Each homework consists of 3 problems, and you are expected to spend 30 min to 1 hour on each problem, but definitely less than 1 hour. If you find yourself spending more than 1 hour, you are probably overthinking about it.

1 Order of magnitude physics - bombs

In this problem, we will practice our order of magnitude (OoM) reasoning by thinking about scaling for bombs.

1.1 Free Fall and terminal velocity

Let us first consider dropping the bombs from a flying bomber aircraft. How big does the bomb needs to be so that it maintains free fall when it hits ground? This is highly desirable, since if it maintains free fall, then its trajectory is ballistic and it becomes much easier to predict where it will hit. (Free fall means the only major force on the bomb is gravitational force.)

1. For macroscopic objects going through the air, this is the high Reynolds number situation, i.e. Reynolds number $Re \gg 1$. In such cases, objects experience free fall at low speed where gravitational force is the only force on the object, and as the speed increases, eventually it reaches terminal velocity where the gravitational force balances with the drag force from air resistance. The terminal velocity v satisfies (assuming $\rho_s \gg \rho_a$, density of solid ρ_s is much greater than density of air ρ_a):

   $$v^2 \propto \frac{\rho_s}{\rho_a} R g, \tag{1}$$

   where R is the radius of the object, assumed spherical, and g is the gravitational constant. For rough estimate, we can treat the proportionality constant to be unity.

   Could you see how the above scaling is derived?

   (Hint: drag force from air resistance scales with the velocity squared, and scales with the surface area. The exact formula is $F_{\text{drag}} = \frac{C_d \pi}{2} \rho_a v^2 R^2$.)

2. If you jump off an aircraft, what would be your terminal velocity? How much time does it take to reach terminal velocity by gravitational acceleration? What's the height needed for you to reach free fall before hitting the ground?

   (Hint: Human body has $\rho_s/\rho_a \approx 10^3$.)

3. If we let the bomb fall from 5km high, and assumes it maintains free fall when hitting the ground, then what's the free fall speed? Do we need to consider the bomb crossing the sound barrier or not? For this to happen, how big the bomb needs to be? (Hint: Speed of sound in air is about $c_s = 340\text{m/s}$.)

1.2 Why build nuclear weapon? More bang for the buck...

This is the famous back-of-envelope calculation done on nuclear bombs in terms of TNT equivalence when the dynamics of the nuclear bomb test was first seen.

The fact is, we see nuclear bomb happen in about 2ms, and the mushroom cloud diameter is about 100m.

1. Let the energy of the explosion be E. The circles or spheres formed are mostly air, hot air, not bomb material when $R > \left(\frac{\rho_s}{\rho_a}\right)^{\frac{1}{3}} R_{bomb}$, where ρ_s is density of bomb material, and ρ_a is density of air.

   The relevant variables are energy released E, duration of expansion t, radius of cloud R, and density of air ρ_a. Temperature and pressure doesn't matter as speed of expansion is much faster than speed of sound, or $E \gg p_{air} R^3$. 4 variables with 3 units, so only one dimensionless quantity.

What is this dimensionless quantity? Denote this dimensionless quantity Π_1.

For air, $\Pi_1 = 1.03$, so very good.

Plug in $t = 2$ms, $R = 50$m, and $\rho_a = 1$g per cube cm. Check that you have $E \sim 10^{14}$J. This is the estimate of energy released by the nuclear bomb.

If you'd like to skip the calculations below, use 4 kJ/g as the burning energy density of TNT to obtain the kilo ton TNT equivalence of the nuclear bomb.

2. (Optional) Now we estimate the energy of burning TNT.

   TNT has molecular formula of $C_6H_2(CH_3)(NO_2)_3$, which is a carbon-based fuel. To calculate the energy of burning carbon-based fuel, we consider the energy released from the covalent bonds broken.

   The energy in covalent bonds are electrostatic, so it should be proportional to the charges squared divided by distance, $E_{\text{covalent bond}} \sim \frac{e^2}{a}$, where a is size of atom, and e is the charge of one electron. Not all energy will be released, as the molecule is only re-configured. Burning reaction is essentially $(C)_n + (O_2)_n \to (CO_2)_n$. So say the energy released in burning is 1/5 of the covalent bond energy. Then

$$E \sim \frac{1}{5}\frac{e^2}{a}$$

   which is approximately 5×10^{-19} J or 2.3eV.

   Estimate the energy released in burning 1 gram of hydrocarbon, and compare your estimate to the actual numbers below.

   Reporting actual numbers for burning energy in units of 10^4 J/g, we have

	heating oil	Natural Gas	Kerosine	Coal	Wood
E	4.4	4.8	4.8	2.8	2.5

   For TNT, molar mass is 227g, or about 20 times carbon molar mass. TNT molecule has 3 strong covalent bonds rearranged. This gives about $1/10$ of energy from burning carbon. So energy per g of TNT is approximately $1/10$ of energy per g of hydrocarbon.

   What's the energy of burning one kilo ton of TNT? What's the kilo ton equivalence of the atomic bomb based on this estimate?

1.3 Why no big bombs anymore

Because smaller bombs destroy larger area... To reason about this, let us calculate the destruction area.

1. Take the equation we obtained from the dimensionless quantity at the beginning of this problem, and rewrite it using the speed of expansion v replacing the t variable. Express R in terms of E, ρ_a and v.

2. The speed of expansion can be considered roughly constant, around the speed of sound, when the mushroom expands. This allows us to consider the destruction area $A \propto R^2$. What's the scaling of A with respect to E?

   If we split the same amount of energy into N bombs, how does A scale with E and N? Does it increase with N or decrease with it?

2 Order of magnitude biology - metabolism vs gene expression

2.1 Which is larger? mRNA or proteins?

From central dogma, we know mRNA encodes the amino acid sequence of proteins. Therefore, mRNA is often called the blueprint of proteins, the molecules that drive life's actions. Which is typically larger in our daily lives, the blueprint or the machine or object it encodes, such as buildings or cars? Now regarding mRNAs and proteins, which is typically larger, in terms of mass and volume, and by how much?

Try to draw to scale a sketch cartoon depicting an mRNA molecule with a typical length, and the globular protein molecule it encodes for.

2.2 Metabolism vs gene expression

When the production and consumption fluxes of a metabolite are not equal, either the metabolite pool will be depleted or overflown. So the fluxes need to be adjusted on the metabolism time scale to maintain a stable balance. Can metabolism be controlled and stabilized by gene expression directly, or does it have to be controlled by mechanisms that take action much faster?

1. What's the turnover time of metabolism? The turnover time is the amount of time it takes to fully produce or consume the pool of a metabolite in the cell. If you need a specific metabolic pathway to think about, consider the glycolysis pathway as a representative example.

2. What's the time it takes to change the concentration of enzymes significantly via gene expression?

3. How does the two time scales compare? Could gene expression be fast enough to directly control metabolism? Does this justify the existence of other regulatory mechanisms of enzyme activity such as allostery and post translational modifications? If you do the estimates for both bacteria and mammalian cells, does the conclusion change?

2.3 How much head space when culturing bacteria?

You probably have heard the rule of thumb that you should leave 5 fold head space when culturing aerobic bacteria, e.g. for a 15 ml culturing tube, you should put in no more than about 2ml of liquid culture. This comes from the estimate for the air in the head space of the tube needed to supply enough oxygen for the bacteria to grow. Let us estimate whether this makes sense.

1. How much oxygen is needed for E coli aerobic growth on glucose? You could express this simply as the number of oxygen atoms needed for each glucose consumed for biomass growth.

   (Hint: If you need numbers to start with, you could consider the concentration of glucose in the media to be 0.2% by mass, and that the biomass yield of glucose is about 0.5, i.e. half is used for energy and half is grown into biomass.)

2. What's the amount of air needed to grow a unit volume (e.g. 1 mL) of saturated E coli culture? How much head space is needed when culturing E coli in a tube, assuming there is no air exchange with outside of the tube once the culture starts? Would the amount of oxygen dissolved in the media be significant?c

3 Chemical reaction networks - write them down

For this problem, glance through the papers referenced and write down a chemical reaction network description for the regulatory pathways of concern. Make sure to keep in mind the distinction between elementary and composite reactions.

3.1 Repressilator and toggle switches

Glance through these two papers [1, 2] that kick started the synthetic biology revolution in 2000, and write down the chemical reaction networks for the genetic circuits they constructed.

3.2 BMP signaling pathway and multifate

Glance through these two papers on combinatorial regulations in cell signaling [3] and cell fate determination for developmental biology [4], write down the chemical reaction networks.

3.3 Glycolytic oscillations

Glance through the paper [5] with a simplified description of the glycolysis pathway, write down the chemical reactions.

3.4 Lac operon

Based on the description for the lac utilization network in [6], `https://www.nature.com/articles/nature02298`, write down the chemical reactions.

References

[1] T. S. Gardner, C. R. Cantor, and J. J. Collins, "Construction of a genetic toggle switch in escherichia coli," *Nature*, vol. 403, no. 6767, pp. 339–342, Jan 2000. [Online]. Available: https://doi.org/10.1038/35002131

[2] M. B. Elowitz and S. Leibler, "A synthetic oscillatory network of transcriptional regulators," *Nature*, vol. 403, no. 6767, pp. 335–338, 2000.

[3] Y. E. Antebi, J. M. Linton, H. Klumpe, B. Bintu, M. Gong, C. Su, R. McCardell, and M. B. Elowitz, "Combinatorial signal perception in the bmp pathway," *Cell*, vol. 170, no. 6, pp. 1184–1196.e24, 2017. [Online]. Available: https://www.sciencedirect.com/science/article/pii/S0092867417309406

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[5] F. A. Chandra, G. Buzi, and J. C. Doyle, "Glycolytic oscillations and limits on robust efficiency," *Science*, vol. 333, no. 6039, pp. 187–192, 2011.

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