MCB137L: Homework 12: Final Project

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Note:

The origin copy files can be found in GitHub:

https://github.com/HULinfengHideki/MCB137_HW12

For the estimations in question 2, they are written in Typora, a markdown compiler. And the screenshot is attached in the word file.

1 Physical Biology of the Cell: Your Turn (syllabus design)

MCB137L / MCB237L: Physical Biology of the Cell

Course Overview

To equip students with a comprehensive understanding of physical biology using quantitative models, and applying mathematics, physics, and computer science to solve biological problems.

Learning Orientations:

Students should leave the course with the ability to:

1. Make simple estimations of common parameters in cell biology, at least at the order of magnitude level.
2. Utilize literature and online resources (such as BioNumbers) to collect basic data, with a fundamental understanding of programming, data fitting, and data visualization tools, and basic skills in using large language models to assist programming.
3. Replicate existing biophysics models and validate empirical data, with advanced skills including questioning basic models and making simple optimizations.
4. Explain biological phenomena based on mathematical models, such as explaining cell fate decisions starting from mathematical models.
5. Have a general understanding of biological processes simulated based on statistical mechanics; know basic idea to analyze biological processes from energy pathways.

Top Insights:

Student should obtain some basic understanding and inspirations into:

1. The root properties of biological problems are essentially physics and chemical processes, which can be described by mathematical modelling (e.g. evolutionary principles).
2. The significance and validation of magnitude, diffusion, and dynamic states and processes in the context of cell biology.
3. The role of probability distribution in understanding biological stochastic processes: how the probability “maps” the real-world cases?
4. The sophistication of biological network: how to study their nature by dynamic approach?
5. The interpretability of the model: what is the models’ range of application? What is the portability of the model?

Course Format:

- Lectures: Twice weekly, focusing on general theory, with a mix of PowerPoint presentations and blackboard calculations.
- Discussion Session: Extension to the content in the lecture; discuss the assignment; hand-on data analysis and simulation.
- Homework: Weekly assignments on the topics covered in the corresponding lectures. There will be estimation calculations, theoretical model conductions, code interpretation, data analysis and visualization.
- Midterm Quiz: One midterm quiz in discussion, mainly focusing on quantification protocol in bounding energy.
- Final Project: Replication of experimental based on given data, experimental design, and guidance protocols. Also, course concepts integration can be incorporated.

Assessment:

Item	Percentage
Attendance and Participation	10%
Homework	60%
Midterm Quiz	10%
Final Project	20%

PowerPoints Arrangement:

Lecture 1-3	- Introduction to MCB 137/237 - Fundamentals: estimation on biology parameters, magnitude in cell biology - Tools tutorial: GPT-assisted coding, pseudo code, and basic prompt
Lecture 4-6	- Simple modeling and reviews on statistics and probabilities - Bacterial growth model (sizer, adder, timer): expectations - Estimation: composition of single cell and synthetic factors - Review: Poisson distribution and Exponential curves
Lecture 7-8	- Role of probability in biological processes - Real-world applications and theoretical understanding - Case studies: mutations, ion channel
Lecture 9-11	- Diffusion as Biology's Null Hypothesis for Dynamics - Detailed exploration of diffusion processes (e.g. axonal transport) - Case studies: calibrating fluorescent protein counts, FRAP measuring diffusion and establish limits for enzyme catalysis and other reactions
Lecture 12-15	- Entropy Rules: basis of thermodynamics - Entropy maximization principles and their implications in biological systems - Ensemble: a set of imagination

	- Case study: entropic forces-DNA as an entropic spring
Lecture 16-17	- Phase transition: theoretical and practical impacts - Entropy maximization and free energy maximization - Hands-on coding: phase transition diagram - Case study: F1B-1 and nucleolar size
Lecture 18-22	- Introduction to the Boltzmann Distribution and its application to ion channels and two-state systems - "Energy favorable" approach: nature of binding problems in biology - Case study: simple repression in the lac operon - Kinetic proofreading and its role in ensuring biological specificity - Maxwell's demon and local entropy reduction
Lecture 23-25	- Simple graph theory and its application in biological network - Case study: lambda switch - Genetic circuit: Logic gate and positive/negative feedback
Lecture 26-29	- Overview of Monte Carlo methods - Simple Monte Carlo simulation in Python: implementing a random walk as a Markovian process - Introduction to ligand-target docking and Markovian sampling - Introduction to AlphaFold 2 and protein structure prediction
Lecture 30	- Comprehensive review of key concepts covered throughout the course, highlighting connections between topics - Discussion on potential future directions in physical biology - how current students can contribute to these areas

Tentative syllabus:

Lectures 1 - 3: Introduction to Physical Biology

- Overview of MCB 137/237, introducing course goals and applications of mathematics, physics, and computer science in solving biological problems.
- Techniques for estimating biological parameters at the order of magnitude level.
- Introduction to GPT-assisted coding, pseudo code, and basic prompts for biological computations.

Lectures 4 - 6: Modeling and Statistical Fundamentals

- Introduction to basic models in biology, focusing on bacterial growth models such as sizer, adder, timer.
- Estimation of compositions in single cells and synthetic biological factors.
- Discussion on the application of Poisson distribution and exponential growth curves in biology.

Lectures 7 - 8: The Role of Probability in Biological Systems

- Exploration of how probability theories apply to biological systems, with real-world applications.

- Case studies on mutations and ion channel dynamics to demonstrate probability in action.

Lectures 9 - 11: Dynamics of Biological Systems

- Examination of diffusion processes, including axonal transport, as fundamental dynamics in biology.
- Case studies using fluorescent protein calibration and FRAP to measure diffusion limits and enzyme catalysis.

Lectures 12 - 15: Thermodynamics and Entropy in Biology

- Exploration of entropy rules and their implications in biological systems.
- Case study on DNA as an entropic spring, illustrating thermodynamic principles in biological contexts.

Lectures 16 - 17: Phase Transitions and Energy

- Examination of phase transitions in biological contexts and their theoretical and practical impacts.
- Hands-on activity with coding for phase transition diagrams and exploring entropy and free energy maximization.

Lectures 18 - 22: Boltzmann Distribution and Molecular Interactions

- Application of Boltzmann principles to ion channels and two-state systems.
- Exploration of kinetic proofreading, Maxwell's demon, and local entropy reduction to ensure biological specificity.

Lectures 23 - 25: Networks and Systems in Biology

- Application of simple graph theory to understanding complex biological networks.
- Investigations into lambda switches and genetic circuits, emphasizing logic gates and feedback mechanisms.

Lectures 26 - 29: Monte Carlo Methods and Their Applications

- Introduction to Monte Carlo methods and their broad applications in biological systems.
- Implementation of simple Monte Carlo simulations in Python, ligand-target docking simulations, and introduction to AlphaFold 2 for protein structure prediction.

Lecture 30: Course Review and Future Directions

- Comprehensive review of key concepts covered throughout the course, emphasizing the integration of physical biology principles.
- Discussion on future directions in physical biology and how current students might contribute to the field.

2 Order of Magnitude Estimation

Question chosen: 4, 6, 8, 9, 10, 12, 18, 20, 22, 29, 30, 31, 34, 36, 38.

Question 4 pH and ion numbers.

At the typical pH of a bacterial cell, how many hydrogen ions does that correspond to?

Answer:

According to BNID 107037, the internal pH of E.coli is 7.85 ± 0.05.

Since pH is the minus value of concentration of hydrogen ion: $[H^+] = 10^{-pH}$.

Thus, the concentration of proton is approximately:

$$[H^+] = 10^{-7.85} \approx 1.4 \times 10^{-8} mol/L$$

As we estimated in the class, an E.coli can be simplified as a cubic with $1\mu m$ side length. The volume can be estimated as $1\mu m^3$.

$1\mu m^3 = 10^{-18} m^3 = 10^{-15} L$.

The molar number of proton is:

$$N_{moler} = 1.4 \times 10^{-8} mol/L \times 10^{-15} L = 1.4 \times 10^{-23} mol$$

The actual number of hydrogen ion in an E.coli at pH=7.85 would be:

$$N = 1.4 \times 10^{-23} \times 6.02 \times 10^{23} \approx 8 \text{ ions/cell}$$

If we simply estimate the **pH value to be 7**, the answer would be approximately **60** ions per cell.

Question 6 Lipids per cell

How many lipids are there in a bacterial cell?

Answer:

As we estimated in the class, an E.coli can be simplified as a cubic with $1\mu m$ side length. Thus the surface of an E.coli is approximately $6\mu m^2$.

According to BNID 106993, surface area per lipid molecule is $0.5nm^2$.

Note that most of the lipids locate in the cell membrane in the form of **bilayer** lipids.

Thus, we can calculate calculate the number of lipids in a single layer:

Surface area: $6\mu m^2 = 6 \times 10^6 nm^2$.

$$\text{number of lipids in single layer per cell} = \frac{6 \times 10^6 \text{nm}^2}{0.5 \text{nm}^2/\text{lipid}} = 1.2 \times 10^7 \text{ lipids}$$

Consider the **bilayer** lipids structure of plasma membrane:

$$\text{number of lipids in bilayer per cell} = 1.2 \times 10^7 \times 2 \text{ lipids} = 2.4 \times 10^7 \text{lipids}$$

Consider the lipids do not only exist in the plasma membrane but occupies most of the lipids usage:

A reasonable estimation is: an E.coli has $\text{few} \times 10^7$ lipids.

Question 8 Water in the Central Valley?

How much water is used to irrigate the Central Valley of California every year?

Answer:

Consider the Mediterranean climate of California, with the average rainfall of about 500 nm, we can just assume central valley grows commercial crops in the whole year. From my experience while driving along Highway 5 in January, most of the fields along with Highway 5 is utilized in January. Which means the crop season could just be whole year in our estimation.

From empirical experience of planting in flowerpot, a cup of water (approximately $250mL = 0.25L$) is needed for irritation per day.

From homework 1, the area of central valley is approximately $300 \times 100km^2$ which is $3 \times 10^{10}\ m^2$.

We can first calculate the water needed per day:

$$\text{water needed per day in a unit area} = \frac{0.25\text{L/day}}{20 \times 20\text{cm}^2} = \frac{0.25\text{L/day}}{0.04m^2} = 6.25\ \text{L/m}^2\text{/day}$$

Then the annual water usage can be estimated as:

$$3 \times 10^{10}\text{m}^2 \times 6.25\text{L/day} \times 365\text{day/year} \approx 6.84 \times 10^{13}\text{L/year}$$

Consider there will be rainfall and there would be different water usage for various crops, few $\times\ 10^{13}$L would be a reasonable estimation.

Question 9 Mass of mRNA and proteins.

What is the mass of an mRNA and a protein?

Answer:

Only consider the general case of mRNA and protein.

Let's assume a typical protein is around 300 amino acid.

According to BNID 103248, the range of amino acid is from 57-186 Dalton.

As a rule of thumb, the average amino acid mass would be **100 Dalton** (BNID 101830).

The mass of a protein is:

$$m_{protein} = \frac{100Da/aa \times 300aa}{6.02 \times 10^{23}/mol} = \frac{3 \times 10^4 g/mol}{6.02 \times 10^{23}/mol} = 5 \times 10^{-20}g$$

Similarly, an mRNA is composed of nucleotides.

According to BNID 104886, average molecular mass of RNA nucleotides in E.coli is 324.3 Dalton.

Let's take $m_{nt} = 300Da$ for simplification.

Knowing that 3 nucleotide coding for a protein, $N_{nt} \approx 3 \times N_{aa}$ and $m_{nt} \approx 3 \times m_{aa}$.

The corresponding mass of mRNA could be:

$$\begin{aligned}\text{mass of mRNA } &= N_{nt} \times m_{nt} = 3 \times N_{aa} \times 3 \times m_{aa} \approx 10 \times N_{aa} m_{aa} \\ &= 10 \times m_{protein} = 5 \times 10^{-19}g\end{aligned}$$

Question 10 Water uptake in dividing bacteria

How many water molecules are taken up each second during the growth of a rapidly growing bacterium?

Answer:

Take E.coli as a bacterial model. In our estimations, E.coli is often considered as a cubic with $1\mu m$ side length. The volume is $1\text{fL} = 1 \times 10^{-15} L$.

Let's consider the cell growth rate to derive the growth of a rapidly growing bacterium.

According to BNID 111284, the experimentally observed specific growth rate of E.coli is **1.14 per hour**.

If we consider the division means a doubled volume, and most of the volume increased is considered water.

Knowing that:

Within 1 hour, E.coli will grow 1.14 volume of E.coli.

Volume increased in 1 hour: $1.14 \times 1\text{fL/hour} = 1.14 \times 10^{-15} L/hour$

1 hour is 3600 second.

Volume of water taken in each second:

$$\frac{1.14 \times 10^{-15}\text{L/hour}}{3600\text{sec/hour}} \approx 3.2 \times 10^{-19}\text{L/sec}$$

The density of water is 1g/L.

Mass of water taken per second during rapid growth: $3.2 \times 10^{-19}\text{g/sec}$

The molecular mass of water (H_2O) is 18g/mol.

Mole of water taken per second during rapid growth:

$$\frac{3.2 \times 10^{-19}\text{g/sec}}{18\text{g/mol}} \approx 1.78 \times 10^{-20} mol$$

Convert mol into exact value:

$$1.78 \times 10^{-20} mol \times 6.02 \times 10^{23}\text{molecules}/mol \approx 1 \times 10^{4}\text{molecules}$$

Consider the growth rate and the conditions in E.coli growth, **few hundreds** or **few thousands** water molecules taken per second during rapid growth.

Question 12 Length of DNA in your cells

What is the length of DNA in one of your cells?

Answer:

Let's just consider a cell with normal autosomal chromosomes in my body. (If we consider cells undergoing cell division or germ cells, the condition would be different.)

According to BNID 103777, the "Rule of thumb" for length of DNA per base pair is $0.333 nm/bp$.

According to BNID 110200, "the size of the total human genome is estimated to be about 3.1Gb".

Gb stands for Giga base pairs. One gigabase is equal to **1 billion bases**.

Length of DNA in my cell in bps is: $3.1 Gb = 3.1\text{billion bases} = 3.1 \times 10^{9}\text{bps}$.

Length of DNA in a typical cell of mine in meter would be:

$$3.1 \times 10^{9}\text{bps} \times 0.333\text{nm/bp} \approx 1 \times 10^{9} nm = 1\text{m}$$

For a sanity check, according to BNID 102980, the length of longest chromosome in human homo sapiens is $10cm = 0.1m$. Since we have 46 chromosomes in somatic cells, **few meters** would be a reasonable estimation.

Question 18 Size of sequence space

How many times the volume of our universe would it take to make a single copy of every 300 aa protein?

Answer:

Consider mainly 20 types of animo acids that can compose the protein. For each position among 300 amino acids, there are 20 choice for each animo acid position. Assume that the probability of occurrence is equal and the position correlation is not considered, we can have:

$$Seq = 20^{300} \approx 2.04 \times 10^{390}$$

By consulting Jena Library in BioNumber (BNID 103241), we can estimate the volume for each amino acid to be $100\text{Å}^3 = 0.1nm^3$. Thus, the volume of such a protein could be approximately

$$300 \times 0.1nm^3 = 30nm^3 = 3 \times 10^{-26}m^3$$

As a sanity check, typical protein with around 300 aa is Green Fluorescent Protein (GFP) with 238 amino acids. According to BNID 108461 and BNID 110498, if we consider the volume of GFP can be considered as a sphere, by utilizing $V = \frac{4}{3}\pi r^3$,the volume is few $\times 10^{-26}m^3$.

By checking the google website and NASA website, the volume of observable universe is $4 \times 10^{80}m^3$.

Consider all the possibilities we could have, in total the volume takes place:

$$3 \times 10^{-26}m^3 \times 2.04 \times 10^{390} = 6.12 \times 10^{364}m^3$$

Thus it occupies:

$$\#\text{ of observable universe} = \frac{6.12 \times 10^{364}}{4 \times 10^{80}} = 1.53 \times 10^{284}$$

It needs approximately $\text{few} \times 10^{284}$ observable universe to contain all the permutations of the proteins.

Question 20 Fraction of body mass in DNA

What fraction of your body mass is DNA?

Answer:

According to BNID 110200, "the size of the total human genome is estimated to be about 3.1Gb".

Gb stands for Giga base pairs. One gigabase is equal to **1 billion bases**.

Length of DNA in my cell in bps is: $3.1Gb = 3.1\text{billion bases} = 3.1 \times 10^9\text{bps}$.

By checking the chemical formula of A/T/C/G, the average molecular weight of base pairs is $(135 + 126 + 111 + 151)/4 \approx 131g/mol$.

Thus, we have the DNA weight per cell is:

$$3.1 \times 10^9\text{bps/cell} \times 131\text{g /mol} \times \frac{1mol}{6.02 \times 10^{23}\text{bps}} \approx 6.75 \times 10^{-13}\text{g/cell} = 6.75 \times 10^{-16}\text{kg/cell}$$

According to BNID 113040, the number of cells in human body is approximately 3.7×10^{13}.

Thus the total mass of DNA is:

$$m_{DNA} = 3.7 \times 10^{13} \times 6.75 \times 10^{-16}\text{kg} \approx 0.025\text{kg}$$

A typical average body weight of human is $70kg$ (so do I).

Fraction of DNA mass in human body can be estimated as:

$$\frac{0.025\text{kg}}{70\text{kg}} \times 100\% \approx 0.036\%$$

The mass of human DNA in body mass is ~0.036%.

Question 22 Number of humans born per year

Make the spurious assumption of a steady state human population size and use Little's theorem to work out the number of humans born every year.

Answer:

By consulting the web source, Little's theorem, commonly applied in queuing theory, states that the long-term average number L of customers in a stationary system is equal to the long-term average effective arrival rate λ multiplied by the average time W a customer spends in the system.

$L = \lambda W$

where L represents the total human population at any given time, W is the average lifespan of human, and λ is the rate of new individuals (births) entering the population.

In the steady-state assumption, by checking the website, there is approximately 8.1 billion people in the world. $L = 8.1 \times 10^9$.

According to the World Bank website, the average human lifespan worldwide is 71.33 years. $W = 71.33 \text{ years}$.

$$\lambda = \frac{L}{W} = \frac{8.1 \times 10^9 \text{people}}{71.33 \text{years}} = 1.14 \times 10^8 \text{ births per year}$$

110 million births per year worldwide would be the result in this context.

Question 29 Intuition for concentration

If there is one copy of a molecule of interest per bacterial cell, what is the concentration in M units?

Answer:

Take the E.coli as a bacterial model.

As we estimated in lectures and previous answers, the volume of an E.coli is $1\mu m^3 = 1 \times 10^{-15} L$.

If there is one molecules in each E.coli, it corresponds to $1 \text{ molecule}/10^{-15} L$

The concentration is: $10^{15} \text{molecules/L}$.

Convert the concentration into mol:

$$\text{concentration in mol} = \frac{10^{15} \text{molecules/L}}{6.02 \times 10^{23} \text{molecules/mol}} \approx 1.66 \times 10^{-9} \text{mol/L} = 1.66 \times 10^{-9} \text{M} = 1.66 \text{nM}$$

This is the molar concentration of this molecule in bacteria, which is about 1.66 nanomoles per liter (nM).

Question 30 Volume of a human body

In m^3 units, what is the volume of a human body?

Answer:

To simplify and model my body, I'd like to consider my body as a sphere and a cube. The sphere is my head and the cube is my body (from leg to shoulder).

The radius of the sphere can be estimated as $r = 7cm = 0.07m$.

The thickness of my body (measured by roommate) is $a = 15cm = 0.15m$. For the width, we apply the "the shoulder width minus the arms", and $b = 30cm = 0.3m$. For the height, from my feet to shoulder is approximately $c = 150cm = 1.5m$

The estimated volume of the sphere (head) is: $V_{sphere} = \frac{4}{3}\pi r^3 \approx 1.4 \times 10^{-3} m^3$.

The estimated volume of the cube (under the shoulder) is: $V_{cube} = 0.15 \times 0.3 \times 1.5 m^3 = 0.0675 m^3 = 6.75 \times 10^{-2} m^3$.

Thus, the total volume estimated can be:

$$V_{total} = V_{sphere} + V_{cube} = (6.75 + 0.14) \times 10^{-3} m^3 \approx 6.9 \times 10^{-3} m^3$$

Question 31 Number of red blood cells in a human

How many red blood cells in a human body?

Answer:

According to BNID 101707, volume of blood in average-sized (70 kg) person is $5.5L$.

According to BNID 102745, concentration of red blood cells in human blood is $5.6 \times 10^6 \text{cells/mm}^3$.

Convert the unit for concentration: since $1mm^3 = 10^{-6}L$, concentration: $5.6 \times 10^{12} \text{cells/L}$.

Total number of red blood cell in a human body:

$$N_{\text{RBC}} = 5.6 \times 10^{12} \text{cells/L} \times 5.5L = 3.08 \times 10^{13} \text{ cells}$$

Question 34 Translation time

How long does it take for a ribosome to translate all of the proteins that are needed to make another ribosome?

Answer:

Consider the E.coli case.

According to BNID 101175, total number of amino acids in the ribosome of E.coli is 7459 amino acids.

According to BNID 111689, the average translation rate of E.coli is ~8 amino acids/sec.

Now we can calculate the time needed:

$$\frac{7459 \text{ amino acids}}{8 \text{ amino acids/sec}} \approx 930 \text{ seconds}$$

It takes approximately 930 seconds (15.5 mins) for a ribosome to translate all of the proteins required for another ribosome.

Note that translation rate differs at different condition. Few tens minutes or 10 mins is logically acceptable.

Question 36 Areas and volumes of your cells

Crudely estimate the total (membrane) surface area, and total (cellular) volume, of all bacterial cells in your body (assuming they are rods like E coli).

Do the same for your eukaryotic cells; how different are these bacterial & human values?

Answer:

According to BNID 113000, the number of bacteria across the whole body of the "reference man" is 3.8×10^{13} bacteria/human.

Assume all of these bacteria are like E.coli, with $6\mu m^2$ surface area and $1\mu m^3$ volume (as we always did in our lecture).

$$A_{bacterial} = 3.8 \times 10^{13} \times 6\mu m^2 \approx 2.3 \times 10^{14}\mu m^2$$
$$V_{bacterial} = 3.8 \times 10^{13} \times 1\mu m^3 = 3.8 \times 10^{13}\mu m^3$$

For eukaryotic cells in my body, let's just use **typical mammalian tissue culture cell or HeLa cells** as our reference.

According to BNID 105906, the volume of a typical cell is $4000\mu m^3$ (in mammalian tissue culture cell). (Sanity check: Volume of HeLa cell is $3700 \pm 1500\mu m^3$). According to BNID 103718, the surface area of HeLa Cell is $1600 \pm 500\mu m^2$.

According to BNID 109716, total cell number in body for human is $(3.7 \pm 0.8) \times 10^{13}$ cells.

Sanity check: BNID 113005:

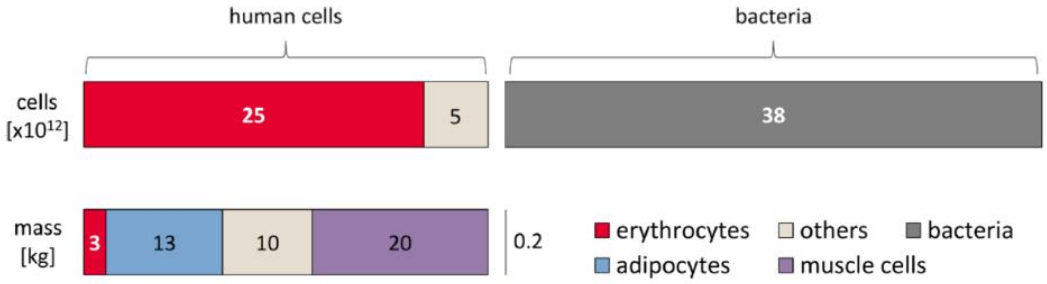

Fig 3. Distribution of cell number and mass for different cell types in the human body (for a 70 kg adult man). The upper bar displays the number of cells, while the lower bar displays the contribution from each of the main cell types comprising the overall cellular body mass (not including extracellular mass that adds another ≈24 kg). For comparison, the contribution of bacteria is shown on the right, amounting to only 0.2 kg, which is about 0.3% of the body weight.

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We can calculate:

$$A_{eukaryotic} = 3.7 \times 10^{13} \times 1600\mu m^2 \approx 5.9 \times 10^{16}\mu m^2$$
$$V_{eukaryotic} = 3.7 \times 10^{13} \times 4000\mu m^3 = 1.48 \times 10^{17}\mu m^3$$

Conclusion:

Although bacteria and human cells are roughly equal in number, the total volume and total surface area of human cells far exceed that of bacterial cells.

Consider the bacterial cell has a higher ratio of Surface Area to Volume than eukaryotic cells in human body; This allows them to be widely distributed in the human body and play important roles in the human microecology.

Question 38 Food and mountain climbing

What is the maximum height of a mountain you can climb after eating just a bowl of ramen?

Answer:

Let's clarify this question: if we only consume the calories by a bowl of ramen, what is the height of mountain that the energy derived allows me to climb?

Combining the search result from Google and menus supplied by Yelp, a typical bowl of Ramen contains 450-600 kcal.

Knowing that 1 calories is approximately 4.2 Joules: $1\ \text{calories} \approx 4.2J$.

Let's take 500 kcal for estimation in this question.

Energy derived: $500\text{kcal} = 2100kJ = 2.1 \times 10^6 J$

My weight is $m = 70kg$, the acceleration of gravity is $g = 9.8m/s^2$. Assume the maximum height is h(m).

Consider all of the energy are transferred into the gravitational potential energy:

$$mgh = 2.1 \times 10^6 J$$
$$70kg \times 9.8m/s^2 \times h = 2.1 \times 10^6 J$$
$$h = \frac{2.1 \times 10^6 J}{686kg \cdot m/s^2} \approx 3061m$$

Incredible. However, in the real case, not all energy can be transferred into the gravitational potential energy. Kinetic energy also account for a certain portion of energy consumption.

By consulting Google and discussing in last lecture, only approximately 25% of energy taken are transferred into mechanical energy, base on this, a more reasonable estimation if all of the energy are transferred into gravitational potential energy would be:

$$h = 3061m \times 25\% = 765.25m$$

Although it is still higher than my gut feeling, but it is more reasonable.

3 Your Philosophy of Biology

The Quantifiable Life:

Harnessing Mathematical Models to Decode and Predict Biological Phenomena

Linfeng Hu

Essay on MCB 137 Final Project, UC Berkeley

Modern biology has fundamentally transformed from a non-quantitative science to a quantitative one, driven by advances in technology and methodology. During my elementary years, I learned how Robert Hooke used a microscope to discover cells, and in high school, I acknowledged that Aristotle had determined whales are viviparous. These early studies prioritized objective observations. In contrast, modern biology relies heavily on quantitative data. Noteworthy examples include the discovery of the genome of extinct species and human evolution. This shift reflects the influence of foundational sciences, which have long embraced quantification. Erwin Schrödinger's seminal question in 'What is Life?'—'How can events within a living organism be accounted for by physics and chemistry?'—highlights this inevitable transition in biological research from qualitative observation to quantitative precision.

Quantitative models serve as bridges between experimental data and theories, moving away from black box approaches to data interpretation. These models allow us to understand the underlying principles of a system, offering an approach to summarize, predict, and verify changes methodically. It enables systematic control over phenomena and even fosters the creation of new systems based on these principles. While trial and error method has its place, it will eventually be replaced by research and production guided by theoretical models.

In this course, we have explored several elegant yet simple quantitative models that demonstrate their practical value in biological contexts. For instance, concepts like bi-stability, hysteresis, and bifurcations explain why equilibrium states differ when approached from two different directions. These models show how biological systems can maintain stability or generate various response to different initial conditions. Furthermore, we've seen how binding probability and fold-change are used to describe repression mechanisms, providing a quantitative framework for understanding gene regulation. Additionally, graph theory has proved instrumental in managing

models of simple activation, helping us visualize and analyze complex networks of interactions within biological systems.

Future advancements in biological technology will increasingly rely on quantitative data and models, with fields like synthetic biology poised for significant breakthroughs. Synthetic biology can now redesign genomics and metabolic pathways, transforming cells and even creating synthetic cells, offering boundless possibilities. Gradually, experimental biologists will require a theoretical basis to estimate how to engineer cells, a foundation that only quantitative biology can provide. While past modeling primarily focused on metabolic networks, modeling at the cellular and multicellular levels is still developing. The recent rise of AI for Science (AI4Sci) could also aid in extracting undiscovered scientific principles from data, optimizing and interpreting models, and gradually demystifying complex processes.

In conclusion, modern biology's transformation into a quantitative science underscores the necessity of using quantitative data and models. As discussed, these models are crucial for understanding complex biological systems and for pioneering advances in areas like synthetic biology. The mantra of this course, "quantitative data demands quantitative models," captures this shift effectively. This approach is essential, as it moves us beyond mere observation to a deeper, systematic understanding of life's complexities. As biology continues to evolve, quantitative models will remain indispensable in driving forward the next wave of scientific discoveries.

4 A Feeling for the Organism: Your Turn

I wonder what the number of lipids is involved in hepatocytes apoptosis in an average person at any given time.

Knowing that under normal conditions, a very small fraction of hepatocytes are actively dividing. At the meantime, hepatocytes have the capability to enter the cell cycle in response to injury or loss.

Data and source:

Cells per gram of liver tissue: According to BNID 110544, there are approximately 1.07×10^8 hepatocytes per gram of liver tissue.

Liver weight: According to BNID 110212, an average adult liver weighs about 1.5 kg.

Lipid content per gram of liver: According to BNID 105885, there is approximately 65 mg of lipid per gram of wet liver weight.

Apoptosis rate: According to BNID 112171, less than 0.1% of hepatocytes are undergoing apoptosis at any given time.

Length of edge of hepatocyte (in a roughly cubical simplification): According to BNID 113236, the length of edge of a typical hepatocytes is 15 μm.

Surface area per lipid molecule: According to BNID 106993, surface area per lipid molecule is 0.5 nm^2.

“Rule of thumb” for the mass of lipid molecule in lipid bilayer: According to BNID 101838, "Rule of thumb" for the mass of lipid molecule in lipid bilayer is 800 Dalton.

Assumptions:

Most of the cells in liver is hepatocytes.

For a simplification model, each hepatocyte can be considered as a cube with a side length of 15 microns.

If a hepatocyte undergoes apoptosis, we consider all the lipids it has are involved in apoptosis.

Hepatocytes turnover is in a common steady state.

Calculations:

Total Hepatocytes in the Liver:

$$N_{hepatocytes} = 1.07 \times 10^8 \frac{cells}{g} \times 1500g \approx 1.6 \times 10^{11} cells$$

Knowing that hepatocytes occupies most of the mass in liver cell, the total lipid in the liver can be considered the lipids for hepatocytes.

Hepatocytes involved in apoptosis:

$$N_{hepatocytes\ in\ apoptosis} = 1.6 \times 10^{11} cells \times 0.1\% = 1.6 \times 10^8 cells$$

The surface area of a hepatocyte cell: given that the cell can be simplified in to a cubic with 15 μm length of side,

$$A_{hepatocyte} = (15\mu m)^2 \times 6 = 1350\mu m^2$$

Consider that most of the lipid is used for plasma membrane composition, and the membrane is a bilayer lipids structure, we can estimate the number of lipids that each cell has:

$$N_{lipids\ per\ hepatocyte} = \frac{1350\mu m^2}{0.5nm^2} \times 2 = \frac{1350\mu m^2}{5 \times 10^{-7}\mu m^2} \times 2 = 5.4 \times 10^9\ lipids/cell$$

Thus, the total number of lipids involved in apoptosis at any given time can be calculated:

$$N_{lipids\ in\ apoptosis} = 5.4 \times 10^9 \frac{lipids}{cell} \times 1.6 \times 10^8 cells = 8.64 \times 10^{17} lipids$$

If we consider all the lipids of a hepatocyte undergoing apoptosis means involvement in apoptosis, an estimation is:

At any given time, the number of lipids involved in apoptosis is $\mathbf{8.64 \times 10^{17}}$. Since hepatocyte is the major cell, but not sole cell type in liver tissue, the magnitude of estimation could be approximately **few$\times\ \mathbf{10^{17}}$ lipids**.

Sanity check:

According to BNID 110212, an average adult liver weighs about 1.5 kg.

According to BNID 105885, there is approximately 65 mg of lipid per gram of wet liver weight.

Total lipids weight:

$$m_{total\ lipids} = 1500g \times 65\,mg/g = 97500mg = 97.5g$$

According to BNID 101838, "Rule of thumb" for the mass of lipid molecule in lipid bilayer is 800 Dalton.

The mass of lipids involved in apoptosis can be calculated:

$$m_{lipids\ in\ apoptosis} = \frac{8.64 \times 10^{17} lipids}{6.02 \times 10^{23} lipids/mol} \times 800 \frac{g}{mol} \approx 1.15 \times 10^{-3} g = 1.15mg$$

Considering only a very small fraction of hepatocytes are undergoing apoptosis at any given time, it lines up with our estimations and assumptions. Also, not only plasma membrane contains lipids, it also contributes to the small fraction.

End of the Final Project.

Thanks for your review and tutorials this semester.