Problem set 8

This problem set covers the content from week 10: systems biology and online resources

Tips and rules:

- You can answer in English or in Thai.
- There can be more than one correct answer. What I am looking for from you is not just the correct answer but <u>the rationale for your answer</u>.
- Please <u>provide evidence</u> of how you think and what <u>sources of information</u> you used.
- AI such as ChatGPT may be used. You can also work together with friends. But you must <u>write the answer in your own words</u>.
- Any incidence of plagiarism and copying of another student's work will be reported to the Graduate Affairs.

Systems biology

 "Cellular memory" is the phenomenon where cells retain molecular responses to external stimuli even long after the stimuli had disappeared.

Q1: Explain how this property can arise from positive auto-regulation mechanisms

Q2: Explain how epigenetics mechanisms can play a role in this process

Simulate the expression pattern over time of the systems in **Q3-Q5**. Use step size $dt = 1.0$. For each system, show the graph of [RNA] over time.

Here is an example of how to perform the simulation for **Q3** in MS Excel for 4 steps.

time	[RNA]	
0	4.00	**formula**
1	7.80	**B3**=*B2*+5-(0.3)**B2*
2	10.46	**B4**=*B3*+5-(0.3)**B3*
3	12.32	**B5**=*B4*+5-(0.3)**B4*
4	13.63	**B6**=*B5*+5-(0.3)**B5*

Q3: d[RNA]/dt = 5 – 0.3[RNA], initial [RNA] = 4.0

Q4: d[RNA]/dt = 100 – 0.3[RNA], initial [RNA] = 4.0

Q5: d[RNA]/dt = 5 – 0.1[RNA], initial [RNA] = 4.0

Q6: From your simulation results in **Q3-Q5**, which factor affect the amount of time it takes for the system to reach an equilibrium, the transcription rate or the degradation rate.

Online resources

Use the GEO2R tool to perform more analyses of the **GSE33113** colorectal cancer dataset explored in class.

4 out of 6 normal mucosa samples have matched cancer tissue samples. Perform a differential expression analysis between the 4 normal mucosa and matched cancer tissues and answer **Q7-Q9**.

Q7: How many genes are **up-regulated in cancer tissues** at the adjusted p-value cutoff of 0.01?

Q8: Show the expression profile of the top **up-regulated gene** across 8 samples.

Q9: Because among 4 cancer tissues, 2 were from patients with metastasis and 2 were from patients without metastasis, we may worry that this affected the differential expression analysis results.

Based on the visualizations in **GEO2R**, do you think the results were affected by this factor?

Download the differential expression result from **GEO2R** to perform a functional enrichment analysis in **WebGestalt** (https://www.webgestalt.org/). Select the **GSEA** algorithm and **Gene Ontology: Biological Process** as the database.

Q10: What is the **ID Type** (gene accession ID system) for this dataset?

Q11: Show a screenshot of the resulting bar plot that shows enriched functions.

Q12: What is the top up-regulated function? What are the top up-regulated genes associated with this function?

For **Q13-Q15**, you are given situations that can be solved using appropriate online resources. Explain which resources you will use and how they can help you solve the problems.

Q13: You suspect that SMAD2, which is a transcription factor, activate your gene of interest. So, you extracted the 5kb upstream DNA sequence of the transcription start site of the gene and want to check whether SMAD2 can bind to it.

Q14: You want to regulate LIB28B gene post-transcriptionally with miRNA but are unsure which miRNA to choose.

Q15: You discovered a novel non-synonymous mutation on ACTB gene in multiple patients and want to investigate how this mutation affects the gene/protein.