) Affected individuals are less likely to conceal their condition as it becomes less stigmatized.

Rationale: This is a Sociology question that evaluates the skill of “Scientific Reasoning and Problem Solving” with a theoretical paradigm that is listed under the content category of “Understanding Social Structure.” Symbolic interactionism focuses on how meaning is constructed through small-scale social interactions. As a concept that is relevant to social interactions and the illness experience, social stigma is also closely associated with symbolic interactionism. Thus, the correct answer is option B, which

rests in reasoning from the perspective of symbolic interactionism to make a prediction about social interaction and stigmatization. The incorrect options make predictions about large-scale social changes or about the disease itself, which are not consistent with the paradigm of social interactionism.

3. Which research project best represents a macrosociological approach to studying the social support networks mentioned in the passage?

- A) A researcher follows the conversation of participants who post messages in an online support forum.
- B) A researcher interviews patients who participate in a local hospital's support group for rare disorders.
- C) A researcher surveys patients for reasons that they joined an online support group for their disorder.
- D) A researcher tracks how the number of websites dedicated to rare disorders has changed over time.

Answer

Correct Answer is D) A researcher tracks how the number of websites dedicated to rare disorders has changed over time.

Rationale: This Sociology question tests on “Reasoning about the Design and Execution of Research” with material that is covered by “Understanding Social Structure.” Option D is the correct answer because tracking changes in websites would provide data on the availability (growth or decline) of information about rare disorders. This type of project is aligned with a macrosociological approach because it would allow a researcher to determine how the organization of health information in a society changes over time. The other options are incorrect because they are more similar to a microsociological approach, as each would result in data that is based on small-scale interactions or individual decisions.

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