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IBO 2013 Theoretical Exam 1



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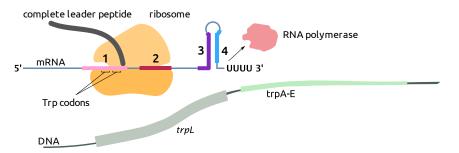
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Cell-, molecular- and microbiology

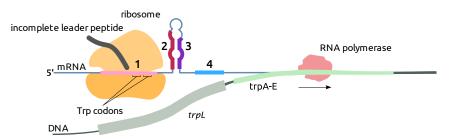
Some bacteria possess an additional mechanism to regulate the production of enzymes involved in tryptophan (Trp) biosynthesis. The (Trp) operon possesses, prior to the actual genes (trpA-E), a leader sequence (trpL), coding for a leader peptide. trpL contains two tryptophan codons next to each other.

Promoter Operator <i>trpL</i>	trpA-E

At high tryptophan concentrations, the ribosome translates the mRNA of the leader peptide and stalls at its stop codon, thereby masking segment 2 of the mRNA and allowing segments 3 and 4 to form a stem loop. A stem loop followed by poly-U is a termination signal for the RNA polymerase (RNA pol), which falls off the DNA.



However, at low tryptophan concentrations, the ribosome gets stalled at the tryptophan codons allowing 2 and 3 to form a stem loop. The whole tryptophan operon can be transcribed by the RNA polymerase.



Indicate if each of the following statements is true or false.

- A. The same regulation mechanism also works for nuclear genes in eukaryotes.
- B. With reduced concentration of the aminoacyl-tRNA synthetase (attaches tryptophan to tRNA^{Trp}), transcription of the *trpA-E* genes will be inactivated at a lower tryptophan concentration.
- C. After deletion of one of the two tryptophan codons in the gene coding for the leader peptide, transcription of the *trpA-E* genes will be inactivated at a lower tryptophan concentration.
- D. In case of a mutation destabilizing the stem loop 2-3, transcription of the *trpA-E* genes will be inactivated at a lower tryptophan concentration.
- A. False B. False C. True D. True

Original commentary

Correct answers

A false

the mechanism works only if the translation begins before the transcription finishes. In eukaryotes, the transcription happens in the nucleus, then the mRNA is exported to the cytoplasm where it is translated and this mechanism cannot work in this form.

B false

by reduced concentrations of the tryptophan's aminoacyl-tRNA synthetase, tRNA loaded with tryptophan will be formed slower than in the normal case, so that less tRNA-Trp will be present. To inactivate the transcription of the trpA-E genes, a higher tryptophan concentration than in the normal case is needed. C *true*

with only 1 Trp codon, a lower concentration of Trp can still allow translation of the leader peptide and therefore inhibit the synthesis of the enzymes.

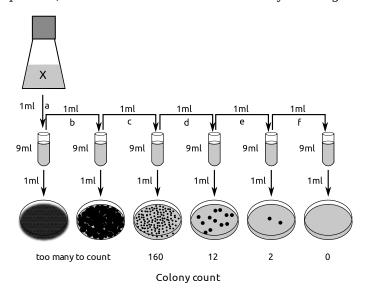
D true

a mutation destabilizing stem loop 1-2 will promote the formation of stem loop 2-3 even at low tryptophan concentrations, inhibiting the transcription of the trpA-E genes.

References Walsh et al, Biochemistry (1979)

Cell-, molecular- and microbiology

Bacterial count of a liquid culture can be determined by different methods: 1) Cells can be counted under a microscope using a counting chamber, 2) the absorbance of the culture can be measured in a spectrophotometer (with $A_{600} = 1$ corresponding to 8×10^8 bacterial cells/ml) or 3) several dilutions of the culture can be plated on agar and the colonies can be counted (see picture) to calculate the number of colony forming units per milliliter (cfu/ml).



Indicate if each of the following statements is true or false.

- A. A culture with $A_{600} = 0.1$ and a doubling time of 30 minutes will reach $4x10^8$ cells/ml in less than two hours of growth.
- B. Counting colonies on plates gives a smaller estimate of the number of bacterial cells than counting cells under a microscope.
- C. Using the plate giving the most accurate results (from the figure), the culture X is estimated to contain 1.6×10^5 cfu/ml.
- D. When repeating the plating of Dilution *f* (from the figure) many times, some plates will show colonies.
- A. True B. True C. True D. True

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Original commentary

Correct answers

A true

A culture with an OD_{600} = 0.1 and a doubling time of 30 minutes will have an OD_{600} = 0.2 after 30 minutes, 0.4 after 1

hour, and 0.8 after 1:30 hour, therefore it will will reach 4*10<sup>8</sup> cells/ml in less than 2 hours (4x10<sup>8</sup>) cells correspond to

an OD = 0.5).

B true

Counting colonies on plates gives the number of cfu/ml, and only living cells can form colonies, whereas under the

microscope, dead cells are also counted.

C true

The plate giving the most accurate results is the one with 160 colonies that corresponds to a 1:1000 dilution of the

starting culture X. 160*1000 = 1.6x10^5

D true

The dilution f contains 0.16 cells/ml. Statistically, by plating it more than six times, colonies should grow.
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Cell-, molecular- and microbiology

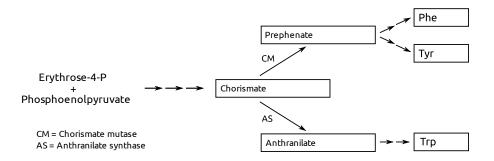
In a living organism, cells die either through apoptosis (programmed cell death) or necrosis (cells swell and burst).

Indicate if each of the following statements is true or false.

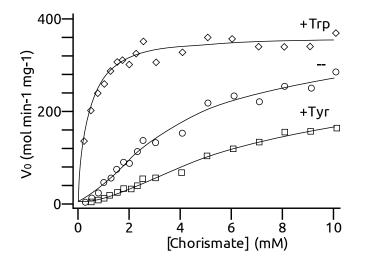
- A. Apoptosis is induced in immature T-cells that recognize self antigens.
- B. Intestinal epithelial cells losing contact with the basal lamina undergo apoptosis.
- C. Neural stem cells undergoing apoptosis expose on their surface a signal promoting phagocytosis.
- D. Necrosis often induces an inflammatory immune response.
- A. True B. True C. True D. True

Original commentary

The chorismate pathway leading to the synthesis of aromatic amino acids in yeast is presented here.



The velocity of the enzyme chorismate mutase (CM) was measured in the presence of either tryptophan (+Trp) or tyrosine (+Tyr), as well as in the absence of both (--).



Based on these results and the pathway scheme, indicate if each of the following statements is true or false.

- A. Tryptophan increases the activity of chorismate mutase.
- B. Tryptophan, but not tyrosine inhibits the synthesis of chorismate.
- C. A high concentration of tyrosine is likely to increase the synthesis of tryptophan.
- D. The prephenate and the anthranilate branches compete for chorismate.
- A. True B. False C. True D. True

Original commentary

Correct answers A true

B false

Under addition of tryptophane, at the same chorismate concentrations, the speed is higher

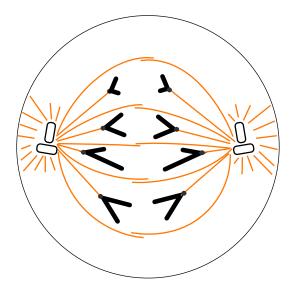
The synthesis of erythrose-4-P is neither inhibited by tryptophan, nor by tyrosine. It would not make sense that only tryptophan inhibits E4P, since E4P is needed for the synthesis of both tryptophan and tyrosine and their synthesis is regulated differently.

C true When the tyrosine concentration is increased, CM gets slower, and the chorismate will be used by AS instead to produce tryptophane.

D true Both pathway branches have chorismate as a starting point and the positive/negative regulation by Trp/Tyr hints that chorismate is not present in unlimited supply.

References Schnappauf et al, Biochemistry (1998)

The following schematic shows a stage of cell division for an eukaryotic diploid cell.



Indicate if each of the following statements is true or not.

- A. The schematic may represent a stage of mitosis.
- B. The schematic may represent a stage of meiosis II.
- C. The cell would have failed to reach this stage if microtubular motor proteins were inhibited.
- D. Transcription of histone genes peaks during this stage.
- A. False B. True C. True D. False

Original commentary

Correct answers A false

as the chromosomes are different from each other in the picture, they cannot arise from pairs of chromosomes, which would need to be the case for mitosis of a eukaryotic diploid cell. B *true*

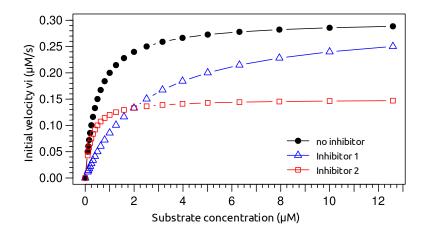
during meiosis II, the 2 chromatids are distributed between daughter cells.

C true

to reach an aphase, molecular motors working on microtubule are needed for the expansion of microtubuli ${\rm D}\ false$

in this stage, the DNA is highly condensed and not available to transcription. Furthermore, new histone proteins are particularly necessary during the S-phase where the DNA is duplicated and needs to be packaged, not in the anaphase.

The sensitivity of an enzyme for different inhibitors is assessed. The rate of product formation was measured at different concentrations of substrate with 10 nM enzyme. The initial velocity v_i (at t = 0 s) was calculated and plotted as a function of the substrate concentration in the absence or presence of two different inhibitors.



Indicate if each of the following statements is true or false.

A. In the absence of any inhibitor, the K_M (Michaelis constant) of the enzyme is 0.15 $\mu M.$

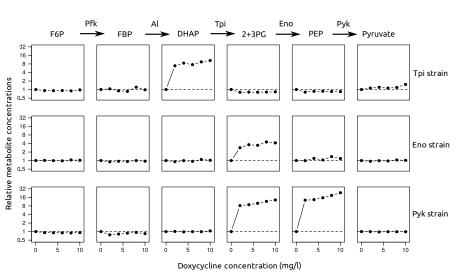
- B. The effect of Inhibitor 1 can be partially compensated for by adding more substrate.
- C. Inhibitor 2 reduces the v_{max} (maximal velocity) of the enzyme.
- D. The turnover number (maximum number of molecules processed per second by one enzyme molecule) under inhibition by Inhibitor 2 is about 10-20/s.
- A. False B. True C. True D. True

Original commentary Correct answers A false K_m is the [substrate] at which half the maximal velocity is reached, in this case v_{max} is 300 nM/s, $v_{max}/2 = 150$ nM/s, which corresponds to $0.5 \,\mu M$ B true With inhibitor 1, only the K_M is affected, not the v_{max} . The reaction to proceed at the same speed as without inhibitor if more substrate is added (corresponds to a competitive inhibitor). C true The v_{max} is reduced (150 nM/s instead of 300 nM/s without inhibitor): corresponds to an uncompetitive inhibitor. D true $k_{cat} = v_{max}$ / [Enzyme] = (150 nM/s) / (10 nM) = 15/s

Cell-, molecular- and microbiology

Three yeast strains (*Saccharomyces cerevisiae*) have been engineered to each contain a gene for a different enzyme from glycolysis (Tpi, Eno or Pyk) under the control of a doxycycline-repressed promoter such that addition of doxycycline down-regulates the synthesis of the corresponding enzyme. Concentrations of some metabolites are measured in each yeast strain grown on glucose at different doxycycline concentrations, relative to the concentrations without doxycycline. Relevant steps of the glycolysis are shown above the measurements with metabolites and enzymes abbreviated as follows:

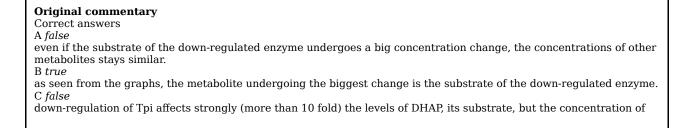
Metabolit	tes	Enzy	mes
F6P	fructose 6-phosphate	Ρſk	ATP-dependent phosphofructokinase
FBP	fructose 1,6-biphosphate	Al	Aldolase
DHAP	dihydroxyacetone phosphate	Трі	Triose phosphate isomerase
2+3-PG	2- and 3-phosphoglycerate	Eno	Enolase
PEP	phosphoenolpyruvate	Pyk	Pyruvate kinase



Indicate if each of the following statements is true or false.

- A. Down-regulating any of these enzymes disrupted metabolite concentrations in the whole pathway.
- B. Down-regulating any of these enzymes affected the concentration of its substrate more than the concentration of its product.
- C. The equilibrium of the reaction from 2+3-PG to PEP is more on the side of the product than the equilibrium of the reaction from FBP to DHAP.
- D. The concentration of F6P is expected to be unaffected by a down-regulation of Al.

A. False B. True C. False D. True



FBP stays constant, thus the equilibrium of FBP \rightarrow DHAP is strongly on the side of DHAP. In contrary, down-regulation of Pyk does not only affect the concentration of PEP, its direct substrate, but also of 2+3PG, the substrate of the previous enzyme in the pathway, Eno. This means that the increased level of PEP is enough to shift the equilibrium of 2+3PG \rightarrow PEP back to 2+3PG, therefore the equilibrium is not as strongly on the side of the glycolytic product than FBP \rightarrow DHAP.

D true

During the reaction of F6P to FBP, ATP is hydrolyzed to phosphorylate F6P. Therefore, the equilibrium is strongly on the side of FBP. Down-regulation of Al would result in an increase of the FBP concentration, but since the equilibrium is strongly on the side of FBP (even more strongly than for the reaction FBP \rightarrow DHAP), the concentration of F6P will stay unaffected.

References

Fendt et al, Molecular Systems Biology (2010)

Cell-, molecular- and microbiology

Some substances need to be transported (actively or passively) from their site of synthesis to the location where they are active.

Indicate for each of the following substances if they are transported from the cytoplasm to the nucleus.

A. tRNAs

- B. Histone proteins
- C. Nucleotides

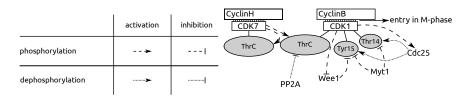
D. ATP-synthase subunits

A. False B. True C. True D. False

Original commentary Correct answers A false tRNAs are synthesized in the nucleus, but need to get to the cytoplasm to be used by the ribosome. B true Histones are proteins synthesized in the cytoplasm, but need to get to the nucleus to bind to the DNA. C true Nucleotides are obtained by endo/picocytosis or synthesized in the cytoplasm, but need to get to the nucleus to be used in DNA replication and transcription. D false The ATP-synthase is a membrane protein synthetised in the cytoplasm (on the ER membrane) and transported to the plasma membrane, but not to the nucleus

Cell-, molecular- and microbiology

Progression through the cell-cycle is mediated by Cyclin-Dependent Kinases (CDKs), which become active only when bound to their respective cyclin and phosphorylated at the ThrC (core threonine). Phosphorylation or dephosphorylation of other amino acids further modulates their activity. The following pathway represents the proteins involved in the entry into the M-phase of the cell-cycle.



Indicate for each of the following mutations if it would promote entry into the M-phase by activating the CyclinB/CDK1 complex.

A. A mutation that reduces the dephosphorylating activity of Cdc25.

B. A mutation that reduces the phosphorylating activity of Wee1.

C. A mutation that changes the ThrC of CDK1 to a valine that cannot be phosphorylated.

D. A mutation that inhibits the binding of CyclinH to CDK7.

A. False B. True C. False D. False

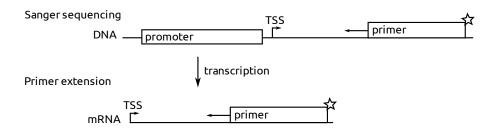
Original commentary

Correct answers A *false* Cdc25 by dephosphorylating CDK1 at Tyr15 and Thr14 activates CDK1 (removes the inactivation). By reducing its activity, CyclinB/CDK1 would be less active B *true* Wee1 inactivates CDK1 by phosphorylating it at Tyr15. C *false* to be active, CDK1 needs to have Thr161 phosphorylated, with a valine at position 161, CDK1 would be always inactive D *false* CDK7 needs to be bound to CyclinH and phosphorylated at Thr170 to be active and able to phosphorylate (and therefore activate) CDK1 in complex with CyclinB. This mutation in CyclinH would make it unable to bind CDK7 which would stay in an inactive state.

References Fussenegger et al, Biotechnol. Prog. (1998)

Cell-, molecular- and microbiology

To determine the precise transcription start site (TSS) of a newly discovered bacterial gene promoter, a radioactively labeled primer complementary to the 3'-end of the gene is used both for Sanger sequencing of the DNA construct and for primer extension of the mRNA. Primer extension (similar to cDNA synthesis) is repeated on mRNA transcribed with addition of the transcription factor α .



The fragments obtained are separated by gel electrophoresis, a radiography is presented below.

Sang	er sec	lneud	Prime	er extens	ion	
G	Α	Т	С	- a	+a	
		=				
					_	
-						
=						

Indicate if each of the following statements is true or false.

- A. Different polymerases are used for the Sanger sequencing and primer extension assays.
- B. mRNAs of this gene with CUCAUGAC as the first eight bases after the TSS are found in these cells.
- C. Multiple TSS exist for this gene.
- D. Transcription is modulated by transcription factor $\boldsymbol{\alpha}.$
- A. True B. True C. True D. False

Original commentary

Correct answers

A true For Songer s

For Sanger sequencing, a DNA polymerase is needed, whereas for primer extension, reverse transcriptase is used. B true

The PE lane on the radiography gives the length of the mRNA. The first (most 5') base of the main mRNA corresponds to the fragment from the sequencing with the same length (here: G). The second most 5' base of the mRNAc corresponds from the sequencing one nucleotide shorter (=one band lower on the radiography) than PE (here: A).

C true For this gene, a main and a secondary TSS exist. D false Transcription in the absence or presence of α produces the same ratio of mRNA starting from the main and the secondary TSS.

Animal anatomy and physiology

High levels of triglycerides in the bloodstream have been linked to higher risks of heart diseases. An agonist (activating molecule) S of receptor Y was observed to reduce the triglycerides levels.

How could one convincingly prove that the effect of S is mediated specifically via receptor Y?

A. Generate genetically modified mice which overexpress (more than physiological) receptor Y.

B. Generate genetically modified mice in which receptor Y is knocked out (deleted).

C. Treat the mice with an antagonist (inactivating molecule) specific for receptor Y.

D. Treat the mice with an antibody that sequesters (removing from circulation) S.

A. False B. True C. True D. False

Original commentary

Correct answers A false

Even if the decrease in triglycerides levels observed would be more important than with wild-type mice, this is not enough to prove that S-Y interaction is either sufficient or necessary for the decrease. B true

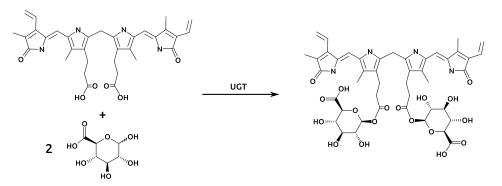
If in these mice, triglycerides levels decrease after addition of S, it is not mediated by Y. If no decrease can be observed, the interaction of S and Y is necessary for the decrease in triglycerides levels

C true

If Y is inactivated by an antagonist, treatment with S should not decrease triglycerides levels, it shows that S-Y interaction is necessary for the decrease in triglycerides levels. If a decrease would be observed, it would show that S mediates triglycerides levels decrease via an other mechanism. D *false*

Even if no decrease in triglycerides levels would be observed, this would only prove that S is necessary to decrease triglycerides, but would not prove that it acts via Y.

Bilirubin is a breakdown product of heme catabolism which is transported to the liver where it is conjugated to two glucuronic acid molecules by the enzyme UGT (see figure below). Conjugated bilirubin is then secreted in the small intestine as a component of the bile.



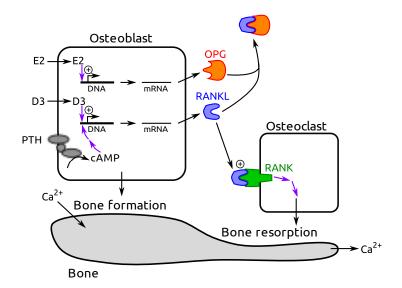
Indicate for each of the following statements if it is true or false.

- A. Conjugation to glucuronic acid increases the solubility of bilirubin in water.
- B. A tumor obstructing the bile duct near the junction into the small intestine leads to a decrease in the blood levels of conjugated bilirubin.
- C. A point mutation reducing significantly the activity of UGT leads to a decreased level of unconjugated bilirubin in the blood.
- D. An increased level of conjugated bilirubin in the blood is a symptom of a malaria infection.

A. True B. False C. False D. True

Animal anatomy and physiology

While osteoblasts are secreting new bone material, they can trigger osteoclasts to break down existing bone by excreting the protein RANKL, which activates its receptor RANK in osteoclasts. This pathway is stimulated by either vitamin D (D3) or parathyroid hormone (PTH). In the presence of oestrogen (E2), however, osteoblasts inhibit that process by secreting osteoprotegerin (OPG), which sequesters RANKL.



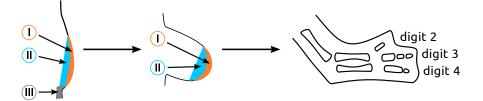
Indicate for each of the following statements if it is true or false.

- A. Oestrogen replacement therapy prevents bone resorption after menopause.
- B. A symptom of hyperparathyroidism (excessive function of parathyroid gland) is loss of bone mass.
- C. D3 and E2 are hydrophilic molecules whereas PTH is lipophilic.
- D. A consequence of Ca^{2+} loss through the urine is a decrease in PTH plasma levels.
- A. True B. True C. False D. False

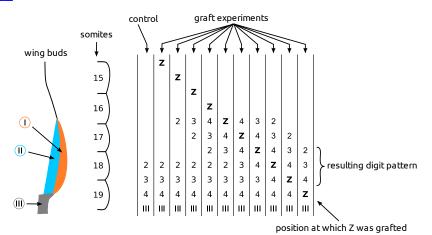
Original commentary

Correct answers A true After menopause the estrogen level declines. Estrogen replacement therapy increases OPG levels and prevents thereby RANKL to bind to RANK, which would activate osteoclasts. B true Loss of bones mass is a symptom of hyperparathyroidism, where increased production of PTH leads to increased levels of RANKL and increased osteoclast activity C false Estrogen and Vitamin D are lipophilic hormones as shown above they have to cross the cell membrane to operate whereas PTH needs to bind to a extracellular receptor as it is hydrophilic and cannot cross the membrane D false Renal loss of calcium leads to a decrease of plasma calcium level which causes a elevation of PTH. PTH indirectly activates osteoclasts which resorb bone, process during which calcium is released into the blood. This reestablishes the calcium plasma level. References Seeman et al, NEJM (2006)

<u>Seeman et al, NEJM (2006)</u> <u>Stavros et al, NEJM (1995)</u> Weinstein et al, NEJM (2009) Wing development in chickens starts with the formation of a wing bud which will develop into a full wing consisting of three digits.



To decipher development of digits, the zone III of the left wing was grafted as an additional zone III in the wing bud of the right wing during early development. The resulting digit morphology relative to the somite position is presented below for different positions of grafting (indicated by Z).



Indicate if each of the following statements is true or false.

- A. Zones I or II are necessary to produce digits.
- B. Zone III seems to produce a signal whose concentration influences the digit type.
- C. <u>Cells at the position of somite 19 are unlikely to form a digit 4 if zone III was transplanted</u> <u>from somite 19/20 to 17.</u>
- D. Formation of digits occurs by sequential induction: formation of digit 2 is induced by digit 3, whose formation is induced by digit 4.

<u>A. True</u> <u>B. True</u> <u>C. True</u> <u>D. False</u>

Original commentary
Correct answers
<u>A true</u>
<u>No digits could develop at position of somites 14/15-16 where zone I is absent.</u>
B true
A high concentration of the signal (near zone III) leads to formation of digit 4, a middle concentration to digit 3, a low
one to digit 2. Grafting a second zone III close enough to the normal one increases the concentration of the signal and
promotes the formation of digits 3/4 (see e.g. when Z is grafted at somite 17, the digit pattern posterior of it is 4-3-3-4,
without digit 2 being formed.
<u>C true</u>
The results suggest that digit number 4 is only formed next to a zone III. In fact, such a transplantation would result in
no digit being formed by somite 19.
<u>D</u> false

If it was the case, a digit 2 could only be formed next to a digit 3 itself near to a digit 4. As seen when Z is grafted at somites 15 or 15/16, this is not the case, a digit 2 can be formed even in the absence of a digit 3/4 next to it.

<u>References</u> <u>Tickle et al, Nature (1975)</u>

Animal anatomy and physiology

A neuron is kept in a solution similar to the extracellular fluid of brain tissue under a pure oxygen atmosphere. After a few minutes, cyanide, a substance that blocks the electron transport chain, is added to the solution.

Indicate if each of the following statements is true or false.

A. The concentration of K^+ ions in the cell increases.

- B. The probability of a spontaneous action potential increases.
- C. The concentration of H⁺ ions in the intermembrane space of the mitochondria increases.

D. The concentration of bicarbonate in the solution decreases.

A. False B. True C. False D. True

Original commentary

Correct answers A false

Addition of cyanide leads to a rapid depletion of ATP in the neuron. As a consequence, the Na⁺ / K⁺ pump will no longer exchange Na⁺ against K⁺ inside the cell. Through diffusion, the distribution of ions will be equalized across the cell membrane, and hence the concentration of K⁺ will decrease in the cell.

B true

With an increase of the membrane potential due to diffusion (see A), the probability of a spontaneous action potential increases.

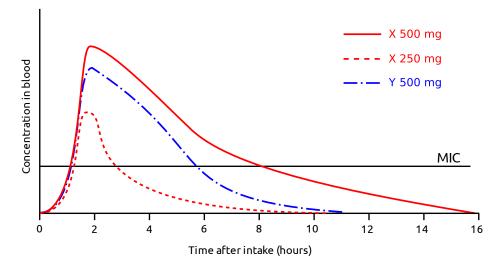
C false

The concentration of H^+ is kept high in the intermembrane space of the mitochondria by the electron transport chain. After blocking this chain, the concentration quickly decreases through the production of ATP at the ATP-synthetase. D true

After adding cyanide, the cell stops emitting CO_2 . The CO_2 dissolved as bicarbonate in the solution from before adding cyanide is entering the atmosphere with an extremely low partial pressure of CO_2 (as it was initially pure O_2).

Animal anatomy and physiology

The effectiveness of antibiotic treatments depends on the time and concentration at which bacteria are exposed to a specific drug, which in turn depends on the dosage, the intake interval and the rate of drug elimination from the body. Two antibiotics X and Y, both somewhat toxic to humans, are excreted by the kidney, but Y is also eliminated in the liver through cytochrome complexes. While X makes the bacterial cell wall permeable for ions, Y inhibits the synthesis of the cell wall during cell division. The figure below shows the average concentration of drugs X (red) and Y (blue) measured in healthy individuals after a single intake of 500 mg or 250 mg, along with the minimal concentration at which target bacteria are inhibited to grow *in vitro* (MIC, solid black line).



Indicate if each of the following statements is true or false.

- A. To safely treat patients with significantly reduced renal function, intake intervals of X have to be prolonged.
- B. When doubling the dosage of X to 500 mg, doubling the intake interval prevents an accumulation of X while ensuring that the concentration stays above the MIC in the blood.
- C. Patients treated with Y should increase their dosage when consuming fruits containing inhibitors of cytochrome complexes (e.g. grapefruit).
- D. Ensuring a drug concentration above the MIC in the blood is more important for X than Y.
- A. True B. False C. False D. False

Original commentary
Correct answers
A true
Drug X is eliminated only renally and thus in renal insufficient patients, the consideration of the risk of accumulation
of drug X is important. By increasing the intake interval, the kidney has more time to eliminate the drug and hence the
risk of accumulation is reduced.
B false
As shown in the graph a dosage of drug X of 250 mg causes blood concentration higher than MC only for 2-3 h but a
dosage of drug X of 500 mg causes blood concentration higher than MC for approx. 8 h, meaning more than double of
a dosage of 250 mg and meaning the interval has to be more than doubled.
C false
Substances inhibiting the cytochrome complexes (e.g. grapefruit) leads to slower inactivation/excretion of drug Y and
hence patients treated with this drug have to be given lower dosages or asked to increase the intake intervals to
prevent accumulation and intoxication.
D false
As bacteria cell division is a continuing process and bacteria divide not simultaneously the concentration of drug Y has

to be as a therapeutic level (higher than MC). A change in the membrane permeability of ions causes rapid bacterial damage and death consecutively.

References Tulane University; MIC & Time- vs Concentration-Dependent Killing

17

Dysfunctions of endocrine glands can be classified into three types, depending on the hormone directly affected:

- Primary endocrine dysfunctions alter the production of hormones with direct systemic effects on metabolism or development.
- Secondary endocrine dysfunctions alter the production of tropic hormones that act on other glands.
- Tertiary endocrine dysfunctions affect the hypothalamus.

Indicate for each of the following statements if it is true or false.

- A. A patient with an elevated cortisol level, a reduced corticotropin-releasing hormone (CRH) level and a elevated adrenocorticotropic hormone (ACTH) level is most likely affected by a primary dysfunction.
- B. An overproduction of the thyroid stimulating hormone TSH can be due to a primary dysfunction.
- C. An increased blood concentration of cortisol may be due to a tumor implying a primary or a secondary dysfunction.
- D. In the case of a tumor leading to a secondary endocrine dysfunctions, the blood concentration of the corresponding releasing hormone is changed.

A. False B. True C. True D. True

Original	commentary
Correct a	nswers

A false

The most likely explanation is a secondary dysfunction leading to an overproduction of ACTH, which in turn leads to an elevated Cortisol level and, due to feedback, an decreased CRH level. B *true* Due to feedback interactions, a primary underproduction leads to an increase in the corresponding tropic hormone. C *true* A hormone-producing tumor of the adrenal gland as a primary dysfunction elevates the cortisol. The same is caused

secondary due a overproduction of ACTH causing a stimulation of the adrenal gland. The latter results in a overproduction of cortisol.

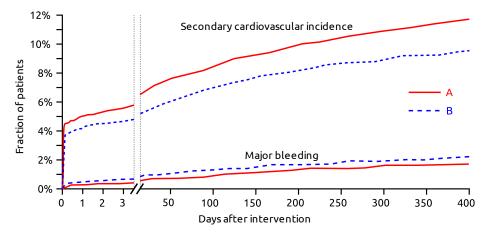
D true

A secondary dysfunction affects the tropic hormone through a feedback mechanism.

References Campbell Biology



Inhibiting platelet aggregation after a coronary intervention has been shown to greatly reduce the risk of complications. The effectiveness of two competing inhibitors was assessed in a clinical study in which 13,608 patients with symptoms of a myocardial infarction were randomly assigned to a treatment with either inhibitor A or B after the intervention. The figure below shows the fraction of patients that suffered from a second cardiovascular incident such as an infarction or a stroke, as well as the fraction of those that suffered from major bleeding in the 400 days post intervention.



Indicate if each of the following statements is true or false.

- A. This study suggests that using inhibitor B instead of A reduces the risk of a secondary cardiovascular event, but does not reduce the risk of major bleeding.
- B. This study suggests that a switch from inhibitor B to the cheaper inhibitor A after 3 days is increasing the risk of a secondary cardiovascular event.
- C. When using inhibitor B instead of A, the total number of patients suffering from a secondary cardiovascular incidence within 3 days after a coronary intervention is reduced by more than 10%.
- D. Repeating the study with a placebo control group is advised.

A. True B. True C. True D. False

Original commentary Correct answers A true Inhibitor B does indeed decrease the risk of a secondary cardiovascular incident, but at the same time increases the risk of a major bleeding. B true The study suggests that patients treated with inhibitor B have a reduced risk of a secondary cardiovascular incidence even after day 3. This can be read from the figure since the absolute difference in the fraction of patients with a secondary cardiovascular incident is increasing from day 3 to day 400. If there were no difference in the effects after day 3, the risk to suffer a secondary cardiovascular incident in the following 397 days would be the same in both treatments. Hence the number of patients with such an incident between days 3 and 400 can be calculated as $n^{(1-f(3))}$ where f(3) is the fraction at day 3, n the total number of patients and r the rate. The total fraction of patients at day 400 is then given by f(400)=(f(3)*n + (1-f(3))*n*r)/n = f(3)+(1-f(3))*r=f(3)*(1-r)+r. The absolute difference at day 400 is thus $(fA(3)^*(1-r)+r) - (fB(3)^*(1-r)+r)=(1-r)^*(fA(3)-fB(3))$, which is always smaller than fA(3)f(B(3)) unless r=0. But note that the students do not need to make these calculations but just realize that the absolute difference increases. C true To calculate the reduction in the total amount of affected patients, one need to compute the reduction from 5.8% to

4.9% of all patients, which is a reduction by 1-4.9/5.8=15.5%. Note that the exact numbers the students read off the graph do not matter, as to get a reduction of less than 10%, the student would need to misread the percentage of inhibitor A to be 9% or more.

D *false* Given the known reduction in the risk of complications when inhibiting platelet aggregation it would not be ethical not to give some patient any platelet inhibitor. In addition, the use of a placebo could only reaffirm the beneficial use of such an inhibitor but not add value to the comparison between inhibitors A and B.

References <u>Wiviott et al, NEJM (2007)</u>

19

There is variability in the proteins transporting O_2 , and their affinities for O_2 , both within and between organisms.

Indicate if each of the following statements is true or false.

- A. At the same partial pressure of O_2 , the saturation of fetal hemoglobin is higher than the saturation of the maternal hemoglobin.
- B. Hemoglobin has a lower affinity to O_2 in the vicinity of cells performing anaerobic glycolysis heavily.
- C. The hemoglobin of deep-diving mammals has a higher oxygen affinity than the hemoglobin of mammals adapted to high altitude.
- D. Hemoglobin is more efficient in transporting O_2 than is hemocyanin, the equivalent protein of many arthropods that binds O_2 non-cooperatively.

A. True B. True C. False D. True

Original commentary

Correct answers

A true

This is an adaptation of the fetal hemoglobin to recruit oxygen from the maternal blood.

B true

Cells relying heavily on anaerobic glycolysis recycle their NADH by fermenting lactate, which increases the acidity of the blood in the vicinity. In a more acidic environment, hemoglobin changes its conformation, which in turn reduces its affinity for oxygen (Bohr effect). This is an effective way to release oxygen where it is needed most.

C false

The opposite is true. Mammals that are deep divers need hemoglobin that releases most of the oxygen in the blood. Mammals adapted to high altitude, in contrast, need to fill their hemoglobin with oxygen in the lungs even at low partial pressure, and hence have hemoglobin with higher affinity. D *true*

The cooperativity between the different hemoglobin subunits allow for a larger difference in affinity between the place of oxygen uptake and oxygen release (a sigmoid dissociation curve).

The Hepatitis B virus contains the antigens HBs, HBc and HBe, of which HBs is commonly used as a vaccine. HBe is expressed in only some strains. The following table shows the presence (+) or absence (-) of viral antigens and antibodies measured in some patients. A question mark (?) indicates that the respective test was not performed.

Patient	HBs	HBc	HBe	Anti-HBs IgG	Anti-HBs IgM	Anti-HBc IgG	Anti-HBe IgG
P1	-	-	?	+	?	-	?
P2	-	-	-	+	-	+	+
P3	+	?	+	-	+	-	?
P4	+	?	?	?	?	+	+
P5	?	-	-	-	+	-	?

Indicate for each of the following statements if it is likely to be true or false.

A. Patient P1 was vaccinated a while ago, but never suffered from a Hepatitis B infection.

B. Patient P2 successfully overcame a Hepatitis B infection.

C. Patients P3 and P4 are currently suffering from a Hepatitis B infection.

D. Patient P5 has been vaccinated recently.

A. True B. True C. True D. True

Original commentary

Correct answers

A true

Since vaccination is done using HBs, a vaccinated person is producing anti-HBs IgG after several weeks. A Hepatitis infection, however would also lead to anti HBc and often anti-HBe antibodies, which were not found in P1. B *true*

While no antigens were found, P2 produces IgG against all three antigens, even those not used in vaccination. C true $% \mathcal{A}$

The antigen HBe was found in P3, which is a good indication that the virus is present. In addition, the immune system of P3 started its first response by producing IgM antibodies. Since P4 shows anti-HBc and anti-HBe IgG, he or she must have been infected at one point. The presence of HBs strongly suggest that the infection is still in progress since the only alternative would be a very recent vaccination, which is unlikely to be applied to an already immunized person.

D true

The presence of anti-HBs IgM suggest a recent and exposure to HBs. However, since HBc and HBe antigens are not present, the likely source of exposure was a recent vaccination.



Participants of the IBO 2013 are going to visit mount Niederhorn. Before and right after a rapid ascent by cable car from 400 m to 2000 m and just before descent 3 hours later, physiological parameters of several participants will be measured and compared to the same measurements obtained from an alpine herder who stayed on the Niederhorn for more than two consecutive months. The participants are expected to hyperventilate at this altitude and get dehydrated.

Indicate if each of the following statements is true or false.

- A. The heart rate of an IBO participant just after arriving on top is expected to be higher than just before the ascent.
- B. The pH of the blood of the alpine herder is expected to be higher than the pH of the blood of an IBO participant when arriving on top.
- C. The pH of the urine of an IBO participant is expected to be higher just before descent than just after arriving on top.
- D. Some IBO participants are expected to show a transient increase in the hemoglobin concentration while on top.

A. True B. False C. True D. True

Correct answers

A true

The hypoxemia due to the lower partial concentration of oxygen will be compensated by an increased heart and respiratory rate .

B false

The blood pH is tightly controlled and is not expected to change substantially. If any change is observed, then the pH of the IBO participant is expected to increase due to hyperventilation, followed by a rapid reduction in the carbondioxyde concentration in the blood.

C true

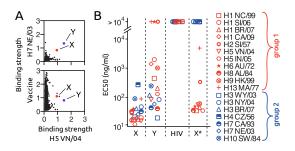
Due to hyperventilation, the carbondioxyde concentration in the blood is decreased rapidly. To prevent an increase of the blood pH, the body excretes basic metabolites through the urine, leading to an increase of the urine pH. D *true*

To avoid an increase of the blood pH (see answer to C), the kidney excretes basic metabolites, often leading to dehydration, which is followed by an increase of the hemoglobin concentration in the blood. What is more hyperventilation (especially on high altitudes) leads to dehydration, too.

References Campell Biology

Animal anatomy and physiology

The rapid evolution of the influenza antigen Hemagglutinin (HA) is a major challenge for the development of efficient treatments. In order to identify antibodies effective against a wide variety of influenza strains, 13,000 plasma cells of a vaccinated person were individually isolated and triggered to produce antibodies. These antibodies were tested against different types of HA (H5 VN/04, H7 NE/03 and the mix present in the vaccine) by measuring their binding strength (figure A). The binding efficacy of two particularly promising antibodies X and Y against several HA types from groups 1 (red) and 2 (blue) was further assessed by measuring the required concentration to achieve half the maximal binding efficacy (EC50, figure B). As a comparison, the EC50 was also measured for an anti-HIV antibody (HIV) and an antibody X* produced by plasma cells originally producing X but in which all mutations have been reverted to obtain the corresponding sequence originally inherited from the parents.

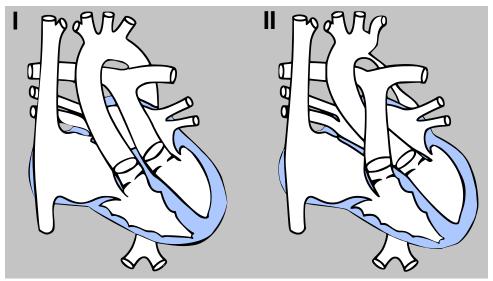


Indicate if each of the following statements is true or false.

- A. An immune response against the influenza vaccine is mediated by a diverse set of antibodies.
- B. While efficient against HA from group 2 strains, antibody Y does not confer immunity against all group 1 strains tested.
- C. The widespread immunity found for antibody X has in part arisen from somatic mutations.
- D. An injection of antibody X confers effective immunity against a wide range of influenza strains for several years.
- A. True B. True C. True D. False

Original commentary Correct answers A <i>true</i>
As can be seen in the lower panel of figure A, there are a large number of plasma cells producing antibodies against the HA present in the vaccine.
B <i>true</i> This can be seen in figure B where antibody Y does not bind all group 1 HA better than the control antibody against HIV.
C true Since the germ line copies of all genes do not concur immunity, the difference between X and X* antibodies must be due to somatic mutations that occurred in the cell line leading to the plasma cell producing X. Note that somatic mutations and rearrangements are common in antibody producing cells, a likely adaptation to deal with a wider range of antigens. D false
While an injection of antibody X concurs passive immunity against a wide range of influenza strains, it does not provide active immunity. Therefore, immunization will not last for more than a couple of weeks or maximally month.
References <u>Corti et al, Science (2011)</u>

The following schematics illustrate two severe congenital heart malformations occasionally found in newborns.



Indicate if each of the following statements is true or false.

- A. In Malformation I, the oxygen saturation is higher in the pulmonary artery than in the carotid artery.
- B. Surgically swapping the aorta and the pulmonary artery in the case of Malformation I restores proper blood circulation.
- C. In Malformation II, the blood pressure in the carotid artery is increased compared to healthy individuals.
- D. Surgically swapping the *venae cavae* and the pulmonary vein in the case of Malformation II restores proper blood circulation.

A. True B. True C. True D. False

Original commentary Note

In the heart Malformation I, the aorta comes out of the right ventricle (instead of the left one) and the pulmonary artery out of the left ventricle (instead of the right one). In Malformation II, the aorta is narrowed.

Correct answers

A true

This is true because there is no connection between the pulmonary blood circulation and the systemic one. B true

As mentioned in the "answer note" the origins of the aorta and pulmonary artery are swapped.

C true

The narrowing of the isthmus of the aorta causes an increased resistance at this location leading to a reduced flow downwards the aorta which increases the blood flow in the arteriae of the upper extremities and the head/brain. The latter increases the blood pressure consecutively.

As a second mechanism the decreased blood flow in the aorta descendens/aorta abdominalis and in the flow renal arteries consecutively. As a physiological mechanism the kidney rises the circular blood pressure to try to increase the renal blood flow.

D false

The suggested operation does not change the patients problem. What is more it would create the same separation of the pulmonary and systemic circulation as in Malformation I.

References

Universitätsklinikum Bonn; D-Transposition der großen Arterien

In a community of marine brown algae (*Phaeophyta*), two multicellular life forms are observed among the species:

- 1) A tall and fast-growing form that is strongly affected by environmental seasonality and shows a high mortality.
- 2) A tiny and slow-growing form that is less sensitive to seasonality and shows a low mortality.

All species alternate between a haploid and a diploid generation. Isomorphic species show the tall form both in the haploid and diploid generation. The life form of heteromorphic species, however, depends on ploidy.

Indicate if each of the following statements is true or false.

- A. Proportion of isomorphic species is likely to increase with more intense seasonality.
- B. In heteromorphic species, the tall and fast-growing life form is observed during the more productive season.
- C. Heteromorphic species are limited to one generation each season (winter/summer).
- D. In these algae, haploid full siblings from diploid parents are genetically less related than diploid full siblings from haploid parents.
- A. False B. True C. True D. True

Original commentary

Correct answers A false

The description of the small life form is giving a hint that it is adapted to endure a tougher, less productive season (winter). A species with the tall and fast growing form alone will have an increasing handicap in regions with a more intense winter compared to heteromorphic species more adapted to endure a tough season.

B true

As the tall life form is adapted to fast growth during summer, it will be more competitive during summer as compared to individuals with the small life form present during summer. *C true*

The small life form is adapted to outlive the unproductive winter - during summer the small life form would implicate a loss of productivity. On the same time, the tall life form would be very vulnerable during winter and most likely not survive. So heteromorphic species only make one new generation at the end of each season. D true

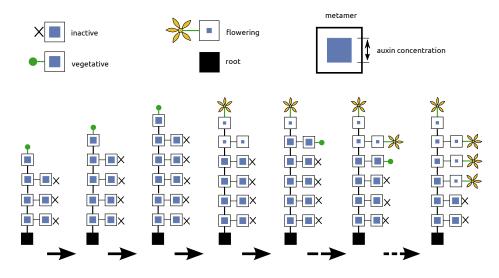
Haploid plants derive from spores which are products of a meiosis and have only one parent. Therefore siblings share half of their genome in average. Diploid plants derive from a zygote out of two gametes, resulting themselves from a meiosis of their parents. All gametes from each parent are genetically identical, as are the full siblings among each other.

References Bessho et al, Evolutionary Ecology Research (2009)



Plant anatomy and physiology

A growing plant can be described by units called metamers (illustrated by boxes) that are produced by a vegetative meristem. Each metamer consists of a stem segment and an additional meristem that is inactive at first, but may become active and develop into a vegetative meristem. Vegetative mersitems can develop into a flowering meristem. Vegetative and flowering meristems produce auxin, which is constantly transported downwards to lower metamers. The figure below shows a plant at different ages ending up flowering and illustrates the auxin concentration found in each metamer.



Based on the observed auxin concentrations, indicate if each of the following statements is true or false.

A. Exceeding a minimal auxin threshold invariably activates meristems.

B. An apex turning to a flowering stage is losing its apical dominance.

C. A high auxin concentration is enough to trigger the development of flowers.

D. Auxin from different apical metamers can have cumulative effects on subsequent metamers.

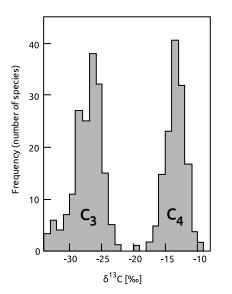
A. False B. True C. False D. True

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Original commentary
Correct answers
A false
The opposite is true, below a certain threshold the apical dominance is lost and the uppermost inactive meristem is
activated.
B true
A metamer turning into a flower is reducing its production of auxin, so the concentration of auxin sinks in the
subsequent metamer and falls under the threshold needed to suppress meristem activation.
C false
If this was true, all meristems would turn into a flowers.
D true
The residual auxin from all four flowering apices accumulates along the stem and prevents the subsequent metamer
from being activated. /br>
References
Przemyslaw et al, PNAS (2009)
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Plant anatomy and physiology

Two stable carbon isotopes ¹²C and ¹³C are present in the atmosphere, but ¹²C is approximately 100 times more frequent. Diverse metabolic processes discriminate against ¹³C in favor of ¹²C, leading to a smaller proportion of ¹³C in biomass than in the atmosphere. The relative difference between expected and observed proportion is indicated by δ^{13} C, with a more negative value indicating a stronger discrimination. The figure shows the distribution of δ^{13} C-values found in plant species with C₃ and C₄ metabolism.



Indicate if each of the following statements is true or false.

- A. RuBisCO is discriminating more strongly against $^{13}\mathrm{C}$ under higher than under lower partial pressure of $\mathrm{CO}_2.$
- B. Fixation of CO_2 into oxaloacetate is discriminating more strongly against ¹³C than the reaction of RuBisCO.
- C. Meat from cattle feeding on a meadow in the Swiss mountains is likely to have a lower 13 C content than from cattle feeding in a central African savanna.
- D. It is possible to distinguish between purified sugar from sugar cane (C_4) and sugar beet (C_3) based on their mass.
- A. False B. False C. True D. True

	iginal commentary
	rrect answers
,	alse
Act	ually the opposite is true. The aim of the C ₄ metabolism is to increase the partial pressure of CO ₂ for RuBisCO to
	rease the proportion of the carboxylase reaction compared to the oxigenase reaction. The higher partial pressure is ually the reason of weaker discrimination of 13 C in C ₄ plants.
B fe	alse
Thi	s reaction is the first fixation step in C ₄ -plants which are less discriminative than C ₃ plants.
C t	rue
C_4	plants are much more present in tropical ecosystems than in temperate or cold ecosystem. The isotope ratio is
rep	orted upwards in the food chain to herbivores and predators.
Dt	1 1
_	

As ^{13}C is slightly heavier than ^{12}C , the mean weight of a sugar molecule from cane is slightly higher.

Seeds of most plants are more resistant to environmental stress before germination has been initiated. To demonstrate this, seeds of wheat (Triticum aestivum) were exposed to one of the following four treatments.

Treatments	Soaked	Incubated	Transferred to wet paper and kept at room T
Α	5 h at room T	5 h; -20°C	+
В	5 h at room T	5 h; 30°C	+
С	-	5 h; 4°C	+
D	-	5 h; 50°C	+

Indicate for each of the following treatments, if the seeds are expected to produce sprouts (true), or not (false).

A. Treatment A.

B. Treatment B.

C. Treatment C.

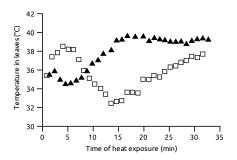
D. Treatment D.

A. False B. True C. True D. True

Original commentary Correct answers A false
B true
C true
D true
References Campbell Biology, 9th ed., p. 84-85 and figure 5.22 ("What determines protein structure?") and pages 807ff. and figure 39.11 ("Seed Development, Form, and Function").

Plant anatomy and physiology

The figure below shows the leaf temperature of two groups of common bean (*Phaseolus vulgaris*) plants exposed to infrared light. One group (open squares) was kept at optimal water supply and the other group (triangles) was drought stressed for 4 month before the experiment.



Based on these results, indicate if each of the following statements is likely to be true or false.

- A. After 8 minutes of heat exposure, drought stressed plants kept more stomata open than control plants.
- B. The ability to regulate the opening and closing of stomata decreases over time in plants of both groups.
- C. Following about 15 minutes of heat exposure, leaves of drought stressed plants absorbed roughly the same amount of thermal energy as they emitted.
- D. Plants experience a trade-off between preventing water loss and protection from over-heating.
- A. False B. False C. True D. True

Original commentary Note

If stomata are open, transpiration increases and therefore leaf temperature decreases (through evaporative cooling). The opposite is true for closing of stomata.

Correct answers A *false*

B false

C true

D true

References <u>Reynolds-Henne et al, Environmental and Experimental Botany et al (2009)</u> Campbell, Biology (9th ed.) page 778 ("Effects of Transpiration on Wilting and Leaf Temperature").



Plant anatomy and physiology

In a buffered suspension of freshly isolated thylakoids incubated in light, the rate of the Hill reaction (photolysis) can be measured using DCPIP. DCPIP is reduced at Photosystem I and changes its colour from blue to colourless.

Indicate for each of the following modifications of the experimental setting if it would significantly reduce the rate of this reaction.

A. Raising the temperature of the solution from 20 °C to 30 °C.

- B. Removing soluble gases from the buffer solution prior to adding thylakoids.
- C. Adding DCMU, a herbicide that binds to Photosystem II.

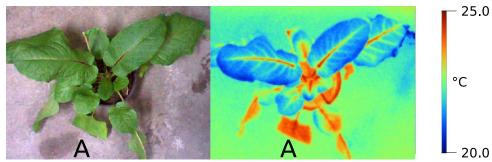
D. Adding 2,4-D, a herbicide acting as a synthetic auxin.

A. False B. False C. True D. False

Original commentary Correct answers A false Temperature remains in the physiological optimum and the rate is expected to increase with temperature. B false No oxygen nor CO₂ is needed for electron transport chain. C true If the electron transport chain is interrupted, DCPIP will not be reduced and the suspension will not turn colourless. D false Auxin has no effect on electron transport chain. References Campbell Biology, 9th ed., p. 193-194 (electron transport chain).

Plant anatomy and physiology

Infrared pictures are used to visualise the temperature of a plant surface. The figure below shows the photograph of a plant and the corresponding infrared picture.



Based on the figure, indicate for each of the following statements if it is true or false.

- A. Due to growing in the shade of older leaves, younger leaves of this plant are cooler than older leaves.
- B. Plant parts with high metabolic activity get several degrees warmer than parts with lower metabolic activity.
- C. Transpiration in leaf veins is significantly lower than in leaf blades.
- D. The high temperature of leaf A indicates that this plant begins suffering drought stress.

A. False B. False C. True D. False

Original commentary

Correct answers A false

Younger leaves are actually warmer than older leaves because they are transpiring less. The really old leaves in senescing state are warmer, but do not provide shade.

B false

While metabolism may indeed increase the temperature of plant parts, this is usually a negligible factor. In addition, the hottest parts of the plant (shoot and veins) are actually not those parts with the highest metabolism. Those would rather be leaves producing starch, actively growing meristems and roots (which are not visible). Finally, non-metabolizing structures such as the pot, the substrate or the small pole with a tag get equally warm as the hottest parts of plants.

C true

The temperature of leaf veins is higher than that of the leaf blade because their transpiration is very low. D false

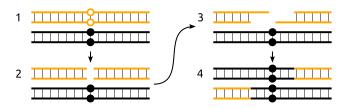
Leaf A is senescing and thus not transpiring any more. Other leaves are healthy and transpiring, hence the reason cannot be that the plant is suffering from drought stress.

References

Campbell, Biology (9th ed.)page 778 ("Effects of transpiration on wilting and leaf temperature")



According to the current model of recombination, a recombination event is initiated by a double strand break (DSB) in one of the two sister chromatids, followed by a trimming of the 5' ends. During the repair process after recombination, the information immediately flanking the DSB site is lost and supplied by the other chromatid.



Consider the situation in which two Alleles A and B of a locus have probabilities rA and rB to initiate a DSB and are initially present at equal frequencies in a large, isolated population.

Indicate if each of the following statements is true or false.

- A. If rA is twice as large as rB, the frequency of Allele A is expected to change faster when rB=0.05 than when rB=0.01.
- B. If rB is large and rA is much smaller, the frequency of Allele A is expected to reach fixation (frequency=1) almost linearly.
- C. If rA=rB, the frequency of Allele A will remain constant even if the population were small.
- D. Unless there is an additional mechanism involved, recombination in the population is expected to decrease over time.
- A. True B. False C. False D. True

Original commentary

Note

It should be clear from both the figure and the text that the allele initiating the DSB is not transmitted, which leads a bias in transmission in heterozygotes if the probabilities rA and rB are different.

Correct answers

A true

The larger the recombination rate, the more often the described mechanism can actually play. Hence the allele frequency changes more rapidly.

B false

While such a setting will lead to a rapid increase in allele A, the increase cannot be linear because the process depends on the frequency of heterozygous individuals, which become rapidly rare as the frequency of A approaches 1. Thus, the frequency of A is expected to increase asymptotically.

C false

In the case of rA=rB, this mechanisms will not necessarily lead to a change. However, due to genetic drift, an allele frequency is never expected to remain constant, unless the population is extremely (infinitely) large. D *true*

This mechanism effectively leads to a reduction in the recombination rate since alleles with a lower recombination rate are favored.



In female fruit flies (*Drosophila melanogaster*), the oocyte is located between maternal nurse cells and follicle cells providing nutrients, proteins and mRNA crucial for the development of the embryo. In one of the genes whose mRNA is transported to the oocyte, a mutation X has been found that leads to deformed, non-viable embryos.

Indicate if each of the following statements is true or false.

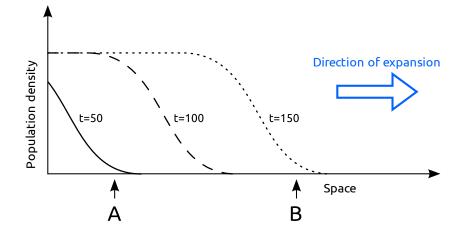
- A. If the mutation is dominant, the female offspring of a heterozygous male and a wild type female will be viable.
- B. If the mutation is dominant, no adult individuals homozygous for X can be observed.
- C. If the mutation is recessive, only the female embryos of a mother heterozygous for X will be deformed.
- D. If the mutation is recessive and two individuals heterozygous for X are crossed to produce the F1, 1/6 of the F2 will be homozygous for X.

A. True B. True C. False D. True

Original commentary
Correct answers
A true
Female with a mutation in a maternal effect gene are viable, even if they are sterile.
B true
To be homozygous for the mutation, an individual need to receive a mutant allele from each parent, however, females
with a dominant mutation are sterile and therefore cannot transmit the mutation to offspring.
C false
If the mutation is recessive, all offspring of a heterozygous mother will be viable.
D true
To be homozygous for the mutation, an individual need to receive a mutant allele from each parent. In the F1 of a cross between heterozygotes, the genotypes are distributed 1:2:1. Males can give the mutant allele with a probability of 1/2, however, the homozygous mutant female are sterile, therefore, only heterozygous females, representing 2/3 of the fertile females can give the mutant allele to their offspring, this with a probability of 1/2. The final probability of being homozygous in the F2 is $1/2 * 2/3 * 1/2 = 1/6$.



Assume a one-dimensional, homogeneous habitat with carrying capacity K that is inhabited by an annual plant species only at the left most point at generation t=0. In each generation, a fraction m=0.01 of the seeds disperses to neighbouring locations while the remaining 1-m seeds remain at the same location. The following figure displays the plant density over the habitat at different generations.



Indicate if each of the following statements is true or false.

- A. A mutation doubling m would increase the speed of the expansion.
- B. A beneficial mutation appearing at time t=100 at Position A will almost certainly become fixed in the population.
- C. A neutral mutation appearing at time t=50 in Position A has a higher probability to become fixed in the whole population than a neutral mutation appearing at time t=150 in Position B.
- D. A harmful but not lethal mutation appearing at time t=150 is expected to persist in the population longer if it appears in Position B than Position A.
- A. True B. False C. True D. True

Original commentary

Correct answers A *true*

The speed of the expansion is primarily dependent on the growth rate and, up to a limit, on the migration rate. If the migration rate is very small (as is the case here), it will, on average, take multiple generations until the next deme is colonized. Hence, an increase in the migration rate does lead to an increased colonization speed. B *false* The most likely fate of every mutation appearing in a population is that it is lost by genetic drift. C *true*

```
While both mutations have the same probability to become common at their receptive positions, a mutation that becomes common at position B will have a very low probability to become common at position A. In contrast, a mutation that becomes frequent at position A is likely contributing to the newly colonized demes and will thus have a higher chance to get fixed in the whole population. D true
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Since the population density will increase rapidly at Position B, selection is very weak and genetic drift is not efficient in losing new alleles. In contrast, both drift and selection are acting more strongly on a new mutation at position A since the population is large and stable in size. Hence, a deleterious mutation is much more likely to persist in the population when appearing at position B than when appearing at position A.

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The red colour of a haploid fungus is produced by a pathway converting a precursor pigment through several intermediates. To study this pathway, several mutant strains (I through IV) of various colours have been obtained. The following table lists their colours along with those observed in the haploid progeny of crosses among them.

Strain or cross	Colours o	Colours observed				
	red	beige	yellow	pink		
wild type	Х					
I		Х				
II		Х				
III			Х			
IV				Х		
I x wild type	Х	Х	Х			
x	Х	Х	Х	Х		
II x IV		Х		Х		
III x IV	Х		Х	Х		

Indicate if each of the following statements is true or false.

A. At least four genes are involved in this pathway.

B. Strain I has mutations in more than one gene involved in this pathway.

- C. In the pathway, the enzyme turning the pigment pink is located upstream of the enzyme turning it beige.
- D. Red progeny can be observed when crossing Strains I and IV.

A. False B. True C. False D. True

Original commentary

Correct answers A *false*

In this pathway, 3 steps catalyzed by a total of 3 enzymes are enough to explain the results.

B true

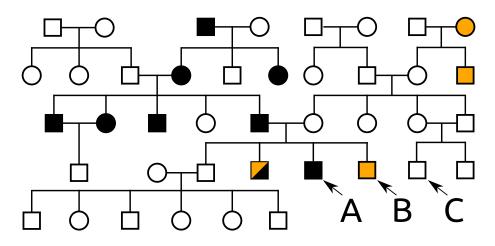
Crossing I (beige) with the wild-type produces, besides beige and red (wild-type) offspring, also yellow offspring which can only be explained if strain I is mutant both for the enzyme metabolizing the beige intermediate and the one transforming the yellow one. Since strain I appears beige, it also means that the yellow pigment is situated further downstream in the pathway as the beige one.

C false

Crossing II (beige) with IV (pink) does not produce any red (wild-type) offspring, this means that at least one of the two strains is mutant for both alleles. Crossing III (yellow) with IV (pink) does not produce beige offspring. Since we know from B that beige is upstream of yellow, this can only be explained if IV is only mutant for the gene metabolizing the pink intermediate, therefore strain II is mutant both for the enzyme metabolizing beige and the one metabolizing pink. Since II appears beige and not pink, the beige intermediate is upstream of the pink one. D *true*

Offspring can only be red if between the 2 parents, at least one copy of each gene is wild-type. We know from B that I is mutant only for the enzymes converting yellow and beige and from C that IV is only mutant for the enzyme converting, therefore red (wild-type) offspring can be observed when crossing I and IV.

Three male members (A, B and C) of a family consult a genetic counsellor. The genealogy of the family is given below with individuals affected by two genetic diseases X (black) and Y (orange) are indicated. While Disease X is extremely rare, the disease causing allele of Disease Y has a frequency of 6% in the population.



Indicate if each of the following statements is true or false under the most likely modes of inheritance.

- A. Individual B must be a carrier of Disease X.
- B. Individual C cannot be a carrier of Disease Y.
- C. If Individual A was to have a son with an unrelated and unaffected woman, the probability that the son will be affected by Disease X is 50%.
- D. If Individual B was to have a son with an unrelated and unaffected woman, the probability that the son will be affected by Disease Y is > 5.65%.

A. False B. True C. True D. True

Original commentary

Note

Mode of inheritance disease X

Since two affected individuals have a healthy son, disease X must be dominant and since both males and females are affected, it cannot be Y-linked. Finally, since we know that the disease is extremely rare and thus most likely absent in the family of the mother of A and B, the disease must be autosomal then an X-linked disease can not be inherited from father to son (individual A).

Mode of inheritance of disease Y

Dominant inheritance can be excluded because two healthy individual have an affected son (individual B). Autsomal recessive is unlikely because the father of individuals A and B has healthy parents, grand parents, uncles, aunts and siblings. Hence the most likely mode of inheritance is X-linked recessive.

Correct answers

A false

Given a dominant inheritance of disease X, individual B cannot be a carrier of this disease. Note that it is enough to realize that the disease must be dominant but not to distinguish between autosomal or gonosomal to answer this questions.

B true

A male cannot be carrier of a X-linked recessive disease.

C true

Since the disease is dominant, individual A will pass on the affected allele in 50% of the cases.

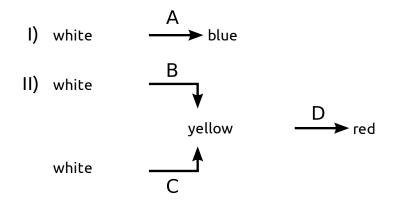
D true

While individual B will pass on his Y-chromosome and hence not the disease causing allele, the probability that the mother will pass it on is non zero. Given the allele frequency of 6% in the population and given that the mother is

healthy, she is a carrier with a probability of (2*0.06*0.94)/(1-0.06*0.06) = 11.32%, in which case she has a probability of 50% to transmit the disease causing allele. Hence, the probability to have an affected son is 5.67%. A common mistake is to assume the probability that the mother is a carrier to be 2*0.06*0.94*0.5 = 5.64%, and hence to ignore the fact that we already know that the mother is not affected.



Several inbred lines with recessive mutations are studied in a plant species. Wild type flowers are purple due to a mix of a red and a blue pigment synthesized by two separate biochemical pathways I and II involving enzymes encoded by genes A-D (all colorless compounds are named "white"):



Indicate if each of the following statements is true or false.

- A. If all genes were unlinked, less than 25% of all F2 individuals of a cross between a red and a blue inbred line are expected to be red.
- B. If back-crossing the F1 of a purple and a yellow inbred line to their yellow parents results in 160 yellow, 40 red, 40 green and 160 purple individuals, genes A and D are 20 cM apart on the same chromosome.
- C. If B was more closely linked to A than to C and A was more closely linked to C than to B, gene B must be between genes A and C.
- D. If the distance between B and C was 28.5 cM and crossing purple F1 individuals from a cross of two purple inbred lines gives rise to blue individuals in the F2, their frequency is less than 5%.
- A. True B. True C. False D. True

Original commentary

Correct answers A true A red inbred line is homozygous for a loss of function mutation in gene A (genotype aaBBCCDD). A blue inbred line is homozygous for a loss of function mutation both in gene B and gene C (genotype AAbbccDD), as otherwise the plants turn green. The F1 of such a cross has the genotype AaBbCcDD. F2 individuals with red flowers must be homozygous for a (which they are with probability 1/2*1/2=1/4) and may not be homozygous for both b and c at the same time, which they are with probability $1-(1/2)^4=15/16$. The total frequency of red individuals among the F2 is thus 1/4*15/16=15/64=23.9%. However, note that the red inbred line might also be homozygous for either b or c, in which case the F1 individuals have genotypes AabbCcDD or AaBbccDD. In this setting, the probability that an F2 individual is not homozygous for both b and c is reduced to $1-(1/2)^2=3/4$, and hence the frequency of red F2 individuals would be 1/4*3/4=3/16=18.75%. So independent of the assumptions, the frequency is always < 25%. B true

Yellow inbred lines must be homozygous for loss of function mutations a and d. In a back-cross setting with an individual homozygous for A and D (as the purple inbred line must be), the genetic distance can easily be computed as the frequency of non-parental phenotypes (green and red) among the progeny (see Campbell chapter 15). Thus, the distance is 80/400=20cM.

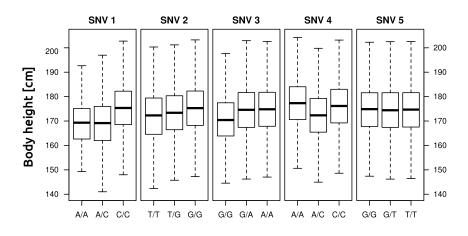
C false

The only possible inbred purple genotypes that result in a purple F1 but some blue F2 when crossed are AAbbCCDD and AABBccDD. Under this setting, the F1 is AABbCcDD, and hence purple. A blue F2 individual has then the genotype

From them stem we know that B and C are linked. We further know that B is closer to A than to C. This leaves us with the orders A-B-C or B-A-C. Since A is closer to C than to B, only B-A-C remains (or C-A-B read from the other side). D true

AabbccDD, which requires a recombination to happen in both F1 parents (from the haplotypes AbCD and ABcD to AbcD and ABCD). This occurs with probability 0.285 (since the two genes B and C are 28.5 cM apart). After recombination, the needed haplotype is transmitted with a 50% chance. Hence the total probability for an F2 individual to be blue is $(0.285*0.5)^2=2.03\%$.

A common strategy to detect genes underlying a particular trait is to test for statistical associations between the phenotype and a very large number of SNVs (single nucleotide variants) in a large sample of individuals. The charts below give the results of such an approach for body height and five independent SNVs typed in 20,000 random individuals from Switzerland.



Indicate if each of the following statements is true or false.

- A. In contrast to SNV2, SNVs 1 and 3 are closely linked to a gene with an allele affecting body height dominantly.
- B. If the frequency of the C allele at SNV 4 decreases from 50% to 30% in the population, the average body height increases.
- C. Since the median body height in the population is 175 cm, the frequency of allele A at SNV 1 has to be below 30%.
- D. These results are sufficient to demonstrate that most of the variation in body height is genetically determined.
- A. True B. True C. True D. False

Original commentary

Correct answers A true

All three SNVs seem to be linked to a gene with an allele affecting body height. The difference to SNV 2 is only that the pattern observed at SNVs 1 and 3 is very likely due to the effect of a dominant-recessive locus in close proximity since the heterozygous genotype results in a very similar phenotype as one of the homozygous genotypes, but the pattern observed at SNV 2 is best explained with incomplete dominance. B *true*

D false

All SNVs together can explain only 10% of the variation. The students are not able to calculate this value from the data. However, they are able to judge that SNVs 1 through 4 each explain about 5cm max, which makes about 20cm difference between the most extreme genotypes ([A/A, T/T, G/G, A/C] vs [C/C, G/G, A/A, A/A]). However, the body height in the populations spans a multiple of this difference. Hence the conclusion from this data that a majority of the variation s genetically determined is false. But note that in fact body height in humans is 60-80% heritable, yet one needs different data to show this.

If the frequency of the C allele decreases from 50% to 30, the number of heterozygous individuals decreases from 50% to 42%, and hence the average body height is expected to increase.

SNV 5 has no effect on body height, and hence gives a direct estimate of the average height in the population (about 175 cm). If the A allele at SNV 1 has a frequency of 30%, the frequency of the dominant C/C genotype is only 49%, which is not possible since the average height for this genotype had then to be > 180cm to obtain a population average of 175cm. Higher allele frequencies of A would even make it worse. Note: the true allele frequency in the example is 7%.

38

Genetics and evolution

In cats, there is a genetic locus with two alleles (A, a). In a population, 1300 cats have genotype AA, 7400 are heterozygous and 1300 individuals carry the recessive genotype aa.

Indicate if each of the following statements is true or false.

- A. The frequency of Allele A in the population is 0.5.
- B. Under Hardy-Weinberg equilibrium, only 6000 cats are expected to be heterozygous for this locus.
- C. If this population was isolated and mating randomly, the next generation of cats is expected to be in Hardy-Weinberg equilibrium.

D. Sterility of homozygous individuals can explain this pattern.

A. True B. False C. True D. False

Original	commentary
Correct a	nswers

A true

The frequency of allele A is given by (2*1300+7400)/(2*(1300+7400+1300))=10000/20000=0.5.

B false

Under Hardy-Weinberg, 2*p*q=2*0.5*0.5=5000 cats are expected to be heterozygous.

C true

A population is always in the Hardy-Weinberg equilibrium after only a single generation of random mating. D *false*

If only heterozygous individuals were fertile, the allele frequency would indeed be 0.5. However, the offspring would still be expected to be heterozygous in only 50% of the cases.

To elucidate the phylogenetic relationship among three fly species of the *Lauxaniidae*, the nucleotide sequence of the 18S RNA and the cytochrome oxidase gene was determined in all species. Dots indicate the same nucleotide as the first sequence (*Minettia*) and hyphens represent deletions or insertions of one or more base pairs.

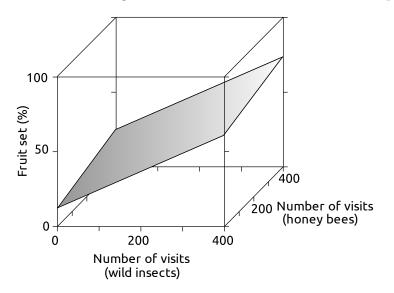
Based on these data, indicate if each of the following statements is true or false.

- A. The gene for cytochrome oxidase accumulates mutations faster than the gene for 18S RNA.
- B. Sequences of *Minettia* are evolutionarily more conserved than those of *Lauxiana* or *Lyciella*.
- C. The fact that the cytochrome oxidase sequence of *Minettia* is 8 nucleotides longer than the sequences of both *Lauxiana* and *Lyciella* suggest that the latter two taxa are more closely related than either is with *Minettia*.
- D. Single nucleotide substitutions of 18S RNA and cytochrome oxidase suggest different relationship between *Minetti, Lauxiana* and *Lyciella*
- A. True B. False C. False D. False

Original commentary Correct answers A <i>true</i> Cytochrome oxidase has13 point mutations and 4 deletions, 18S RNA has 6 point mutations and 1 deletion. B <i>false</i> Minettia was arbitrarily chosen as reference to align the other two species and do not mean that it is the most primitive one.
<i>C false</i> Between Lyciella and Minettia is only one deletion, Lauxiana has 3 independent deletions compared with Minettia and Lyciella. D <i>false</i> False, 18S RNA and cytochrom oxidase do show the same general topology of the genetic tree.



Flowers of cherry trees (*Prunus avium*) can be pollinated by both domesticated honey bees and wild insects such as wild bees or bumblebees. To study the influence of these pollinators on the fruit set (percentage of flowers of a tree that develop into fruits), flower visits of domestic honey bees and wild insects were counted during a standardized observation period for cherry trees worldwide. The figure below shows a linear model best explaining the data.



Indicate if each of the following statements is true or false.

- A. Cherry trees produce no fruits when domesticated honey bees and wild insect are completely absent.
- B. Domestic honey bees were more efficient pollinators than wild insects, needing fewer visits to increase fruit set.
- C. To maximize fruit set, cherry farmers are advised to limit the number of visits by wild insects when domestic honey bees are visiting.
- D. An isolated cherry tree is likely to have a higher fruit set when situated in a flower-rich backyard than in the middle of a wheat field.

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A. False B. False C. False D. True
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Original commentary
Correct answers
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A false

- B false
- The slope of wild bees~fruit set is steeper than the one for honey bees, thus wild insects are more efficient.
- C false

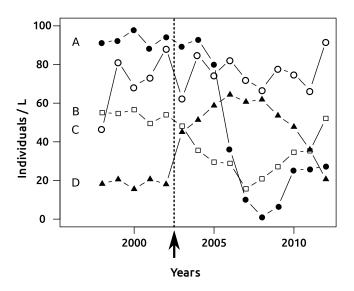
Both regressions (domestic bees~fruit set and wild insect~fruit set) are linear. Wild pollinators enhance fruit set regardless of the abundance of domestic honey bees. D true

In a flower-rich backyard the density of both wild pollinators and domestic bees is expected to be higher than in a monoculture of wheat because the backyard is likely to offer a more breeding sites and a more diverse flowers spectrum to feed on.

References Garibaldi et al, Science (2013)

The regression predicts that about 10% of cherries would still be pollinated. This might be due to wind pollination or self-pollination.

In an accident in spring 2003, a large quantity of fertilizer was spilled into a small lake in Switzerland. The figure shows the abundance of four species of zooplankton measured during August for several years before and after the accident. The accident is indicated with an arrow



Indicate if each of the following statements is true of false.

- A. Species C reacts on the accident with a quick decline in population density.
- B. The fertilizer is likely to be poisonous for species A.
- C. Species D is more useful as a bioindicator than is species B or C.
- D. The relative species densities in the community are re-established within ten years of the accident.
- A. False B. False C. True D. False

Original commentary

Correct answers

A false

The decline in density of species C after the accident is in the range of its normal annual fluctuation. A causal relation with the accident is very unlikely. B *false*

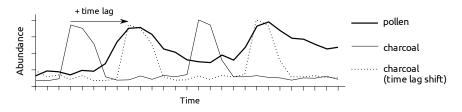
Zooplankton has short generation times. If the fertilizer itself were poisonous, the effect would be a drastic reduction already within the first two years after the accident. C true

After the accident, species A and D show drastic and stable shifts in population densities. Those shifts are much bigger than the stochastic fluctuation before and some years after the accident and therefore seem to be reliable. The shift in population density of species B is much smaller. Species C does not seem to react at all. D *false*

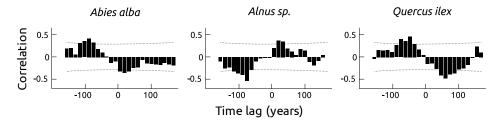
After 10 years, species is likely to still have a much smaller density than before the accident. During the years 7-9 after the accident, no significant increase in population density happened.



To study the effects of fire events on forest ecosystems around a Mediterranean lake, the amount of microscopic (smaller than 10 μ m) charcoal particles and pollen of three different tree species were counted in several slices of sediment layers dating from approximately 6000 years before present. Since the response of forest ecosystems may be visible only after many years, the correlation between the abundance of charcoal and pollen of a tree species was analyzed for different time lags. The hypothetical tree species in the figure below, for instance, reaches the highest abundance many years after the actual fire event. Hence, the highest correlation is achieved when the charcoal abundance is shifted with a specific time lag.



The figure below shows the results of such an analysis for three tree species, of which Abies alba has recently become locally extinct. Correlation coefficients exceeding the threshold (dotted lines) are statistically significant at α =0.05.



Indicate if each of the following statements is true or false.

- A. An increase in the frequency of fire events may have contributed to the extinction of Abies $\ alba$
- B. The pattern observed for *Alnus* trees can be explained by smoke from the fire events stimulating their flowers to produce more pollen.
- C. The dominance of *Quercus ilex* in recent Mediterranean forests can be explained by its tolerance to periodic fire events.
- D. The abundance of *Abies*-pollen is affected by fire events more quickly than the abundance of *Quercus*-pollen.

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A. True B. False C. False D. True
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Original commentary

Correct answers A *true*

According to the data shown the amount of Abies pollen is negatively correlated with the amount of charcoal for a few decades after a fire. Therefore the species seems not to be tolerant to fire. An increase of frequency of fires will lead to successive regression of this species.

B false

The positive correlation between charcoal and pollen approximately 20-40 years after fire event cannot be explained by a reaction of individual flowers or even trees to fire stimulus. The period of increased pollen production lasts several decades what is much too long for being explained by a punctual stimulus. C *false*

As it is for Abies, Quercus seems to be less present during the period after a fire event. The recent dominance must have other reasons than tolerance to fire.

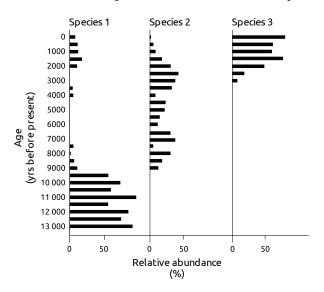
D *true* The negative correlation to fire events is significant after a time lag of about 10-15 years in Abies, but only after about 40 years in Quercus.

References Colombaroli et al, Journal of Ecology (2007)

Many chironomid species (non-biting midges) are known to be abundant only within well-defined ecological niches, as is shown below for three species commonly found in Switzerland.

	Optimal trophic state	Mean T of air in July	Most common adjacent vegetation
Species 1	Oligotrophic	7.1 - 12.9 °C	Alpine grassland
Species 2	Mesotrophic	9.3 - 17.6 °C	Mixed forests
Species 3	Hypertrophic	10.7 - 19.2 °C	Farmland

Fossil chironomids in lake sediments can be used to reconstruct the past climatic and ecological conditions in the vicinity of the lake. In a sequence of sediment layers of a small swiss lake, head capsules of all chironomid species have been identified and counted. The relative abundance of the three listed species in each sediment layer is shown in the figure.



Indicate if each of the following statements is true or false.

- A. Human impact is evident since 9000 years BP.
- B. An intermittent cooler period can be presumed between 2000 years BP and the present.
- C. Species 3 seems to be a better indicator species for the trophic state than for average temperature.
- D. Fluctuation in abundance of Species 2 is likely to be best explained by the Lotka-Volterra (predator-prey) model including an insectivorous predator.
- A. False B. True C. True D. False

indicated by species 2. D *false*

Interactions between predators and prey show fluctuation periods of several years at maximum (insects are short living), but will not be visible on a time scale of several hundreds of years.

References <u>Heiri et al, Palaeogeography, Palaeoclimatology, Palaeoecology (2003)</u>



Cladistic analysis is an approach to infer the evolutionary relationship among organisms based on the presence or absence of morphological or molecular characters. In order for cladistics to work correctly, the following three assumptions have to be met:

- Along a lineage, characters change over time.
- Any pair of two organisms shares a common ancestor.
- Evolutionary lineages split in a bifurcating manner.

Indicate if each of the following statements is in line with these assumptions (true), or whether one or more of them are violated (false).

- A. The presence or absence of nematocysts can be used in a cladistic analysis to reconstruct phylogenetic relationship of metazoa. Nematocysts are complex cells of cnidaria (e.g. sea anemone) that certain sea slugs incorporate into their own body for self defense by feeding on sea anemones.
- B. Cladistics can be used to reconstruct the phylogenetic relationship of ecologically distinct plant species, of which one arose by hybridisation of two distinct parental species.
- C. Cladistics can be used to reconstruct the phylogenetic relationship of two finch species that arose from a generalist finch that colonized a remote island. The species differ in bill length and depth, tarsus length and plumage color.
- D. Cladistics can be used to reconstruct the phylogenetic relationship of lichen multicellular eukaryotes. Lichen are a symbiotic interaction between green algae or cyanobacteria with fungi.
- A. False B. False C. True D. False

Original commentary Correct answers

A false

Although both taxa have nematocysts, this trait cannot be used to put both of them in a distinct clade within metazoa, as sea slugs do not produce nematocyst themselves. In regard of this trait the evolutionary lineages do not split in bifurcating manner.

B false

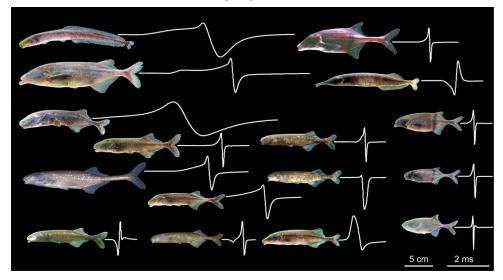
Here, evolutionary lineages do not split in bifurcating manner, but the origin of one lineage is the fusion of two initially separated lineages. C true

This example is in agreement with all assumptions.

D false

Lichen behave functionally a single organism, but consists of two independent organisms with a completely different phylogenetical background. Therefore the principle of splitting lineages in bifurcating manner is violated.

Fish species of the family *Mormyridae* are known for their ability to locate objects and communicate by weak electric fields called electric organ discharges (EOD). They are also able to sense EODs of other *Mormyridae*. The figure shows body shape, relative body size and and EOD-waveform used for communication (white lines) for 16 *Mormyridae* species living in a central African rainforest drainage system.



Indicate if each of the following statements is true or false.

- A. *Mormyridae* show characteristics typical for fish specialized on preying on other fish of similar size.
- B. *Mormyridae* show characteristics typical for a group of fish warning their predators of an electric shock via shared visual warning signs (Müllerian mimicry).
- C. *Mormyridae* show characteristics typical for fish living in highly turbid water or are mainly nocturnal.
- D. Mormyridae show characteristics typical of fish that attract mates with non-visual cues.

A. False B. False C. True D. True

Original commentary

Note

Since the students cannot be expected to know these fish, the question focuses on testing if the students can think of typical features of fish of a specific lifestyle, and are then asked to check if the *Mormyridae* show such features. This gets us around asking the students to judge the life style of *Mormyridae*.

Correct answers

A false

Fish specialized on preying other fish of similar size typically have a relatively large mouth with large conical teeth, both absent from all species of *Mormyridae*.

B false

If Müllerian mimicry would be important to reduce pressure from predators, all shown Mormyrids should show very similar, extremely contrasting colours most likely in combination of yellow and black or orange/red and black. In contrast, all shown *Mormyridae* are of dull / camouflage color. Furthermore, *Mormyridae* do not produce harmful electric shocks which could be used as an anti-predation behavior (mentioned in the text). C true

Mormyridae live in turbid water and are mostly nocturnal. They have very small eyes compared to body size what indicates that vison is limited and seems to play a minor role for these fish. Large eyes are common in diurnal fish species that live in clear water. The complex systems for object localization and communication via the generation and reception of weak electric fields are very useful for nocturnal fish in turbid water. D *true*

All Mormyroiadea are of dull color and have impaired vision. Hence, a system to attrackt mates using non-visual cues

is highly expected. In addition, the electric signals produced vary greatly between species and are used to attract mates. /br>
References
<u>Hopkins, Electroreception (1986)</u>