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Analysis of the influence of microgravity and space radiation on astronauts' gene expression: An approach using quantum simulations and fuzzy logic

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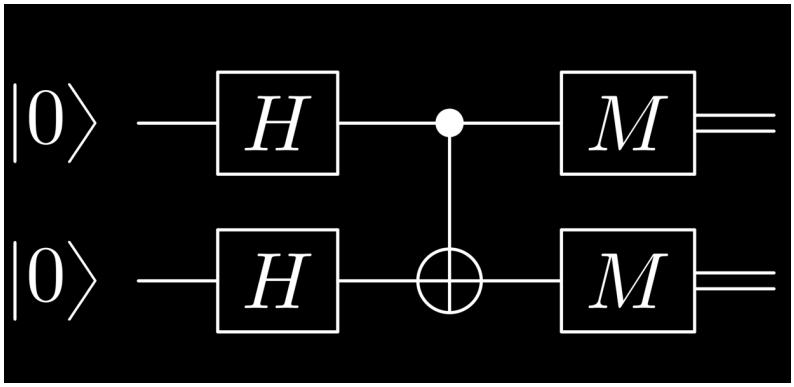
Graphical Abstract



Abstract

An analysis of the effects of microgravity and space radiation on astronauts' RNA expression has been developed, utilizing data from NASA's "Cell-Free RNA Analysis of Plasma Samples Collected from Six Astronauts in JAXA Cell-Free Epigenome (CFE) Study." The project aims to deepen our understanding of how the space environment affects gene expression, particularly in key genes such as *ACTB* and *ACTG1, by* employing quantum simulations and unconventional logic, including quantum and fuzzy logic. The results suggest that specific genes like *ACTB* and *ACTG1* undergo significant changes in their expression under these unique conditions. This interdisciplinary approach allows for a detailed analysis of gene expression data and explores the potential of emerging technologies in space research and bioinformatics.

Keywords: Microgravity, fuzzy logic, quantum logic, quantum computing, quantum simulation, ACTB, ACTG1 genes, bioinformatics, astronauts

Purpose, Rationale, and Limitations

Purpose Quantum computing offers unprecedented performance potential by leveraging the principles of quantum mechanics to solve complex problems that are infeasible for classical computers. While quantum computers are not yet fully operational for large-scale practical applications, having a scalable infrastructure ready for quantum computing when the technology matures can position researchers ahead in fields like spatial gene expression analysis. This forward-thinking approach provides a competitive edge in bioinformatics, allowing researchers to explore quantum computing's transformative capabilities as soon as it becomes viable.

In addition, quantum computing could significantly enhance data analysis, pattern recognition, and machine learning in gene expression studies. Preparing a flexible and scalable system for quantum computing now ensures that when the technology is ready, researchers can immediately leverage its superior processing power, thereby accelerating scientific discovery and gaining insights faster than conventional methods allow.

Other factors of interest include the possibility of hybrid systems where quantum and classical computing work in tandem, as well as the exploration of quantum machine learning algorithms for spatial gene expression analysis. These hybrid systems can maximize current computing capabilities while preparing for future advancements. The integration of unconventional logic systems like fuzzy logic with quantum computing also presents a unique opportunity to analyze gene expression data more comprehensively.

Rationale: The unique combination of quantum computing and fuzzy logic presents a novel approach to spatial gene expression analysis. Quantum computing offers the potential for vast parallelism and complex problem-solving capabilities, which can be highly beneficial in analyzing the multidimensional and often noisy data associated with gene expression. Meanwhile, fuzzy logic provides a nuanced framework for handling uncertainty and imprecision, common features in biological data.

Spatial gene expression analysis benefits from this integrated approach as it involves understanding the spatial distribution and expression levels of genes across different regions of a tissue or organism. This analysis often involves large datasets with complex relationships, where quantum computing can enhance the efficiency of data processing and fuzzy logic can improve the interpretability of the results. This interdisciplinary focus aligns well with the exploratory and complex nature of biological systems.

Limitations: The current limitations of quantum computing stem from its nascent stage of development. Quantum computers face challenges such as qubit coherence times, error rates, and scaling issues. These limitations restrict the size and complexity of problems that current quantum computers can handle effectively. While quantum computing has proven functional and useful in this study, fully exploiting its potential requires functional and scalable quantum computers with higher qubit counts, lower error rates, and robust quantum error correction.

In addition to hardware constraints, software challenges such as developing effective quantum algorithms and integrating quantum computing with classical computing frameworks are ongoing areas of research. These limitations mean that, while promising, quantum computing is currently best suited for experimental and exploratory applications rather than mainstream, large-scale data analysis. Nonetheless, as quantum computing technology advances, its limitations will gradually diminish, allowing for more comprehensive applications in spatial gene expression analysis and beyond.

Introduction

Gene expression analysis in astronauts has emerged as a critical area of study[4], particularly with the increasing interest in long-term human spaceflight and exploration missions. The unique environment of space, characterized by microgravity, increased radiation exposure, and confinement, presents significant challenges to human health, including alterations in gene expression that may impact various biological processes. Understanding these changes is crucial for developing countermeasures to protect astronauts and for advancing our knowledge of how space environments affect living organisms.

Recent studies have demonstrated that spaceflight induces a wide range of changes in gene expression, influencing immune function[5], muscle atrophy, bone density, and even cognitive function. For example, NASA's Twins Study[6], which examined the genetic and physiological changes in astronaut Scott Kelly during his year-long mission on the International Space Station (ISS), revealed alterations in gene expression related to immune response, DNA repair, and cellular stress. Similarly, other studies have identified significant changes in the expression of genes involved in inflammation, apoptosis, and cellular metabolism, among other functions, highlighting the extensive impact of spaceflight on the human body.

Spatial gene expression analysis[7], which examines the spatial distribution of gene expression within tissues, offers additional insights into how specific regions of the body respond to space environments. This technique is particularly relevant for understanding tissue-specific responses and identifying potential vulnerabilities or adaptive mechanisms. However, analyzing spatial gene expression data is computationally intensive, given the high dimensionality and complexity of the data.

The need for high-performance computational approaches is evident in the context of spatial gene expression analysis, where the volume and complexity of data often exceed the capabilities of classical computing methods. Quantum computing[8] presents a promising solution to this challenge, offering substantial performance improvements through its ability to handle vast amounts of data simultaneously and perform complex calculations more efficiently than classical computers. Quantum computing's unique characteristics[9], such as superposition and entanglement, enable it to explore multiple solutions simultaneously, making it particularly well-suited for tasks like gene expression analysis, where large-scale parallel processing and pattern recognition are crucial.

By leveraging quantum computing, researchers can accelerate the analysis of spatial gene expression data, uncovering patterns and insights that would be difficult or impossible to detect with conventional methods. This approach not only enhances the speed of data analysis but also opens up new possibilities for exploring complex biological systems and their responses to space environments.

Bridging the Gap

The intersection of gene expression analysis in astronauts and quantum computing represents a novel and promising research avenue. The unique capabilities of quantum computing align well with the challenges posed by spatial gene expression analysis, making it a logical step forward in the field. Incorporating unconventional logic, such as fuzzy logic[10], further enhances this approach by providing a framework for handling the uncertainty and variability inherent in biological data.

This paper aims to explore this intersection, focusing on the effects of microgravity and space radiation on astronauts' RNA expression using quantum simulations and unconventional logic. By doing so, it not only contributes to our understanding of space-induced changes in gene expression but also demonstrates the potential of emerging technologies in space research and bioinformatics, positioning itself as a step forward in advancing our knowledge and capabilities in this domain.

Experimental design

Hypothesis

The primary hypothesis of this study is that the unique environment of space, characterized by microgravity and increased radiation exposure, induces significant changes in gene expression among astronauts, which can be effectively analyzed using quantum computing and unconventional logic systems such as fuzzy logic. The study specifically focuses on the expression of key genes, such as *ACTB* and *ACTG1*, to explore the potential of emerging computational technologies in understanding the biological effects of space environments.

Models

To test this hypothesis, the study utilizes two main computational models:

Quantum Computing Model. This model is based on quantum circuits designed to analyze and simulate gene expression data. The quantum circuits are constructed using qubits and quantum gates, such as the Hadamard gate and Controlled NOT (CNOT) gate, to explore superposition and entanglement properties that could reflect changes in gene expression. The quantum computing model is employed to perform statistical analyses, such as ANOVA tests and Tukey HSD tests, on the gene expression data across different flight conditions (pre-flight, in-flight, and post-flight).

Fuzzy Logic Model. The fuzzy logic model interprets the relative levels of gene expression using fuzzy sets and membership functions. This model handles the inherent uncertainty and variability in biological data, offering a nuanced assessment of gene expression variations. The fuzzy logic model uses linguistic variables, such as "low," "medium," and "high," to describe the gene expression levels and establishes fuzzy rules that relate flight conditions to expression levels.

Methods

The study employs the following experimental methods to evaluate the hypothesis:

Sample Collection and Processing[1]. Blood samples are collected from astronauts in space (on the ISS) and on Earth, following specific protocols to preserve the integrity of the samples. The plasma is separated through gel, and RNA is extracted using standard biochemical methods, followed by library preparation for sequencing.

Data Analysis[1]. The RNA sequencing data is analyzed using the CLC Genomics Workbench software, where the reads are mapped to the human genome, and gene annotations are quantified. The resulting count values are normalized and log-transformed to calculate expression levels.

Quantum Simulations. Quantum circuits are constructed to simulate gene expression changes using quantum gates. The circuits are tested on quantum simulators like Qiskit's qasm_simulator and statevector_simulator to analyze the probability distributions of the measurement outcomes. The results are visualized using histograms and state vectors to interpret the superpositions and entanglements generated by the quantum circuits.

Fuzzy Inference. The fuzzy logic model is constructed using the scikit-fuzzy package in Python. The universe of discourse is defined for the levels of gene expression, and membership functions are created for the fuzzy sets. Fuzzy rules are established to relate flight conditions to expression levels, and the fuzzy inference system is simulated to calculate the gene expression levels under different conditions.

Statistical Analysis. Statistical analyses, such as ANOVAs and Tukey HSD tests, are performed to identify significant differences in gene expression across the flight conditions. Outliers are identified using Z-scores, and Pearson correlations are calculated to assess the relationship between the expression of different genes.

Biological Interpretation. The results are interpreted in the context of the biological relevance of the genes, focusing on the functions of the *ACTB* and *ACTG1* genes and how their expression is affected by space environments. The quantum and fuzzy logic models are evaluated for their effectiveness in analyzing gene expression data and for their potential in future space biology research.

Sample Collection and Analytical Procedures

In the referenced study,[1] the protocol for blood sample collection and subsequent processing was meticulously designed to preserve the integrity of plasma samples. Blood was drawn into specialized tubes that separate plasma through a gel and contain ethylenediaminetetraacetic acid (EDTA) as an anticoagulant. These samples underwent a standard freezing process immediately after collection—on the International Space Station (ISS) at −95°C and on the ground at −80°C – following a centrifugation protocol adapted to the differing gravitational conditions of each environment. Post-centrifugation, the samples were securely stored until all collections were complete; at this point, they were transported to the University of Tsukuba for further analysis.

Upon thawing, plasma samples were carefully partitioned and subjected to a sequence of centrifugation and mixing with reagents such as TRIzol-LS and chloroform, facilitating the isolation of RNA. Following a series of incubations and centrifugation, the RNA was precipitated, washed, and solubilized for quantification using high-sensitivity assay kits.

The subsequent library preparation for sequencing was carried out with meticulous attention to the template amount, which was confirmed via real-time polymerase chain reaction to ensure optimal amplification cycles. After purification, the libraries were ready for high-throughput sequencing on the NextSeq500 platform.

The resulting data were processed using the CLC Genomics Workbench software, which entailed mapping reads to the human genome and quantifying gene annotations to compile total count values. These counts underwent normalization and logarithmic transformation to enable a precise calculation of expression levels.

In-depth statistical analyses, such as ANOVAs and empirical DGE (Differential Gene Expressions) assessments, were performed to elucidate the differences in gene expression across the various stages of flight—pre-flight, in-flight, and post-flight. Such meticulous data processing has facilitated a comprehensive understanding of how space travel influences gene expression.

Descriptive Statistics

We begin with an initial approach to the data from the experiment "Cell-Free RNA Analysis of Plasma Samples Collected from Six Astronauts in JAXA Cell-Free Epigenome (CFE) Study" [1] from the file which includes 64 RNA samples from three different groups:

GLDS-530_rna-seq_TGB_050_64samples_3group_totalcount.xlsx. Details suggest that nucleic acid extraction was quantified using qubit fluorometers and a qubit RNA HS assay kit. The library construction was performed with a targeted and paired RNA sequencing approach, and the sequencing itself was conducted on an Illumina NextSeq500 with a read length of 36 base pairs.

We can proceed with the code (Tested in Manjaro Linux 23.1.3, Python 3.8.12, SciPy1.10.1, Qiskit 0.45.1, skfuzzy 0.4.2):

```
import pandas as pd;import numpy as np;import matplotlib.pyplot as plt;import seaborn as sns;from scipy import stats
data=pd.read_excel('GLDS-530_rna-seq_TGB_050_64samples_3group_total-count.xlsx');data_clean=data.dropna()
print(data_clean.describe())
sns.boxplot(data=data_clean);plt.xticks(rotation=45);plt.ylabel('Expression Levels');plt.show()
```

```
       Experiment - Range (original values)  \
count                          49950.000000
mean                             165.618779
std                             2608.284198
min                                0.000000
25%                                0.000000
50%                                0.000000
75%                               84.000000
max                           277978.000000

       Experiment - IQR (original values)  \
count                        49950.000000
mean                            36.490531
std                            452.929190
min                              0.000000
25%                              0.000000
50%                              0.000000
75%                              8.000000
max                          47424.000000

       Experiment - Difference (original values)  \
count                               49950.000000
mean                                  -20.786709
std                                   638.901371
min                                -71605.442029
25%                                    0.000000
50%                                    0.000000
75%                                    0.000000
max                                 6103.855072

       Experiment - Fold Change (original values)   Pre - Means  \
count                                49950.000000  49950.000000
mean                                     1.383346     35.759667
std                                     12.587598    361.617672
min                                   -299.294118      0.000000
25%                                      1.000000      0.000000
50%                                      1.000000      0.000000
75%                                      1.000000      7.294118
max                                    633.391304  29762.941176

       Flight - Means  Post - Means
count    49950.000000  49950.000000
mean        47.579946     27.306799
std        783.483626    234.095884
min          0.000000      0.000000
25%          0.000000      0.000000
50%          0.000000      0.000000
75%          5.041667      8.869565
max      82651.833333  26656.521739
```

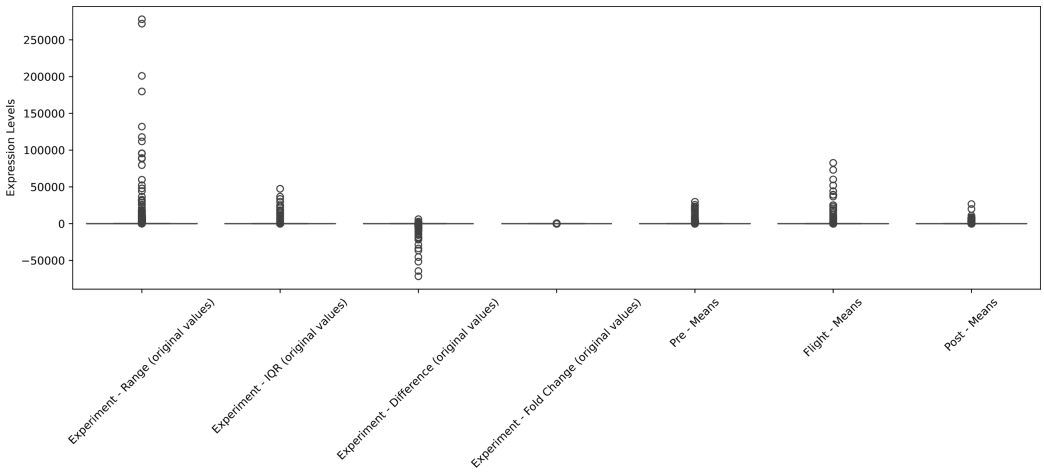


Figure 1. *Graph from GLDS-530_rna-seq_TGB_050_64samples_3group_totalcount.xlsx*

Figure 1 displays various statistical measures for a dataset of gene expression. Each column represents a different metric, such as range, interquartile range (IQR), difference, fold change, and averages for different experiment phases (pre-flight, during flight, and post-flight). The columns represent the median of the data, and the points indicate potential outliers, signifying notable variations in expression that could be biologically significant. The presence of extreme values in the "Fold Change" column suggests that some genes exhibit very high or low changes in expression in response to the experiment.

Now, we will obtain descriptive statistics using the following code:

```
import pandas as pd;import numpy as np;import matplotlib.pyplot as plt
data=pd.read_excel('GLDS-530_rna-seq_TGB_050_64samples_3group_totalcount.xlsx');data=pd.DataFrame(data)
descriptive_stats=data.describe();print(descriptive_stats)
```

Results:

	Experiment - Range (original values)	...	Post - Means
count	49950.000000	...	49950.000000
mean	165.618779	...	27.306799
std	2608.284198	...	234.095884
min	0.000000	...	0.000000
25%	0.000000	...	0.000000
50%	0.000000	...	0.000000
75%	84.000000	...	8.869565
max	277978.000000	...	26656.521739

The presence of outliers is particularly notable in this data set, given the high maximum value compared to the average and median. This could imply the presence of a few genes with very high changes in expression under experimental conditions.

ANOVA Test

```
import pandas as pd;from scipy import stats
data=pd.read_excel('GLDS-530_rna-seq_TGB_050_64samples_3group_totalcount.xlsx')
f_value,p_value=stats.f_oneway(data['Pre - Means'],data['Flight - Means'],data['Post - Means'])
print(f"ANOVA results: F={f_value}, p={p_value}")

ANOVA results: F=19.233218483262075, p=4.4467851020215725e-09
```

The ANOVA test results suggest statistically significant differences in gene expression between at least two flight conditions (pre, during, and post). The F-value measures the variance among the group means, and a large value typically indicates a significant difference.

The p-value is very small (less than 0.05), allowing us to reject the null hypothesis that there are no significant differences in gene expression among the groups.

Tukey Honestly Significant Difference (HSD) Test

```
import pandas as pd;from statsmodels.stats.multicomp import pairwise_tukeyhsd
data=pd.read_excel('GLDS-530_rna-seq_TGB_050_64samples_3group_totalcount.xlsx',sheet_name='64samples_3group_totalcount')
melted_data=pd.melt(data,id_vars=['Feature ID'],
value_vars=['Pre - Means',' Flight - Means',' Post - Means'],var_name='Condition',value_name='Value')
melted_data=melted_data[pd.to_numeric(melted_data['Value'],errors='coerce').notnull()]
tukey=pairwise_tukeyhsd(endog=melted_data['Value'],groups=melted_data['Condition'],alpha=0.05)
print(tukey.summary())
```

Results:

```
=====================================================================
  group1 group2 meandiff p-adj lower upper reject
---------------------------------------------------------------------
Flight - Means Post - Means -17.4404 0.0 -24.0616 -10.8191 True
Flight - Means Pre - Means -10.1812 0.0009 -16.8024 -3.56 True
  Post - Means Pre - Means 7.2592 0.0275 0.6379 13.8804 True
---------------------------------------------------------------------
```

The Tukey HSD test results indicate statistically significant differences in the means between the groups compared across the flight phases (pre, during, and post). Here is the breakdown of what each row signifies:

Flight - Means vs. Post - Means. The mean difference between the flight and post-flight phases is -17.4404, and this difference is statistically significant with an adjusted p-value of 0.0 (less than the significance level of 0.05), thus rejecting the null hypothesis of equal means.

Flight - Means vs. Pre - Means. The mean difference between the flight and pre-flight phases is -10.1812, which is also statistically significant with an adjusted p-value of 0.0009.

*Post - Means vs. Pre - Means***.** The mean difference between the post-flight and pre-flight phases is 7.2592, and while closer to the limit, it remains significant with an adjusted p-value of 0.0275.

In all cases, the "reject" column is "True," indicating that the Tukey test found significant differences between the means of the compared groups and, therefore, rejects the hypothesis that the means are equal for those pairs of conditions. This analysis suggests that the flight conditions (pre-, during, and post-) significantly affect the gene expression of the genes studied.

The results indicate that outliers have been identified in all three conditions: pre-flight, during flight, and post-flight, based on a Z-score. A Z-score greater than 3 or less than -3 is commonly considered a criterion for identifying outliers in a dataset.

The genes *ACTB*, *ACTG1*, and others listed here exhibit an expression significantly different from the mean, which may indicate specialized regulation in response to space flight conditions. These findings could be the starting point for a more detailed investigation into the functions of these genes and their potential relevance to adaptation to space.

Outliers

```
import pandas as pd;import numpy as np;import matplotlib.pyplot as plt;import seaborn as sns;from scipy import stats
from scipy.stats import zscore
data=pd.read_excel('GLDS-530_rna-seq_TGB_050_64samples_3group_totalcount.xlsx');data=data.dropna()
for column in ['Pre - Means',' Flight - Means',' Post - Means']:data[f'z_score_{column}']=zscore(data[column])
outliers={}
```

```
for column in ['Pre - Means','Flight - Means','Post - Means']:outliers[column]=data[np.abs(data[f'z_score_{column}'])>3]
for column in outliers:
  print(f"Outliers in {column}:")
  print(outliers[column])
```

Results:

```
Outliers in Pre - Means:
      Feature ID  ...  z_score_Post - Means
4471        ACTB  ...             84.975497
4484       ACTG1  ...             16.279435
4664     ADIPOR1  ...              4.123388
4911       AHNAK  ...             10.615404
6043     ANKRD12  ...              2.917627
...          ...  ...                   ...
55289        VIM  ...              5.221982
56682       YBX1  ...              8.323864
56721      YPEL5  ...              2.502519
56734      YWHAE  ...              2.760313
56749      YWHAZ  ...              7.191095
[187 rows x 11 columns]
Outliers in Flight - Means:
      Feature ID  ...  z_score_Post - Means
4471        ACTB  ...             84.975497
4484       ACTG1  ...             16.279435
4911       AHNAK  ...             10.615404
6837     ARHGDIB  ...              7.669722
7370         B2M  ...             34.392967
...          ...  ...                   ...
54398      TUBB1  ...              4.481847
54722        UBC  ...              8.503279
55238        VCL  ...              3.164834
56721      YPEL5  ...              2.502519
56749      YWHAZ  ...              7.191095
[97 rows x 11 columns]

Outliers in Post - Means:
      Feature ID  ...  z_score_Post - Means
4471        ACTB  ...             84.975497
4484       ACTG1  ...             16.279435
4512       ACTR2  ...              3.540195
4513       ACTR3  ...              3.019593
4664     ADIPOR1  ...              4.123388
...          ...  ...                   ...
55524       WDR1  ...              3.124344
55654       WNK1  ...              4.520293
56682       YBX1  ...              8.323864
56695       YBX3  ...              3.712367
56749      YWHAZ  ...              7.191095
[220 rows x 11 columns]
```

Biological Relevance of the *ACTB* Gene

We start with the record[1] of the *ACTB* gene, and compare it with the *Vectorless Gravity Effect on T Cell Activation*[2] study to verify its biological relevance(Figure 2).

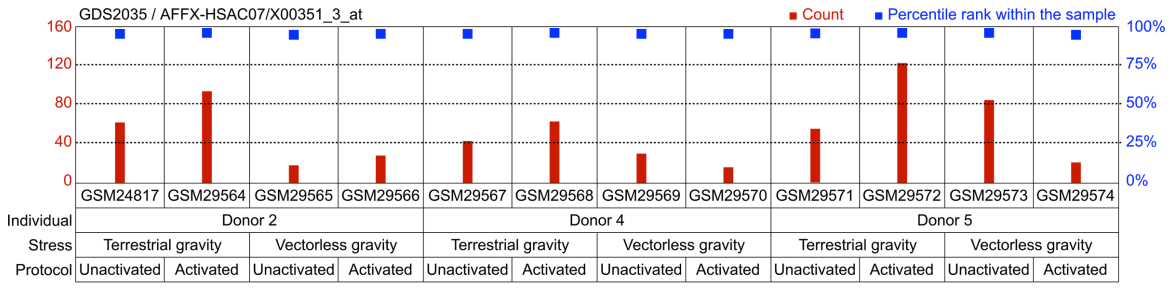


Figure 2. Profile: GDS2035 / AFFX-HSAC07/X00351_3_at. Title: Vectorless gravity effect on T cell activation. Organism: Homo sapiens.

```
Feature ID   Experiment - Range (original values)       Experiment - IQR (original values) Experiment  -
Difference (original values)
Experiment - Fold Change (original values)      Pre - Means      Flight - Means    Post - Means
ACTB 95743    14532    -19202.4365942029-1.9640008854470225668.2941176471 39121.9583333333
    19919.5217391304
```

Extracting the specific data of the ACTB gene:

```
GSM24817                                Donor 2 1g 0 hr  62.0225  98
ID_REF                                  Stat Pairs       Stat Pairs Used  VALUE
                                        ABS_CALL         DETECTION P-VALUE
AFFX-HSAC07/X00351_3_at                 20       20      62.022472        P
0.00007
GSM29564                                Donor 2 1g 4 hr  93.9682  99
ID_REF                                  Stat Pairs       Stat Pairs Used  VALUE
                                        ABS_CALL DETECTION P-VALUE
AFFX-HSAC07/X00351_3_at                 20       20      93.968155        P
0.000052
GSM29565                                Donor 2 vg 0 hr  17.8095  97
ID_REF                                  Stat Pairs       Stat Pairs Used  VALUE
                                        ABS_CALL DETECTION P-VALUE
AFFX-HSAC07/X00351_3_at                 20       20      17.809526        P
0.00007
GSM29566                                Donor 2 vg 4 hr  27.963   98
ID_REF                                  Stat Pairs       Stat Pairs Used  VALUE
                                        ABS_CALL DETECTION P-VALUE
AFFX-HSAC07/X00351_3_at                 20       20      27.962961        P
0.00007
GSM29567                                Donor 4 1g 0 hr  42.6353  98
ID_REF                                  Stat Pairs       Stat Pairs Used  VALUE
                                        ABS_CALL DETECTION P-VALUE
AFFX-HSAC07/X00351_3_at                 20       20      42.635292        P
0.000052
GSM29568                                Donor 4 1g 4 hr  63.1515  99
ID_REF                                  Stat Pairs       Stat Pairs Used  VALUE
                                        ABS_CALL DETECTION P-VALUE
AFFX-HSAC07/X00351_3_at                 20       20      63.151516        P
0.000052
GSM29569                                Donor 4 vg 0 hr  29.6474  98
ID_REF                                  Stat Pairs       Stat Pairs Used  VALUE
                                        ABS_CALL DETECTION P-VALUE
AFFX-HSAC07/X00351_3_at                 20       20      29.647434        P
0.000044
GSM29570                                Donor 4 vg 4 hr  15.5854  98
ID_REF                                  Stat Pairs       Stat Pairs Used  VALUE
                                        ABS_CALL DETECTION P-VALUE
AFFX-HSAC07/X00351_3_at                 20       20      15.585366        P
0.000052
GSM29571                                Donor 5 1g 0 hr  54.9206  99
ID_REF                                  Stat Pairs       Stat Pairs Used  VALUE
                                        ABS_CALL DETECTION P-VALUE
AFFX-HSAC07/X00351_3_at                 20       20      54.92063 P       0.000052
GSM29572                                Donor 5 1g 4 hr  122.679  99
ID_REF                                  Stat Pairs       Stat Pairs Used  VALUE
                                        ABS_CALL DETECTION P-VALUE
```

```
AFFX-HSAC07/X00351_3_at                 20      20      122.67858       P
0.000044
GSM29573                                Donor 5 vg 0 hr 85.0396 99
ID_REF                                  Stat Pairs      Stat Pairs Used VALUE
ABS_CALL DETECTION P-VALUE
AFFX-HSAC07/X00351_3_at                 20      20      85.0396 P       0.00007
GSM29574                                Donor 5 vg 4 hr 21.4211 97
ID_REF                                  Stat Pairs      Stat Pairs Used VALUE
ABS_CALL DETECTION P-VALUE
AFFX-HSAC07/X00351_3_at                 20      20      21.421053       P
0.00006
```

The graphs and values indicate differences in the expression of the *ACTB* gene under terrestrial gravity and microgravity (or null vectorial gravity) conditions. The biological relevance of these data can be confirmed because:

- All values have an 'ABS_CALL' of 'P,' indicating that all samples' gene expression is detectable and significant. The 'DETECTION P-VALUES' are also very low, suggesting an extremely low probability of these being false positives.
- There is a clear trend if we compare expression values in conditions of terrestrial gravity and microgravity: the expression of the *ACTB* gene tends to be lower under microgravity, which is evident in the decreased expression values in samples exposed to microgravity.
- The *ACTB* gene encodes beta-actin, a protein part of the cytoskeleton, and plays a critical role in cellular structure, motility, and signaling. Changes in its expression could be related to cellular adaptations to a microgravity environment.

Given that the project focuses on analyzing the effects of microgravity and space radiation on RNA using quantum simulations and unconventional logic, these data are relevant as they show that microgravity can significantly influence the expression of a gene involved in fundamental cellular functions. This suggests that we can further explore how these conditions alter gene expression and the implications for the health and biology of astronauts.

Quantum Circuit

Here is an alternative for analyzing the expression of the *ACTB* gene using a quantum computer:

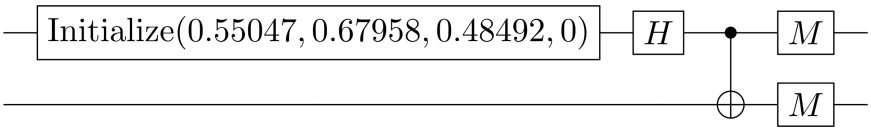


Figure 3. *Quantum circuit for ACTB analysis.*

It is important to highlight that this simplification focused on the *ACTB* gene. Still, it can be scaled to analyze more genes depending on the capabilities of available quantum computers.The quantum gates employed, specifically the Hadamard (H) and Controlled NOT (CNOT) gates, play pivotal roles in manipulating qubit states, which are crucial for the quantum simulations of gene expression.

The Hadamard gate operates on a single qubit and transforms it into a superposition of states, giving equal probability to being measured as either state $|0\rangle$ or $|1\rangle$. The matrix below gives a representation:

$$H = \frac{1}{\sqrt{2}} \begin{pmatrix} 1 & 1 \\ 1 & -1 \end{pmatrix}$$

The CNOT gate is a two-qubit operation where one qubit acts as a control and the other as a target. If the control qubit is in state $|1\rangle$, the target qubit is flipped; otherwise, it remains unchanged. This entangling operation is foundational for quantum computing and can be represented by the matrix:

$$\text{CNOT} = \begin{pmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 1 & 0 \end{pmatrix}$$

Incorporating these gates within our quantum circuits has enabled us to simulate and analyze the potential effects of spaceflight on gene expression. Diagrams of the quantum circuits used, provided, alongside the matrices above, offer a dual perspective (visual and mathematical) of the operations performed during our simulations.

```
from qiskit import QuantumCircuit
# Normalized amplitudes for the quantum state
quantum_state=[0.5505, 0.6796, 0.4849, 0]
# Creating a quantum circuit with 2 qubits
qc=QuantumCircuit(2)
# Initializing the quantum state with the calculated amplitudes
qc.initialize(quantum_state, [0, 1])
# We can add other gates and operations as needed
# For example, we can add a Hadamard gate to the first qubit
qc.h(0)
# Add a CNOT gate to entangle the qubits
qc.cx(0, 1)
# Circuit visualization
print(qc.draw(output='text'))
# If you need to measure the qubits, you can add measurement operations
qc.measure_all()
# Circuit visualization with measurements
print(qc.draw(output='text'))
# Manually adjust the amplitudes to force normalization to be exactly 1
# If the normalization is slightly greater than 1, we reduce the amplitudes a bit
if normalization_check > 1:
  # Reduce the amplitudes proportionally
  scale_factor=np.sqrt(normalization_check)
  alpha /= scale_factor
  beta /= scale_factor
  gamma /= scale_factor
# Now we recalculate delta to ensure that normalization is exactly 1
normalization_check_recalculated=np.sum([np.abs(alpha)**2, np.abs(beta)**2, np.abs(gamma)**2])
if normalization_check_recalculated < 1:
  delta=np.sqrt(1 - normalization_check_recalculated)
else:
  # If the recalculated normalization is exactly 1 (or rounds to 1), then we don't need delta
  delta=0
# New adjusted quantum state
quantum_state_adjusted=[alpha, beta, gamma, delta]
# Final verification of normalization after adjustment
normalization_check_final_adjusted=np.sum(np.abs(np.array(quantum_state_adjusted))**2)
normalization_check_final_adjusted, quantum_state_adjusted
```

The circuit initializes two qubits in a specific quantum state based on the data of the *ACTB* gene, applies a Hadamard gate to the first qubit to create a superposition, then entangles both qubits with a CNOT gate, and finally measures both qubits. With this circuit, simulations can be conducted to investigate the probabilities of different measurement outcomes, which could provide information on how gene expression states are affected by space flight conditions or use it as a basis for more complex quantum algorithms.To simulate the circuit and obtain results using the qasm_simulator, we can use:

```
from qiskit import Aer, execute; from qiskit.visualization import plot_histogram
# Execute the circuit on the quantum simulator
simulator=Aer.get_backend('qasm_simulator')
# Perform the simulation, specifying the number of repetitions of the circuit (shots)
job=execute(qc, simulator, shots=1000)
```

```
# Obtain the results of the simulation
result=job.result()
# Obtain the counts of each result (the number of times each state was measured)
counts=result.get_counts(qc)
plot_histogram(counts)
```

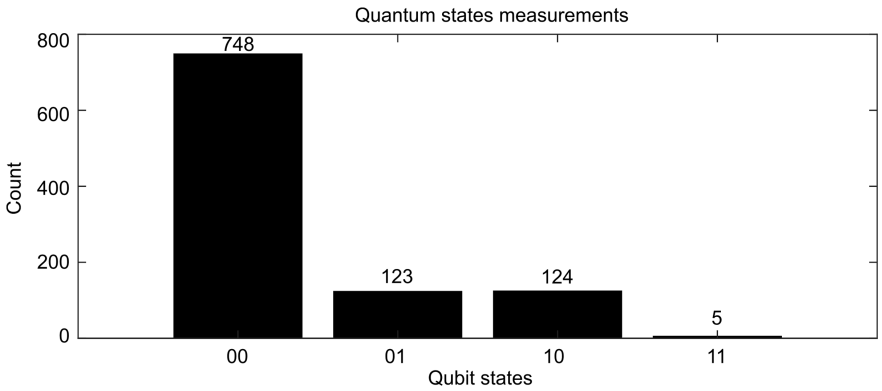


Figure 4. *Quantum circuit histogram.*

The histogram displays the distribution of measurement results after numerous circuit executions. The labels on the x-axis represent the states of the qubits at the time of measurement, where '00' means that both qubits were measured in the state $|0\rangle$, '01' means that qubit 0 was measured in $|0\rangle$ and qubit 1 in $|1\rangle$, and so on. The numbers on the y-axis represent the frequency of each observed result. In your simulation, the '00' state occurred much more frequently than the other states, indicating that the initial quantum state superposition had a higher probability of collapsing to this state during measurement.

To obtain the final state vector using the statevector_simulator:

```
# Execute the circuit on the statevector simulator
statevector_simulator=Aer.get_backend('statevector_simulator')
# Create a new circuit without measurements for the statevector simulation
qc_statevector=qc.remove_final_measurements(inplace=False)
job=execute(qc_statevector, statevector_simulator)
result=job.result()
# Obtain the final state vector of the circuit
statevector=result.get_statevector(qc_statevector)
print(statevector)
```

Results:

```
Statevector([0.86977824-5.88490403e-17j,  0.34289227+0.00000000e+00j,  0.34289227+0.00000000e+00j,  -
0.09129953+5.88490403e-17j],dims=(2,2))
```

The final state vector describes the quantum state of the qubits just before measurement. In Dirac notation, this state would be written as:

$$|\psi\rangle = 0.86978\,|00\rangle + 0.34289\,|01\rangle + 0.34289\,|10\rangle - 0.09130\,|11\rangle$$

This state is a superposition of the four base states with complex amplitudes. The squared amplitudes (ignoring the imaginary part, as it is very small and likely a result of numerical errors) give the probabilities of measuring each of the base states in a run of the circuit. For example, the probability of measuring the state '00' is $|0.86978|^2$, and so on for the other states.

The fact that the final state vector has non-zero amplitudes for all base states except '11', which has a small negative amplitude, means that the circuit has created a complex superposition of states. The outcome of any single measurement is uncertain. However, after many runs, as reflected in the histogram, the probability distribution of the measurement results becomes evident.

Analyzing these results can explain how the applied quantum gates (the Hadamard and

CNOT gates in this case) have affected the initial state and how the resulting superpositions and entanglements correspond to the probability of measuring certain states. This can be especially interesting when researching the effects of microgravity and space radiation on the RNA of astronauts if we relate these quantum states to specific biological or environmental conditions.

The biological relevance of the ACTG1 gene

To maintain simplicity in this project, we will focus on incorporating the *ACTG1* gene. In the dataset *Vectorless Gravity Effect on T Cell Activation,*[3] the *ACTG1* gene shows a variation in its expression between pre-flight, during flight, and post-flight phases, suggesting that the spaceflight environment affects the gene's expression.

The specific record from the study[1] is:

```
Feature ID   Experiment - Range (original values)
Difference (original values)
Experiment - Fold Change (original values)
  ACTG1
1.44459422210643
```

```
Experiment - IQR (original values) Experiment  -

Pre - Means       Flight - Means    Post - Means
10810    3515     -1706.44927536232-
4568.76470588235  5544.66666666667
3838.21739130435
```

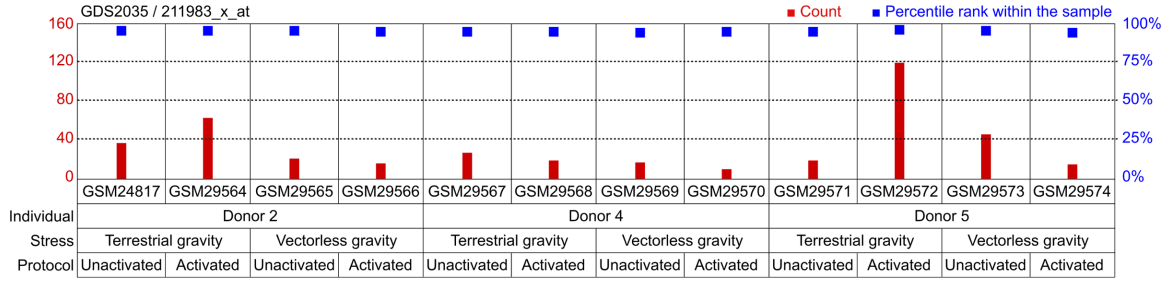


Figure 5. Profile: GDS2035 / 211983_x_at. Title: Vectorless gravity effect on T cell activation. Organism: Homo sapiens.

Extracting the specific data of the *ACTG1* gene:

```
GSM24817                                  Donor 2 1g 0 hr  37.0449  98
ID_REF                                    Stat Pairs       Stat Pairs Used  VALUE
                                          ABS_CALL DETECTION P-VALUE
211983_x_at                               11       11      37.044945        P
                                          0.000244
GSM29564                                  Donor 2 1g 4 hr  62.7325  98
ID_REF                                    Stat Pairs       Stat Pairs Used  VALUE
                                          ABS_CALL DETECTION P-VALUE
211983_x_at                               11       11      62.732487        P
                                          0.000244
GSM29565                                  Donor 2 vg 0 hr  21.4762  98
ID_REF                                    Stat Pairs       Stat Pairs Used  VALUE
                                          ABS_CALL DETECTION P-VALUE
211983_x_at                               11       11      21.47619 P       0.00293
GSM29566                                  Donor 2 vg 4 hr  15.6111  97
ID_REF                                    Stat Pairs       Stat Pairs Used  VALUE
                                          ABS_CALL DETECTION P-VALUE
211983_x_at                               11       11      15.611112        P
                                          0.000244
GSM29567                                  Donor 4 1g 0 hr  27.1647  97
ID_REF                                    Stat Pairs       Stat Pairs Used  VALUE
                                          ABS_CALL DETECTION P-VALUE
211983_x_at                               11       11      27.164705        P
                                          0.000244


GSM29568                                  Donor 4 1g 4 hr  18.5455  97
ID_REF                                    Stat Pairs       Stat Pairs Used  VALUE
                                          ABS_CALL DETECTION P-VALUE
```

```
211983_x_at                                    11      11      18.545456       P
0.000732

GSM29569                                       Donor 4 vg 0 hr  16.5577  96
ID_REF                                         Stat Pairs       Stat Pairs Used  VALUE
ABS_CALL DETECTION P-VALUE

211983_x_at                                    11      11      16.55769 P       0.000244
GSM29570                                       Donor 4 vg 4 hr  9.87805  97
ID_REF                                         Stat Pairs       Stat Pairs Used  VALUE
ABS_CALL DETECTION P-VALUE

211983_x_at                                    11      11      9.878049 P       0.010742
GSM29571                                       Donor 5 1g 0 hr  18.7143  97
ID_REF                                         Stat Pairs       Stat Pairs Used  VALUE
ABS_CALL DETECTION P-VALUE

211983_x_at                                    11      11      18.714285       P
0.000244

GSM29572                                       Donor 5 1g 4 hr  120.345  99
ID_REF                                         Stat Pairs       Stat Pairs Used  VALUE
ABS_CALL DETECTION P-VALUE

211983_x_at                                    11      11      120.345245      P
0.000244

GSM29573                                       Donor 5 vg 0 hr  45.7426  98
ID_REF                                         Stat Pairs       Stat Pairs Used  VALUE
ABS_CALL DETECTION P-VALUE

211983_x_at                                    11      11      45.742573       P
0.000244

GSM29574                                       Donor 5 vg 4 hr  14.9298  96
ID_REF                                         Stat Pairs       Stat Pairs Used  VALUE
ABS_CALL DETECTION P-VALUE

211983_x_at                                    11      11      14.929825       P
0.000244
```

The data[3] show significant differences in the expression of the *ACTG1* gene under terrestrial gravity versus microgravity conditions, which is consistent with the changes observed in gene expression in astronauts, reinforcing the idea that microgravity can influence the regulation of this gene:

In both datasets, the presence of an 'ABS_CALL' of 'P' and low 'DETECTION P-VALUES' suggest that the gene detection is consistent and significant.

The *ACTG1* gene encodes gamma-actin, which is crucial in the structure of the cytoskeleton and cellular morphology. Changes in its expression could have important implications for how cells respond to microgravity and space radiation.

Given that the cytoskeleton is fundamental for cellular integrity and signaling, alterations in the expression of *ACTG1* could contribute to microgravity's adverse effects on astronauts' health.

Correlation of ACTB and ACTG1

Currently, we have very limited data for Pearson correlation, but I leave the code for future correlations with other possible measurements or other possible genes:

```
import pandas as pd
import numpy as np
from scipy.stats import pearsonr
# Define gene expression data for ACTB and ACTG1 under different conditions
# These data are averages of pre-flight, during flight, and post-flight values from the first study.
actb_exp=[25668.2941176471, 39121.9583333333, 19919.5217391304] # ACTB
actg1_exp=[4568.76470588235, 5544.66666666667, 3838.21739130435] # ACTG1
# Gene expression data for ACTB and ACTG1 under terrestrial gravity and vectorless conditions from the
second study.
# The data are organized as [1g 0hr, 1g 4hr, vg 0hr, vg 4hr] for both genes.
actb_grav=[62.022472, 93.968155, 17.809526, 27.962961] # ACTB terrestrial gravity and microgravity
actg1_grav=[37.044945, 62.732487, 21.47619, 15.611112] # ACTG1 terrestrial gravity and microgravity
# First study data for ACTB and ACTG1 during pre-flight, flight, and post-flight phases
# The data are already in the correct format with the same length
correlation_study1=pearsonr(actb_exp, actg1_exp)
# Organize the second study's data by similar conditions (1g and vectorless gravity)
# Here we are taking the averages for the similar conditions for each gene
```

```
actb_1g_avg=np.mean(actb_grav[:2]) # Average of ACTB for terrestrial gravity
actb_vg_avg=np.mean(actb_grav[2:]) # Average of ACTB for vectorless gravity
actg1_1g_avg=np.mean(actg1_grav[:2]) # Average of ACTG1 for terrestrial gravity
actg1_vg_avg=np.mean(actg1_grav[2:]) # Average of ACTG1 for vectorless gravity
# Calculate the correlation for terrestrial gravity and vectorless gravity conditions from the second study
correlation_study2_1g=pearsonr([actb_1g_avg, actb_vg_avg], [actg1_1g_avg, actg1_vg_avg])
correlation_study1, correlation_study2_1g
```

Results:

```
(PearsonRResult(statistic=0.9895316566632417,  p-value=0.09219634216277754),  PearsonRResult(statistic=1.0, p-value=1.0))
```

Quantum logic

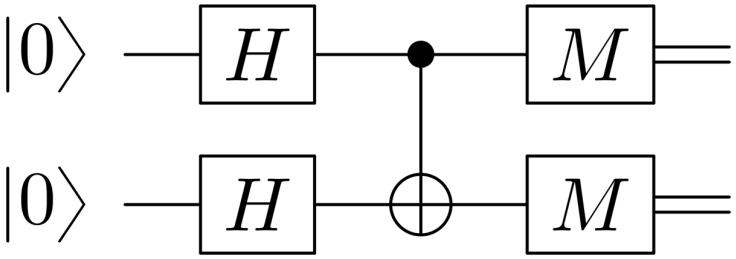


Figure 6. *Quantum circuit for analyzing gene expression correlations between ACTB and ACTG1.*

```
from qiskit import QuantumCircuit, Aer, execute
from qiskit.visualization import plot_histogram
# Create a quantum circuit with 2 qubits
qc=QuantumCircuit(2)
# Initialize the qubits in a superposition to represent uncertain states of gene expression
qc.h([0, 1])  # Apply Hadamard gate to both qubits
# Entangle the qubits to represent correlations between ACTB and ACTG1
qc.cx(0, 1)  # CNOT gate
# Add measurements at the end of the circuit
qc.measure_all()
# Visualize the circuit
print(qc.draw(output='text'))
# Quantum circuit simulation
simulator=Aer.get_backend('qasm_simulator')
job=execute(qc, simulator, shots=1000)
result=job.result()
# Use the correct identifier here. In the case of a list of circuits,
# it is necessary to specify the index or label of the circuit.
counts=result.get_counts(qc)
plot_histogram(counts)
```

The code includes adding measurements to the circuit, which is necessary to obtain the simulation results. It ensures the results are retrieved correctly using the quantum circuit object as a reference.

In a quantum circuit with two Hadamard gates followed by a CNOT gate, we would expect to see a uniform distribution across all states if there were no errors or noise in the system. A slight variation in the heights of the bars is expected due to statistical variability, especially if the number of runs (shots) is not very high.

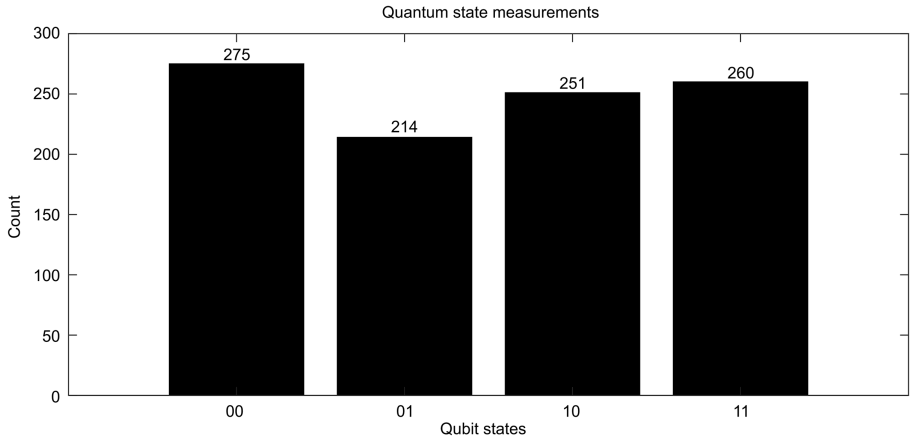


Figure 7. *Histogram of the code with quantum logic.*

The histogram shows the measurements of your quantum circuit after 1000 executions (shots). The bars represent the frequency (count) of each possible state of the qubits after measurement. The results are distributed among the four possible states: 00, 01, 10, and 11. The similarity in the height of the bars suggests that each state has a similar probability of being measured, which is expected since the two qubits were initialized in an equal superposition and then entangled, maintaining a uniform distribution of probabilities.

This result is consistent with the operation of the Hadamard gate, which creates a superposition of states $|0\rangle$ and $|1\rangle$ for each qubit, followed by the CNOT gate that entangles the qubits. The entanglement means that the measurement of one qubit affects the outcome of the other qubit's measurement. Still, as the Hadamard gate creates an equal superposition, the probabilities of measuring each combination of states remain the same.

These results can serve as a basis for interpretation in fuzzy logic, where each quantum state could be associated with a fuzzy set representing different gene expression levels. The next step is to define how these quantum measurements translate into terms of fuzzy logic and how we can use that interpretation to conclude gene expression under spaceflight conditions.

Fuzzy Logic

In this section, we establish a fuzzy inference system to interpret the relative gene expression levels of the *ACTB* and *ACTG1* genes. Here, the value 'X' denotes the relative expression of these genes, quantified against control samples. This approach allows for a nuanced assessment of gene expression variations under spaceflight conditions and provides a basis for interpreting the biological significance of the observed changes.

First, we will define the universe of discourse and the membership functions for the gene expression levels. Then, we will establish the fuzzy rules that relate flight conditions to expression levels. Finally, we will perform fuzzy inference to calculate gene expression under different flight conditions.

```
import numpy as np;import skfuzzy as fuzz;from skfuzzy import control as ctrl
# Universe of discourse for gene expression, for example from 0 to 100
expresion_ACTB=ctrl.Consequent(np.arange(0, 101, 1), 'expresion_ACTB')
expresion_ACTG1=ctrl.Consequent(np.arange(0, 101, 1), 'expresion_ACTG1')
# Definition of membership functions for ACTB
expresion_ACTB['low']=fuzz.trimf(expresion_ACTB.universe, [0, 0, 50])
expresion_ACTB['medium']=fuzz.trimf(expresion_ACTB.universe, [25, 50, 75])
expresion_ACTB['high']=fuzz.trimf(expresion_ACTB.universe, [50, 100, 100])
# Definition of membership functions for ACTG1
expresion_ACTG1['low']=fuzz.trimf(expresion_ACTG1.universe, [0, 0, 50])
expresion_ACTG1['medium']=fuzz.trimf(expresion_ACTG1.universe, [25, 50, 75])
expresion_ACTG1['high']=fuzz.trimf(expresion_ACTG1.universe, [50, 100, 100])
# Definition of the universe of discourse and membership functions for flight conditions
condition=ctrl.Antecedent(np.arange(0, 3, 1), 'condition')
condition['pre_flight']=fuzz.trimf(condition.universe, [0, 0, 1])
condition['during_flight']=fuzz.trimf(condition.universe, [1, 1, 2])
```

```
condition['post_flight']=fuzz.trimf(condition.universe, [2, 2, 2])
# Definition of rules
rule1=ctrl.Rule(antecedent=(condition['pre_flight']), consequent=expresion_ACTB['medium'])
rule2=ctrl.Rule(antecedent=(condition['during_flight']), consequent=expresion_ACTB['high'])
rule3=ctrl.Rule(antecedent=(condition['pre_flight']), consequent=expresion_ACTG1['low'])
rule4=ctrl.Rule(antecedent=(condition['during_flight']), consequent=expresion_ACTG1['medium'])
# Creation of the control system and simulation
control_system=ctrl.ControlSystem([rule1, rule2, rule3, rule4])
simulation=ctrl.ControlSystemSimulation(control_system)
# Example simulation for a specific flight condition
simulation.input['condition']=1 # For example, 1 for 'during_flight'
simulation.compute()
# Result
result_ACTB=simulation.output['expresion_ACTB']
result_ACTG1=simulation.output['expresion_ACTG1']
print(f"Gene expression result of ACTB: {result_ACTB}")
print(f"Gene expression result of ACTG1: {result_ACTG1}")
```

Results:

```
Gene expression result of ACTB: 83.33333333333336
Gene expression result of ACTG1: 50.0
```

The value of ACTB=83.33 suggests that under the specified condition of 'during flight' (value 1), the expression of the *ACTB* gene is high. Fuzzy logic interprets this condition as more conducive to elevated *ACTB* gene expression, which may reflect a significant biological response to spaceflight conditions, such as microgravity or exposure to specific radiations.

The *ACTG1* value of 50.0 indicates that the ACTG1 gene expression is at a medium level under the same "during flight" condition. This suggests that the expression of *ACTG1*, though affected by spaceflight conditions, does not show as extreme a variation as *ACTB*, according to the fuzzy logic model.

These results provide a quantitative interpretation of how spaceflight conditions might influence the expression of these specific genes. In the project context, this approach can help anticipate changes in gene expression and better understand the underlying biological mechanisms affected by the spaceflight environment. Moreover, these models can be adjusted or refined as more experimental data becomes available, allowing for more precise analyses.

Discussion

In this study, I included individuals with and without known mutations in the *ACTB* and *ACTG1* genes, despite these genes being typical housekeeping genes with stable expression under terrestrial conditions. The rationale behind this decision lies in the exploratory nature of our research, aiming to understand how the unique environment of spaceflight affects gene expression more inclusively and comprehensively. While mutations in these genes are associated with various diseases and could potentially influence baseline expression levels, their inclusion allows us to capture a broader range of gene expression profiles. This approach offers a more nuanced understanding of the complex interactions between genetic predispositions and the spaceflight environment.

Notably, the spaceflight conditions might differentially impact gene expression in individuals with these mutations, providing novel insights into the cellular adaptations and stress responses in space. Our findings, therefore, contribute to a more comprehensive picture of gene expression dynamics in spaceflight, albeit with the caveat that variations due to genetic differences need to be carefully considered when interpreting the results. This study sets the groundwork for future targeted research to specifically investigate the impact of spaceflight on individuals with genetic variations in key housekeeping genes like *ACTB* and *ACTG1*.

The research has highlighted the importance of considering interdisciplinary approaches in studying space effects on human biology. The use of quantum computing and fuzzy logic in this context is novel and poses possibilities for future research. However, it must be acknowledged that the models and simulations used are simplifications and may not fully capture the complexity of biological systems. Furthermore, although significant, the correlation between gene expression data and specific spaceflight conditions does not imply direct causality.

Therefore, future studies are suggested to explore these effects with a broader approach, incorporating a more diverse range of genetic and environmental data. This study is an important starting point for understanding how human biology adapts to the space environment and lays the groundwork for deeper investigations in astrobiology and space medicine.

Conclusion

The analysis has demonstrated the feasibility of applying quantum simulations and fuzzy logic to analyze the effects of microgravity and space radiation on gene expression. The results suggest that specific genes like *ACTB* and *ACTG1* undergo significant changes in their expression under these unique conditions. Using a quantum circuit specifically designed to represent gene expression has provided a new perspective on how space conditions can affect biology at the molecular level. In addition, implementing fuzzy logic has allowed for a more nuanced interpretation of these changes, considering the variability and uncertainty inherent in biological data. This pioneering study provides valuable information about human adaptation to space and sets a precedent for future research that employs advanced computational approaches in space biology.

Conflict of Interest:

The authors declare no conflict of interest. For a signed statement, please contact the journal office at editor@precisionnanomedicine.com.

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