Solution to Homework Problems

Introduction to Biomedical Engineering

Second Edition

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Chapter 0

These are open-ended and time-dependent questions; hence, answers are not provided. However, some notes or reminders may be useful. They do engage students early in a course, and I have found that many do pursue REU and other opportunities after gaining the exposure provided in these questions. For the accreditation of engineering programs, ABET now likes to see documented outcomes. Assigning these exercises and keeping some samples could be helpful in documenting that your program attempts to address and assess ethics, knowledge of contemporary engineering issues/developments, etc.

Introduction to Biomedical Engineering, Second Edition, by Michael M. Domach. ISBN 0-13-602003-8.

Chapter 1

1. (a) If our DNA contained combinations of three bases instead of four, how many amino acids could be encoded when a codon contains one, two, or three bases?

Number of words = $n(\text{letters})^{m(\text{word length})}$
$3^1 = 3$; $3^2 = 9$; $3^3 =$ **27**. Can cover the coding of 20 amino acids with three bases and by using a triplet to code for a particular amino acid

(b) Why do you suppose living systems use 4 bases instead of 3 bases in the genetic code?

With four bases and more synonyms, the system is more robust. A mutation could wind up coding for the same amino acid, and the same protein would be made. Also stop and start signals can be composed of additional “words.”

2. If a cell is maintaining 200 proteins and the average number of amino acids per protein is 75, what is the total number of A, G, C, and T bases used to code for the construction of the proteins?

200 prot * 75 AA/prot * 3 bases/AA = 45,000 bases.

3. Match the statement on the left with the best analogous match on the bottom

A car is either a Toyota
or a Ford. a_____

The Naval Tomcat aircraft
was based on the F14 prototype. d_____

Ford water pumps do
not work in Toyotas. b_____

Each musical measure has the
same number of beats. e_____

A taped message in Mission
Impossible incinerates after it is read. c_____

(a) Taxonomy (b) 16S RNA gene in archaea vs. eucarya (c) mRNA lifetime (d) Phylogeny (e) codon triplet (f) universal genetic code (g) Prions.

4. Which compound(s) below would *not* likely be used by a heterotroph for energy?

   (a) carbon dioxide (b) glucose (c) methane (d) fructose (d) reduced iron (Fe^o)

Cannot oxidize carbon dioxide further and Fe^o is not an organic, C-containing compound.

5. A microbe was found in a fossilized meteor in Antarctica. It appears to have a DNA-like molecule made of 5 different types of base-like molecules. An analysis of other molecules suggests that 25 different amino acid-like molecules make up something that resembles proteins. If there is a genetic code in use, then what is the minimum number of base molecules per codon? Why is the value a minimum?

   $5^2 = 25$, so with two bases per codon, can cover minimally. More bases per codon would provide more redundancy/degeneracy as well as start and stop signals.

6. If the yield for the growth of *E. coli* on glucose is 0.3 g cell (water-free basis)/g glucose, answer the following:

   (a) What will be the mass concentration of *E. coli* on a water-free basis when provided 5 g glucose/liter?

5 g gluc/lit * 0.3 g cell dry wt/g gluc = **1.5 g cell dry wt/lit.**

   (b) What will the total mass of *E. coli* per liter?

1.5 g cell dry wt * 1 g cell total (hydrated)/0.3 g cell dry wt = **5 g cell total/lit.**
Note: In any multicomponent system, concentrations can be on different bases just as income can be on a pre-tax or after-tax basis. A good engineer always asks what basis a concentration or other number is on to make sure everyone is talking about the same thing.

7. Assume that a typical protein has 100 amino acids and a "ballpark" molecular weight for an amino acid is 100 g/mol. How many protein molecules are present per 70 kilograms (i.e., average weight of a human) of hydrated animal cells? If a protein's

typical dimension is 10 Angstroms (1 A = 10^{-8} cm), could the distance between Pittsburgh and Los Angeles be spanned by aligning the protein molecules end-to-end?

100 mol AA/mol prot * 100 g/mol AA * 1 g prot/g AA = 10^4 g prot/mol prot.

70,000 g person * 0.3 g solid/g person * 0.6 g prot/g solid * mol prot/10^4 g prot * 6.0 (10^{23}) molecules/mol = 7.56 (10^{23}) protein molecules.

A protein is about 10 Angstroms in size (10^{-7} cm), which means if all these proteins were laid end to end the total length would be 7.56 (10^{23}) protein molecules * 10^{-7} cm/prot molecule * m/10^2 cm * km/10^3 m = **7.56 (10^{11}) km**, which will get one from California and back quite easily.

8. What type of cell on average has more transcription going on, a growing bacterial cell or a stem cell residing in the bone marrow?

Bacterial cell. Stem cells are typically quiescent and undergo division and differentiation only when required for development or repair.

9. Where would one most likely look to isolate a new *Archaea*--spoiled hamburger or in a boiling hot spring in Yellowstone National Park?

While spoiled hamburger can be pretty nasty, some environments in Yellowstone are more akin to early Earth and present the environmental extremes that Archaea are adapted to.

10. Identify what is not true about the following statement: *Bacteria and animal cells use the same genetic code (i.e., codons) to store protein "recipes" and use the same ribosomal machinery to translate the information into functional proteins*.

The genetic code is fairly conserved, so that part is true. If that were not true, bacteria would not be able to produce human or other proteins, and rDNA technology would be not be as advanced as it is. The parts of the ribosomal machinery do, however, exhibit differences. The similarities and differences are now used as the basis for modern taxonomy.

11. Assume a cell possesses 1000 genes, but at any point in time, ten percent are being used (i.e., "expressed"). If a typical protein has 100 amino acids, what is the total number of A, G, C, and T bases that encode the cell's (a) expressed and (b) total genetic repertoire?

(a) 1000 (0.1) genes expressed * 1 prot/gene * 100 aa/prot * 3 bases/aa = **3 10^4.**

(b) total repertoire = **3 10^5.**

12. A codon in a Martian bacterium contains combinations of four of the five base-like molecules that makes up what passes for Martian DNA. An average bacterium on Earth has 4000 genes. On Mars life is quite different; hence, a larger repertoire of 6000 genes is needed to provide flexibility. By what factor is the DNA larger in a Martian bacterium compared to an Earthling bacterium? Assume a Martian protein contains about as many amino acids as an Earthling protein.

(a) 1.2 (b) 1.33 (c) 1.67 (d) 2.0 (e) 2.66

Application of basic modern biology. Information is stored in DNA. Each gene codes for a protein. A codon specifies each part (amino acid) of the protein. A codon possesses three bases on Earth. So the Martian DNA is larger than Earth's by

(6000/4000)* (4/3) = 24/12 = **2** = (factor of more genes) (factor by how much larger codons are).

13. A new organism may have been found in the University Center dining hall in the cole slaw. What is the best thing to do *first* to characterize the new cell?

(a) Sequence the entire genome.

(b) Measure mRNA stability.

(c) Look for similarity with the 16S RNA encoding stretch of DNA in other known organisms.

Modern biology is based on molecular determinism. A key concept is that cells are classified into three groups (Bacteria, Eucarya, and Archaea). They can be distinguished by not having "interchangeable" 16S RNA. If the cell appears to be "new," then it seems first "best" thing to do is to see which family it belongs to, before getting into more detailed studies. So answer (c) makes the most sense. Another way to view this is that genome sequencing is expensive so eliminate (a). Other data are meaningless if you do not even know what kind of organism it is.

WEB-BASED MATERIAL EXERCISES & RESEARCH

W1. Visit the Protein Data Bank. What is the "Molecule of the Month?" What role does it play in a cell, and in general terms, how does the molecule work?

In November 2008, mechanosensitive channels were featured. These proteins open and close an internal channel in response to the mechanical forces a cell experiences. One can imagine a fist opening and closing and in the process, the "hole the hand makes" opens and narrows. The opening and closing, in turn, allows for water to enter and leave a cell. Water movement is important because it allows the cell to adjust to changes in the osmotic strength of the environment.

W2. The basic work of Theodor (The) Svedberg on colloid systems has made a significant impact on life science where, for example, people now speak of "16S RNA." Via the Companion Website, obtain and read Svedberg's biography on the web to learn more about him. Report on the following

(a) He constructed a device that allowed him to investigate colloid and macromolecule systems in a new way. What is the device called and what does it do?

The device is an ultracentrifuge. It fractionates molecules and colloids according to size. He found, for example, a given protein has a particular size. Now that we know about genes and codons, that makes sense. At the time, it was quite an interesting finding.

(b) Did he seem to be a boring or interesting person?

He had interesting hobbies (painting, botany). He was married a number of times, had 12 children, so one could conjecture that he was pretty interesting. How he could do all that work with 12 kids is also pretty amazing.

W3. You read in an article a medical term new to you. The term you saw was "craniosynsotis." Is it spelled correctly, and what does it mean?

The correct spelling is craniosynostosis.
From **http://www.genome.gov/glossary.cfm?search=protein+structure**

A birth defect whereby an infant's skull bones are already fused at birth. Because this defect may interfere with the ability of the brain to grow normally, it is often necessary to operate on affected children.

Chapter 2

This chapter has a lot of exercises. To enable the assignment of problems, or the selection of additional practice ones, an index is provided below. Some problems are cross-referenced in two categories.

Index to Problem Types:

• Basic units: 2.1, 2.5
• Math techniques: 2.11, 2.12, 2.16, 2.18, 2.24
• Balances in physical analog systems: 2.4, 2.9, 2.10, 2.11, 2.18
• Biosystem balances: 2.2, 2.6, 2.7 (challenging), 2.14, 2.20, 2.22, 2,23
• Iron cycling: 2.3, 2.15, 2.17, 2.19, 2.21
• Kinetics: 2.8, 2.12, 2.13, 2.20, 2.22, 2.23

1. A typical cylindrical-shaped bacterial cell is 2 μm long and has a radius of 0.5 μm. Assuming that the yield is 0.3 g cell/g glucose and the density of a hydrated cell is 1.05 g/cm^3, how many molecules of glucose are needed to build one cell?

Volume of Cell = $\pi R^2 L = \pi\ (0.5)^2\ 2 = 1.57\ \mu m^3$.

Mass of one cell = $1.57\ \mu m^3 * 10^{-18}\ m^3/\mu m^3 * 10^6\ cm^3/m^3 * 1.05$ g/cc * 0.3 g dw/g = $5\ 10^{-13}$ g dw.
Mass glucose needed = $5\ 10^{-13}$ g dw *g gluc/0.3 g dw = $16.7\ 10^{-13}$ g glucose.
Molecules glucose needed = 1 mol gluc/180 g * $16.7\ 10^{-13}$ g glucose * $6.02\ 10^{23}$ molecules/mol = $\mathbf{5.6\ 10^9}$ molecules of glucose.

2. A life science experiment is to be flown on a space shuttle mission. The experiment entails studying the effects of microgravity on cell growth kinetics. This experiment is one of many that will be performed, so to manage weight only 1 kg of raw materials can be flown for this particular experiment. What are the optimal amounts of the materials, glucose ($C_6(H_20)_6$), ammonium chloride (NH_4Cl), and phosphate salt (KH_2PO_4), that can be brought on the mission if one gram of glucose yields 0.3 g cell on a dry weight basis? Optimal means that no excess mass was flown or occupied space.

We want to pick each component such that none is in excess and thus represents mass that was flown for no reason. First find the proportions needed so that none of the N, P, or C sources are in excess.

Basis: 1 g cell dry weight.

Glucose = 3.33 g.
Nitrogen = 1 * 0.14 = 0.14 g N so NH_4Cl = 53/14 * 0.14 = 0.53 g.
Phosphate = 1 * 0.04 = 0.04 g P so KH_2PO_4 = 136/31 * 0.04 = 0.175 g.
The component masses that add to one kg must also be in this proportion to maximize the cells grown while minimizing the mass of raw materials flown.

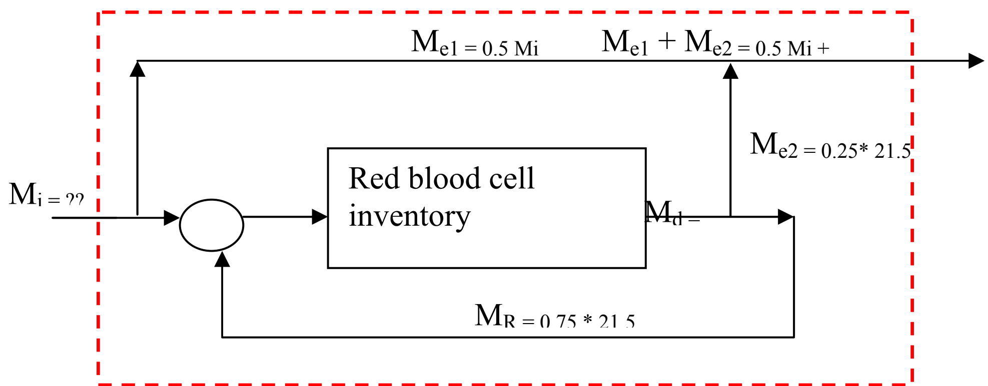
Basis: 1 kg total of C, N, and P source.
x = glucose, y = NH_4Cl, and z = KH_2PO_4.

$1 = x + y + z$.
y/x = 0.53/3.33 = 0.159.
z/x = 0.175/3.33 = 0.0526.

We now have three independent equations and three unknowns.

$1/x$ = 1 + 0.159 + 0.0526 = 1.21 so $\boldsymbol{x} =$ **0.825**.
Now having x, we find that $\boldsymbol{y} =$ **0.131** and $\boldsymbol{z} =$ **0.0434**.
Check 1 =??= 0.825 + 0.131 + 0.0434 = 0.9994; close enough for NASA work.

3. If 50% of ingested iron is not absorbed by the body and 75% of the iron in red blood cells is recycled, estimate how much iron must be ingested per day to maintain the iron content of the blood. Assume 21.5 mg iron/day is available for recycle.



Basis: 21.5 mg iron/day available from spent red blood cells (from reading) = M_d. Recycle efficiency = 75%; hence, M_R = 0.75 * 21.5 and M_{e2} = 0.25 *21.5. M_{e1} = 0.5 M_i. There are five variables and we know the values of four; hence, only one equation is needed. An overall mass balance will suffice.

$M_i = M_{e1} + M_{e2}$.
M_i = 0.5 M_i + 0.25 * 21.5.
$\boldsymbol{M_i} =$ **10.75 mg iron/day.**

4. A 1,000,000 m^3 lake has a phosphorous content of 5 mg/m^3. A river provides the lake with new water and nutrients. Rainfall provides nutrient-free water. Another river drains the lake. The local precipitation on the lake surface provides 100,000 m^3/year of water. The flow rate of the outfall is 1,000,000 m^3/year. What must the

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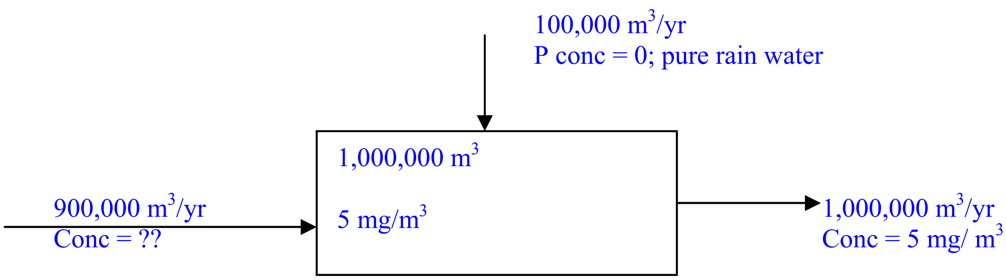
phosphorous content of the incoming river water be to maintain a constant phosphorous concentration in the lake?



Mass flow P in = mass flow P out at steady state, and volumetric flow rate of water into the lake will maintain constant lake volume

900,000 x + 100,000 (0) = 1,000,000 * 5 [mg/yr].
x = 5.56 mg/m^3.

5. The surface area of a typical human is 1.8 m^2. If you shed and replace the outer skin cells every 30 days, estimate how many cans of soda are represented by the carbon content of the lost skin cells. Assume that the typical dimension of a skin cell is 50 μm, the density of a hydrated cell is 1 g/cm^3, and a can of soda contains 36 grams of sugar as glucose.

Basis: 1.8 m^2 of exterior area of skin cells.
Number of skin cells ~ 1.8 m^2 /[50*50 10^{-12} m^2] = 7.2 10^8.
Carbon content of a skin cell ~ [50*50*50 10^{-12} cm^3] * 1 g/cm^3 *0.3 g dw/g * 0.5 g C/g dw = 1.88 10^{-8} g C.
Cans of soda equiv = total skin cell C/soda C = (7.2 10^8 * 1.88 10^{-8})/(36 *72/180) = **0.94 ~ 1 can of soda**.

6. Average daily water inputs and losses for a human at rest are summarized below

Food	1000 g
Drink	1200 g
Air In	50 g
Air Out	400 g
Metabolic Water Production	300g
Sweat	350 g (evaporated) + 200 g (damp)
Urine	1400g
Feces	200 g

If you do not drink any water, will you think that you lost weight and if so, how much?

Check the water balance to see if there is a deficit when one does not drink. This problem is also relevant to the now frowned on practice of shunning fluids (and/or wearing a sweat package) prior to a wrestling match in order to "make weight." It can also explain why you weigh less in the morning.

Water in = 1000 + 50 + 300 = 1350 g.
Water out = 400 + 350 + 200 +1400 + 200 = 2550 g.

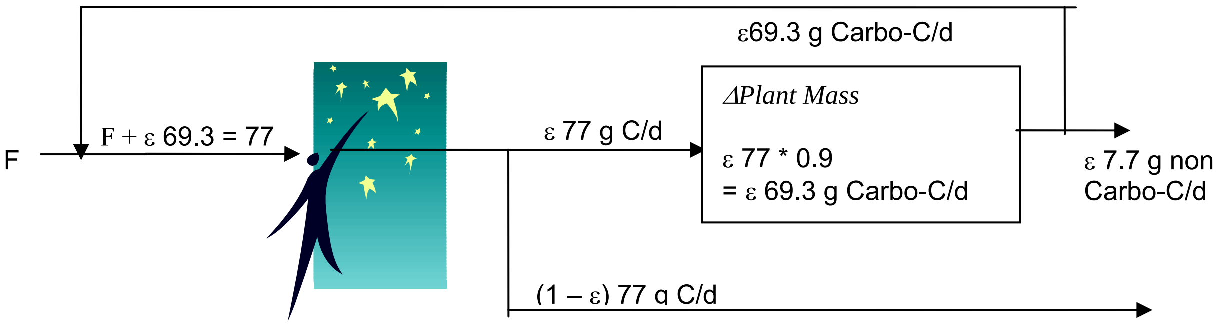
You would appear to loose 1200 g (1.2 kg, 2.6 lbs). Indeed this is the basis for why you weigh less in the morning. For eight hours or more you do not drink fluids, yet you still lose water through your lungs and other ways. That first thing in the AM elimination before you get on the scale helps the weight picture as well.

7. Consider the following proposal that has been put to a bioengineer for evaluation. If we put food crops in a space station, then the carbon dioxide released due to the activity of metabolic processes could be used to produce plant material via photosynthesis. Then, once the process was up and going, the astronauts could eat some of the plants and lower the amount of supplemental food they need to bring with them. That is a steady state inventory of plant mass can be established where new growth from fixing CO_2 by photosynthesis is harvested. Develop an operating diagram that relates how the fraction of the total glucose respired that can be derived from plants depends on the efficiency of carbon capture by photosynthesis. Assume that an astronaut exhales on average, 100 ml/min of carbon dioxide. Also assume that plants are 70% by weight water, 50% by weight carbon (water-free basis), and 90% of the plant carbon is equivalent to the carbon in glucose-like carbohydrate (i.e., can be metabolized for energy by respiration). Does this proposal seem feasible? Do you have any ideas about how to improve the process?

Basis 144 lit CO_2/d output ~ burn rate. Plants --70 wt% water, 50 wt % C water-free basis, 90% of the carbon in plants equiv to glucose-C.

Assume for now that although the plant carbohydrate could be assimilated by an astronaut, we will just look at the astronaut's energy needs. The astronaut's burn rate (CO_2 output) will be compared to the burn rate plant carbohydrate could provide.

Process Diagram



144 lit/d * 12 g C/22.4 lit = 77 g C/d; ε = efficiency of C capture

In general, F [g new C/d] = 77 – 69.3ε (basis for operating diagram).

Consider a test case. If 50% efficient at C capture & use each day's increment in plant carbo, can supply (0.5*69.3)/77 = 0.45 of total respiration. That sounds pretty good, but look at the whole picture on the space station. How much total plant material needs to be on board?

Total new plant mass production/d is 0.5*77 gC d^{-1} [g dw/0.5 g C] [g total/0.3 g dw]= 256 g new plant material/d. Here we eat each day's increment to maintain a steady state value of total plant biomass.

Thus need more than 256 g of plant mass as a standing crop to support this daily harvest. If a fast growing plant (kinetics) can increase its mass by 1 percent per day, then will need 25.6 kg total plant biomass. There will be more mass associated with the plant mass due to soil, water, or a hydroponics setup unless growth in air with a spray mist is used. There will be mass associated with horticulture supplies and equipment. Maintaining and/or finding the space for that much plant biomass and supporting gear could prove to be a challenge and has to be compared to total station size, science/technology mission requirement.

8. The doubling time of an infectious microbe is 20 minutes. How long will it take for the cell population to expand 1000-fold?

$N = N_o \exp(\mu t)$.
$\mu = 0.693/0.33\text{h} = 2.1\ \text{h}^{-1}$.
$N/N_o = 1000 = \exp(\mu t) = \exp(2.1t)$.
2.1 t = ln (1000) so t = **3.3 hours**. They can multiply pretty quickly. If not, then we probably would not get sick.

9. A sink can hold 5 liters of water. When the drain is closed, how long will it take to overflow when the flow from the faucet is 0.50 liter/min?

5 lit * min/0.5 lit = **10 minutes.**

10. A sink can hold 5 liters of water and the drain is closed. You turn on the faucet and then run to answer the phone. The outflow from the faucet is now 0.50 lit/min. After the faucet runs for 8 minutes while you are on the phone, your roommate notices that the faucet is on. The faucet is turned off by your roommate, but due to a worn washer, the faucet drips at 0.0022 lit/min. You both forget about the sink and go to sleep for eight hours. Will there be water on the floor in the morning when you wake up?

Here, have to make a balance and keep track of total allowed and how much is present at a certain point in time, which is somewhat reminiscent of S_o = present + used. After eight minutes, 8 min * 0.50 lit/min = 4 lit. So we are 1 lit away from overflow. While dripping overnight, the volume added is 8*60*0.0022 = 1.056 lit. Exceed capacity by **0.056 lit so there will be a small volume of water on the floor.**

11. A sink with the drain closed initially holds 5 liters of water (V_o = 5 lit). The drain is opened and water begins to drain. The rate that water drains from the sink is proportional to the volume remaining in the sink; hence, $dV(t)/dt = -\alpha V(t)$. Derive an equation that shows how the volume remaining depends on the initial volume (V_o) and α.

$dV/dt = -\alpha V$ can be separated as $dV/V = -\alpha dt$. Integrating both sides using the limits, $t = 0$, $V = V_o$ and t, V yields: $\boldsymbol{V(t) = V_o \exp(-\alpha t)}$.

12. A ten-fold cell proliferation in cell mass occurs. Assume that internal control of the kinetics occurs over the majority of time with X_o = 0.1 g/l; μ = 2 h^{-1}; and Y = 0.5 g cell/g glucose. Derive how S depends on t and then plot $S(t)$ versus time (t) when S_o is 1.8 g/l and 5 g/l. Discuss how the internal control assumption can cause the long time behavior of $S(t)$ on your plot to differ from reality. What would the long-time section of the curve look like in reality?

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Mass Balance on reactant (e.g. glucose; aka "substrate"):

$S_o = S(t) + \frac{[X(t) - X_o]}{Y}$ = initial present = that which remains + that which got used.

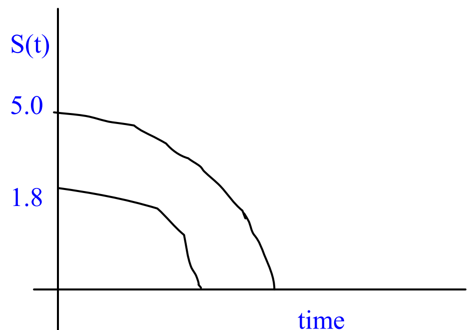
Now for internal control, $X(t) = X_o \exp(\mu t)$. So combining the kinetics and mass balance yields S as a function of time, t.

$$S(t) = S_o - \frac{[X_o \exp(\mu t) - X_o]}{Y} = S_o - \frac{X_o [\exp(\mu t) - 1]}{Y}.$$

Does this answer make sense? If $t = 0$, $S(t)$ should equal S_o because no time has been allowed for growth and nutrient consumption to occur.

Lim t tends to 0, $S(t) = S_o - \frac{X_o [1 - 1]}{Y} = S_o$; makes sense, therefore probably did math OK.

The general shape of the curves will look like.



Note: As S becomes small, internal control will likely not be the case. The initial and medium time behavior may be described OK, but long time behavior will be predicted to drop off faster than may actually happen. If we had a kinetic model that described how cell growth rate depends on both high and low concentration, rather than limiting extremes, we could be more accurate at long time.

13. Often a nutrient or energy source is not in excess and the concentration limits the cellular growth rate. For example, some leukemia cells require the amino acid asparagine, and this amino acid is not prevalent in the blood stream. Consequently, one therapy for leukemia is to inject a patient with the enzyme asparaginase, which catalyzes the removal of the amino group, thereby lowering the availability of asparagine to leukemia cells even further. When external control exists on growth kinetics, estimate by what factor the time will increase for a one thousand-fold

expansion of cells when the asparagine concentration in the blood stream is reduced from 10^{-7} mol/lit to 10^{-9} mol/lit. Assume that $k = 10^5$ h^{-1} mol^{-1} lit.

When external control is the case, the concentration of some nutrient will influence the rate. A low value will provide a low rate and increasing concentration will increase rate. So we need to compare how much time is required for the cells to expand in number when (1) no drug is used ($S_1 = 10^{-7}$ mol/lit) to (2) when the drug is used ($S_2 = 10^{-9}$ mol/lit) to gain a sense of the effect. First find out how much time is required for the general case, then use the numbers. Often a general analysis will boil down to something simple, so we do not have to use the numbers and solve the problem for each set of numbers.

$dN/dt = kSN$; for a given case, k and S are constant so let $k' = kS$.

$dN/dt = k'N$; this looks like something we have dealt with before: $dy/dx = ay$.

Separating and rearranging into things we have been taught how to integrate

$\int dN/N = k'\int dt$ where the lower limits are $t = 0$, $N = N_o$ and upper limits are t and N.
$\ln (N/N_o) = k't$ or $t = 1/k \ln (N/N_o)$

$\ln(N/N_o)$ is the same for both the w/o drug and with drug cases; it equals ln (1000). A fixed amount of expansion is the basis for which the different times needed are being compared. So the factor time increases for a 1000-fold expansion for case 1 vs. case 2 is

$t_2/t_1 = [1/k'_2]/[1/k'_1] = k'_1/k'_2 = kS_1/kS_2 = S_1/S_2 = 10^{-7}/10^{-9}$ = **100-fold more time is required.**

Answer makes sense. Less amino acid concentration, the slower the bad cells will increase in number and progress the disease. **Note:** some exercises in other chapters will refer back to this problem.

14. When at rest, a typical person's ventilation rate is 6000 ml/min (at STP). When one exhales, carbon dioxide is emitted at a rate of 200 ml/min (STP). In a 20 m * 15 m * 8 m lecture hall, there are 50 people.

(a) Estimate the carbon dioxide concentration (mol/lit) in the room after 50 minutes, assuming the concentration was zero at the start of class. Assume that the room is roughly at STP conditions and no one passes out.

Total CO_2 output = 200 ml/min-person * 50 people * 50 minutes = 500 liters.
CO_2 conc = 500 liters * mol/22.4 lit * 1/(20*15*8 m^3) * 10^{-3} m^3/lit = **9.3 10^{-6} mol/lit.**

(b) Re-estimate the concentration at the end of class, assuming this time that each dimension of the room is cut in half.

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The volume is reduced by a factor of eight so the concentration increases by eight to **7.4 10^{-5} mol/lit.**

(c) Why does the pressure not rise due to all that CO_2 release?

Because for every mole of CO_2 produced, a mole of oxygen was removed by respiration, thereby not adding or subtracting net moles. The water can condense on the cooler windows. It is a reaction in a closed system with no net change in the number of gas molecules if the water condenses and fogs the windows. There is probably a lot of "fog" in the room already.

(d) There are places in Africa where lakes emit CO_2. The gas disperses over the surrounding land. Because CO_2 is dense, it tends to sink into the depressions in the surrounding landscape. Small animals fall into these depressions and die from asphyxiation. Larger animals attempt to feed on the smaller animals and they, in turn, perish in the toxic environment. Only animals with suitable physiology and stature can survive the high CO_2 concentration that can be established close to the ground, and they prosper from these asphyxiation events by foraging on the victims of asphyxiation. Lakes Nyos and Monoun are particularly infamous for their CO_2 releases, which can also kill humans in surrounding communities. For humans, a CO_2 concentration that exceeds 4.46 10^{-3} mol/lit (10 percent) can be lethal. In view of these facts, what do you conclude about the need for ventilation in the lecture hall?

If the air in the room never turns over, eventually there could be a problem. Leaky windows and opening the door between classes will probably help freshen up the air. So the workload in the class will probably kill me before the CO_2 in the classroom does.

15. A patient has impaired iron elimination. All iron ingested is absorbed (i.e. $M_{e1} = 0$) so feedback control with respect to absorption in the digestive track is defective due to disease.

(a) Show that at steady state, $M_i = M_d (1 - \varepsilon)$.

$M_i = M_{e2}$ from overall balance.

$M_d = M_R + M_{e2} = \varepsilon M_R + M_{e2}$ from balance at recycle boundary; hence, $M_{e2} = M_d(1 - \varepsilon)$.

Combining the above two equations yields the result.

(b) If M_d still equals 21.5 mg iron/day and the recycle efficiency (ε) is 90 percent, would you advise the patient to continue to ingest 8 mg iron/day?

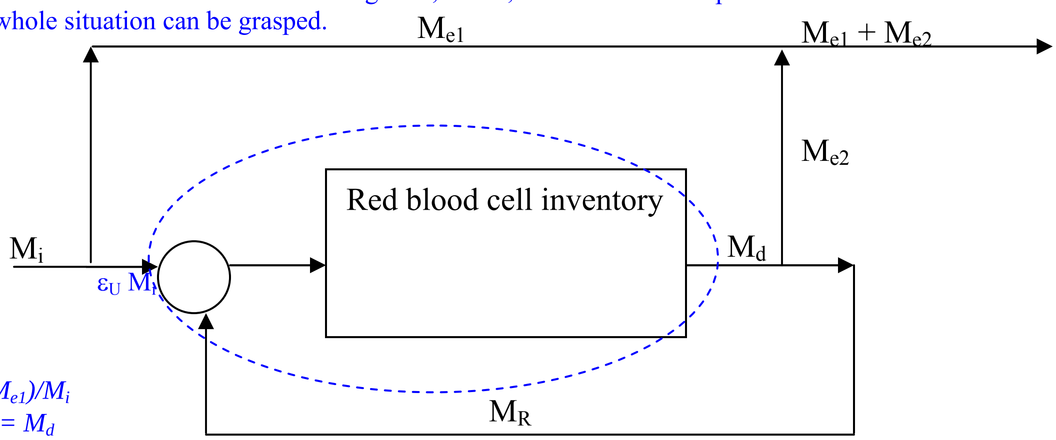
No. M_i should be 21.5 (0.1) = **2.15 mg/d.**

16. Some solution techniques were reviewed/introduced and will be used again. What is the solution to $dy/dt = -ky^2$ for $y = 1$ at $t = 0$. "Solution" means how does y depends on time, t.

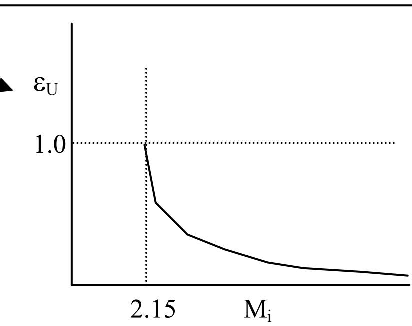
$\boldsymbol{y = (1 + kt)^{-1}}$ using separation of variables.

17. A patient has impaired iron absorption. However, 90 percent of the iron in red blood cells is still recycled and 21.5 mg of iron is available for recycling per day. Generate an operating diagram that depicts how the efficiency of uptake of ingested iron (ε_U; $\varepsilon_U = 1$ means all ingested iron is absorbed rather than eliminated) depends on the daily mass ingested (Mi). Such a diagram could provide disease management guidance.

Analysis of a mass flow network and looking at the iron problem again. Also a picture (i.e., operating diagram) is often more informative to an engineer, nurse, or doctor than a pile of numbers. With one glance, the whole situation can be grasped.



$\varepsilon_U = (M_i - M_{e1})/M_i$
$\varepsilon_U M_i + M_R = M_d$
$\varepsilon_U M_i + 0.9\,(21.5) = 21.5$
$\varepsilon_U M_i = 0.1(21.5) = 2.15$
$\varepsilon_U = 2.15/M_i$



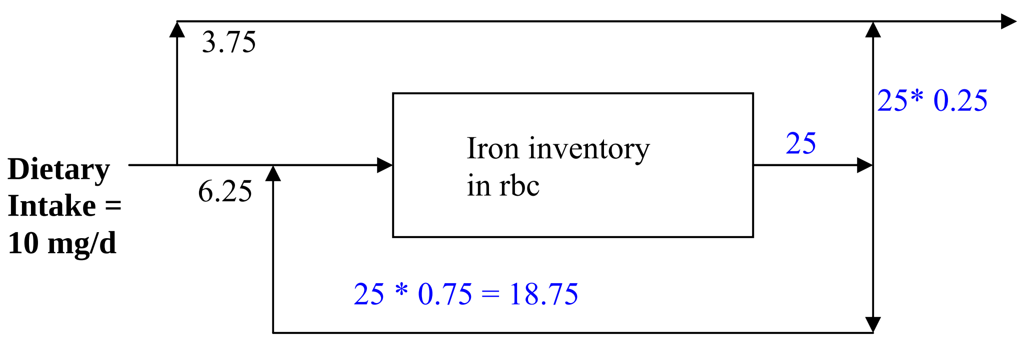
18. A sink holds of total volume V_T. Water flows in at a constant volumetric rate Q (volume that flows in/time). Water drains out of the sink at the volumetric rate αV, where V is the volume of water in the sink and α is a constant. Find a general relationship that relates how long it will take to fill the sink for the case, $Q > \alpha V_T$.

$dV/dt = Q - \alpha V$ where $V = 0$ when $t = 0$. Separation of variables results in

$\int dV/(Q - \alpha V) = \int dt$

$\mathbf{t = (-1/\alpha) \ln (1 - \alpha V Q^{-1})}$ so time to fill is $(-1/\alpha) \ln (1 - \alpha V_T Q^{-1})$.

19. A patient ingests 10 mg of iron per day. His ability to recycle iron from worn out red blood cells is abnormally low and equals 75 percent. What percentage of the ingested iron is actually absorbed through the digestive system and used by the patient? Assume that the patient has 25 mg iron/day released from burned-out red blood cells.



Equation 2.5 works where $M_i = 10$, $M_d = 25$, and $\varepsilon = 0.75$. Or the easier way of using inspection can be pursued if one understands how the bodily processes map onto the flow sheet. Numbers are shown on Figure when inspection is used.

18.75 is recycled. Need a total of 25 to keep the rbc inventory balanced. So 25 – 18.75 = 6.25 must be absorbed from the dietary intake. **Thus, 6.25/10 ~ 60% of eaten is absorbed/used.** 40% of iron eaten is discarded by the activity of the cells in the GI track and their iron binding proteins.

20. A growth medium contains, in part, 1 g glucose/lit and 0.6 g NH_4Cl/liter. The cells to be grown have a yield on glucose equal to 0.3 g cell dry weight/g glucose. It is

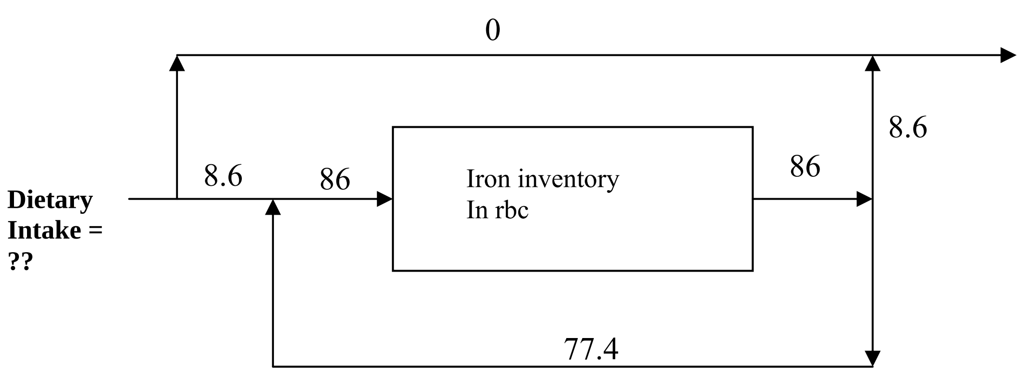
desired to grown more cells per batch; hence, 5 g glucose/liter will now be used. Is 0.6 g NH_4Cl/liter sufficient or should a higher concentration be used?

Basis: 1 g glucose/lit
Cells produced = 0.3 * 1 = 0.3 g dwt/lit
NH_4Cl required = 0.3 * 0.14 g N/g cell dwt * 53 g NH_4Cl/14 g N = 0.3 * 0.53 = 0.158 g NH_4Cl/lit
So initially, NH_4Cl is in excess, so maybe using 5 g/lit of glucose will yield 5X more cells.

NH_4Cl required when 5 g glucose/lit used = 5 * 0.3 g cell dwt/g glucose * 0.14 g N/g cell dwt * 53/14 > 0.6
So 0.6 g NH_4Cl/lit is insufficient to react the entire 5 g/lit of glucose. Another way to look at it is there will be more cells, but not all of the glucose added will be used.

21. A patient with hemolytic anemia suffers with short red cell lifetime. The lifetime of a red blood cell is 30 days as opposed to the typical case of 120 days and an iron release rate of 21.5 mg/day. What is the minimum amount of iron per day that the patient should ingest if 90% of the iron released from red cells is recycled? Assume that the hematocrit is at its normal value.

The iron release rate of 21.5 mg/day is based on a normal hematocrit and red cell lifetime. If the lifetime of a red cell decreases and the hematocrit is the same, the release rate increases by 21.5 (120/30) = 86 mg/day. The minimum to ingest corresponds to when there is zero loss through the digestive system. The answer, **8.6 mg/day**, can be easily determined by inspection as shown below.



22. A recombinant bacteria is to be grown in a batch process for the production of interferon. The cell has a specific growth rate of 1 h^{-1} and a yield on glucose = 0.3 g cell dry weight/g glucose. What is the minimum amounts (in grams) of glucose and ammonium chloride (NH_4Cl) that should be in 1 liter of growth medium in order to produce 10 g cell dry weight/liter when the initial cell concentration in the bioreactor is 0.01 g cell dry weight/liter?

Assume other nutrients like phosphate are in excess. What is the minimum length of time it will take to produce the 10 g cell dry weight/liter?

Basis: 1 Liter
ΔX = 10 – 0.01 = 9.99 g cell dry wt/lit; so produce 9.99 g cells in one liter.
Glucose used = 9.99/0.3 = 33.3 g glucose
NH_4Cl used = 9.99 g cell (0.14 g N/g cell) (53.5 g NH_4Cl/g N) = 0.0026 g NH_4Cl
The minimum time would corresponds to when growth is entirely exponential.
$X = X_o \exp(\mu_m t)$ = 10 = 0.01 exp (1 t) → **t = ln 1000 = 6.9 h**.

23. In lab culture, a cancer cell has a maximal specific growth rate of 0.04 h^{-1} and a yield on glucose equal to 0.3 g cell dry weight/g glucose. The goal is to grow a lot of cancer cells over 24 hours, because after growing them, you plan to investigate the response of different samples of cells to different drugs. Initially there is 0.2 g dry weight/liter of cells present. Will 2 g glucose/liter be sufficient to support growth for 24 hours?

μ_m [h^{-1}] was given, not k [lit mol^{-1} h^{-1}] so internal control applies. If the hint/meaning of parameters was missed, then logic can still prevail. Internal control will result in the fastest growth rate and the highest glucose consumption. Thus, determine if any glucose is left over after the cells grow at their max for 24 h.

$X = X_o \exp(\mu_m t)$ = 0.2 exp (0.04 * 24) = 0.522 g/lit
$(X - X_o)/Y = S_o - S$ = glucose "eaten" = (0.522 – 0.2)/0.3 ~ 1 g/lit.

Cells eat 1 g/lit over 24 h when growing at max rate, which leaves ~ 1 g/lit left, so **YES** 2 g glucose/lit is plenty.

24. How *y* changes with time (*t*) is given by

$$dy/dt = 1/y, \text{ where } y = 2 \text{ when } t = 4.$$

At what time will $y = 10$, where t in the above equations has units of hours.

Separation of variables: $\int y\, dy = \int dt$
Integration: $\frac{1}{2} y^2 = t + c$
Use initial value info to determine c: $\frac{1}{2}(2^2) = 4 + c$; hence, c = -2
Thus, time for y = 10 is $\frac{1}{2}(10^2) = t - 2$, resulting in **t = 52 h**.

WEB-BASED MATERIAL EXERCISES & RESEARCH

W1. From the statement "How much iron you need and other facts," (see Companion Website) answer the following.

(a) A patient takes 66.7 mg/day of ferrous gluconate as a supplement under a physician's supervision. If instead, ferrous fumarate was taken as an iron supplement, what would be the correct daily dosage?

http://ods.od.nih.gov/Health_Information/Vitamin_and_Mineral_Supplement_Fact_sheets.aspx

There one finds that ferrous gluconate is 12% by weight iron. A 66.7 mg dose thus provides 66.7*0.12 = 8 mg. The alternative supplement is 33% iron; hence, should use 12/33 * 66.7 = 24.2 mg/day.

(b) Why do you think that children between 7-12 months of age require more iron per day than adults?

Thinking kinetically, their relative rate of mass increase is higher than adults. Thus, while their total mass is less than an adult, faster assembly and cell division occurs, which if not accounted for, will dilute out the inventory in the body unless intake is maintained at a somewhat higher level.

(c) Can one ingest too much iron?

Yes! Organ damage can result and be excaberated by the condition known as **hemochromatosis.**

W2. What is one life-threatening complication that a physician may have to contend with when administering asparingase? Define this complication further in terms of symptoms. Feel free to use the on-line medical and life science glossaries indexed on the Companion Website for Chapter 1.

Anaphylaxis, where the definition can be found as follows—

1. Hit link below on Companion Website
   Science Magazine Guide to On-Line Life Science Glossaries
   http://www.sciencemag.org/feature/plus/sfg/education/glossaries.shtml

2. Once there, look under **Medical Genomics** header, and hit link to **On-Line Medical Dictionary,** which carries one to http://cancerweb.ncl.ac.uk/omd/

3. Enter **Anaphylaxis** as a search term and retrieve the definition below

Anaphylaxis <immunology> An inflammatory reactions produced by an antigen combining with IgE bound to a mast cell that produces degranulation of the mast cell and subsequent release of histamine and histamine like substances.

This can produce a localised or global immune reponse that results in an acute allergic reaction with shortness of breath, rash, wheezing, hypotension.