BDS Brazilian
Dental Science

Dear Carlos M Ardila, Pradeep Kumar Yadalam:

Your submission Stochastic Gene Expression Modeling Using the Gillespie Algorithm: Insights into Oral Cancer Genomic Variability to Brazilian Dental Science, has been revised and according to reviewers' comments, there are questions to be addressed and/or points to be clarified/corrected.
Please answer the reviewers considerations point-by-point in a separate document and also please make all the corrections in the text highlighted in yellow.

Deadline: 30 days

Thank you for considering Brazilian Dental Science for publishing your research.
We are looking forward the revised version of you manuscript.

Sincerely,

Reviewer D:
Recommendation: Accept Submission

Questionnaire

Does the manuscript contain new and significant information to justify publication?*

Yes

Does the Abstract (Summary) clearly and accurately describe the content of the article?

Yes

Is the problem significant and concisely stated?

Yes

Are the methods or research design described comprehensively? Is the statistical analysis adequate?

Yes

Are the interpretations and conclusions justified by the results?

Yes

Is adequate reference made to other work in the field?

Yes

Is the language acceptable?

Yes

Manuscript Structure

Length of article is:*

Adequate

Number of tables is:

Adequate

Number of figures is:

Adequate

Please state any conflict(s) of interest that you have in relation to the review of this paper (state “none” if this is not applicable).

None.

Rating

Interest*

Excellent

Quality

Good

Originality

Good

Overall

Good

Recommendation

Accept

Would you be willing to review a revision of this manuscript?

Yes

Comments

Comments to the Author

The authors presented an interdisciplinary study that combines advanced computational techniques, molecular biology, and bioinformatics. They emphasize that the Gillespie algorithm enables the simulation of gene expression events, allowing researchers to examine probabilistic interactions between genes, regulatory elements, and environmental factors. This approach could be useful for identifying cellular subpopulations with distinct gene expression profiles, predicting resistance mechanisms, and discovering biomarkers for therapeutic efficacy, contributing to better outcomes in oral cancer treatment. This field of research may enhance our understanding of the relationship between genetics, environment, and cellular evolution.

Reviewer H:
Recommendation: Decline Submission

Questionnaire

Does the manuscript contain new and significant information to justify publication?*

Yes

Does the Abstract (Summary) clearly and accurately describe the content of the article?

Yes

Is the problem significant and concisely stated?

No

Are the methods or research design described comprehensively? Is the statistical analysis adequate?

No

Are the interpretations and conclusions justified by the results?

No

Is adequate reference made to other work in the field?

Yes

Is the language acceptable?

Yes

Manuscript Structure

Length of article is:*

Adequate

Number of tables is:

Adequate

Number of figures is:

Adequate

Please state any conflict(s) of interest that you have in relation to the review of this paper (state “none” if this is not applicable).

none

Rating

Interest*

Average

Quality

Average

Originality

Excellent

Overall

Average

Recommendation

Reject

Would you be willing to review a revision of this manuscript?

Yes

Comments

Comments to the Author

In the Materials and Methods section, the manuscript presents an extensive conceptual description of each bioinformatic analysis; however, it lacks clear and detailed information of analytical tools employed —details that would be expected in a methodological description, particularly in the “Analysis Framework” and “Gene Expression Analysis” subsections.

In the “Analysis Framework” section, the description remains largely conceptual and does not provide sufficient methodological detail for reproducibility. For example, the “Temporal Statistics Analysis” subsection states: “The study aims to analyze the change in mRNA levels and noise in gene expression over time using running averages, coefficients of variation, and line plots. It also compares theoretical mean and noise levels to observed data.” While this outlines the general analytical approach, it does not specify the software or programming environment used to implement the SSA, the exact variant of the algorithm (e.g., Gillespie’s direct method or modifications), parameter values and their sources, initial conditions, number of simulations, duration of runs, or convergence criteria. Furthermore, the statement “The study aims to analyze…” reflects research objectives rather than a precise methodology. Without these details, the analysis cannot be independently reproduced or critically evaluated.

On page 10, there is a “Type error,” and several paragraphs appear to be missing (e.g., “ate (k_degradation): 0.1This”). While this is not my primary area of expertise and I acknowledge that I may be mistaken or demanding more than the method realistically allows, my reading of the Discussion section gave me the impression that the authors were primarily presenting a literature review rather than engaging in a critical discussion of their own findings. In fact, it appears that the actual discussion of results only begins on page 17, with the sentence: “The study analyzed mRNA.” The authors state that stochastic models “can inform therapeutic strategies, improve personalized medicine outcomes, and enhance management and treatment”; however, based on the presented results, I did not perceive such implications, despite the use of a stochastic model. Moreover, the first full paragraph on page 18 contains relevant information but lacks appropriate references. Finally, I am left questioning why the authors did not employ their stochastic models to shed light on pathways that underpin tumorigenesis and metastasis.
