Advanced Computational Framework for Simulating Multiple Myeloma Proliferation Dynamics: Development, Calibration and Experimental Validation

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Abstract
Controlling cancer cell proliferation under controlled experimental conditions remains a complex challenge due to the intricate interplay of biological, mechanical, and biochemical factors involved. This work presents a computational framework for multiple myeloma proliferation calibrated and validated against experimental in vitro data, successfully reproducing the characteristic proliferation dynamics observed under both free-cell and hydrogel environments.

1. Introduction
Multiple myeloma (MM) is a hematological malignancy characterized by the uncontrolled proliferation of malignant plasma cells in the bone marrow [1]. The progression of the disease is strongly influenced by the mechanobiological conditions of the surrounding microenvironment [2], [3]. Traditional in vitro experiments in laboratory culture vessels often involve elevated economic costs and long experimental times, limiting the exploration of complex biological scenarios [4].

Computational modeling has emerged as a complementary approach for studying cancer proliferation through predictive *in silico* simulations [5], [6]. Recent advances in Computational Fluid Dynamics (CFD) and mechanobiological numerical models have enabled the simulation of increasingly complex biological systems [7], [8].

The present work focuses on the development, calibration, and experimental validation of a computational framework capable of reproducing the proliferation dynamics of multiple myeloma cell cultures under different experimental conditions while incorporating the influence of environmental mechanical interactions.

This work continues a research line previously explored by the author [2], [9].

2. Methods
The proposed computational framework was developed within the ANSYS Fluent environment integrating Computational Fluid Dynamics (CFD), Discrete Phase Modeling (DPM), and the Discrete Element Method (DEM) [6], [7]. Multiple myeloma cells were represented as discrete interacting particles, while the surrounding culture medium was modeled as a continuous phase.

The numerical framework integrates DPM for cellular individualization together with DEM for collision management and Hertzian-Dashpot contact interactions, enabling the simulation of mechanically regulated proliferation behavior and aggregate evolution [3], [6], [7], [9].

To reproduce biological proliferation dynamics, customized User-Defined Functions (UDFs) and additional computational routines developed in Visual Basic were implemented [3], [7]. A maturation index (MI) dynamically regulated the cellular cycle according to the frequency of mechanical contacts perceived by each cell.

The model was progressively calibrated and validated using experimental proliferation data obtained from laboratory vessel experiments [2], [10]. Two experimental conditions were considered during the calibration process: free-cell proliferation and hydrogel environments, allowing the analysis of how mechanical resistance influences cell growth and proliferation dynamics [2], [3].

3. Results and Discussion

The calibration and experimental validation of the proposed computational framework were successfully achieved using proliferation data obtained from laboratory vessel experiments. The resulting model accurately reproduced the experimental proliferation curves under both free-cell and hydrogel conditions as shown in Figures 1 and 2.

Under free-cell conditions, the framework replicated the characteristic exponential growth behavior observed experimentally. After extending the model to hydrogel microenvironments, the simulations reproduced the evolution of proliferation under mechanically constrained conditions, highlighting the influence of mechanical interactions on cell growth dynamics [3], [9].

Overall, the developed framework successfully reproduced the lag, exponential, and saturation phases observed experimentally, supporting its application in future predictive mechanobiological studies.

4. Conclusions

A computational framework for simulating multiple myeloma proliferation dynamics was successfully calibrated and validated under both free-cell and hydrogel conditions. The obtained model reproduced the characteristic proliferation behavior observed experimentally, supporting future applications involving vascular-inspired and mechanobiological environments while contributing to the reduction of experimental and animal-based studies.

Acknowledgements

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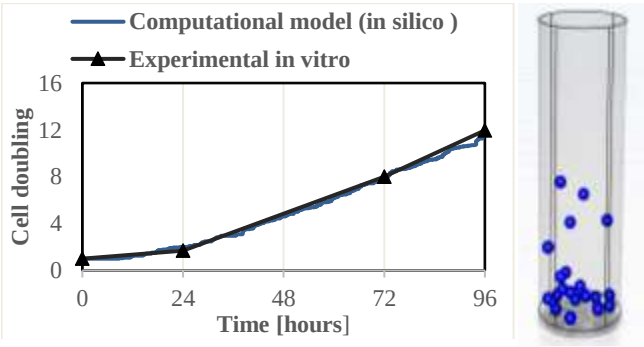

Figure 1. Computational and experimental *in vitro* cell doubling under free-cell conditions after 96h. Right: ANSYS snapshot at 19 h.

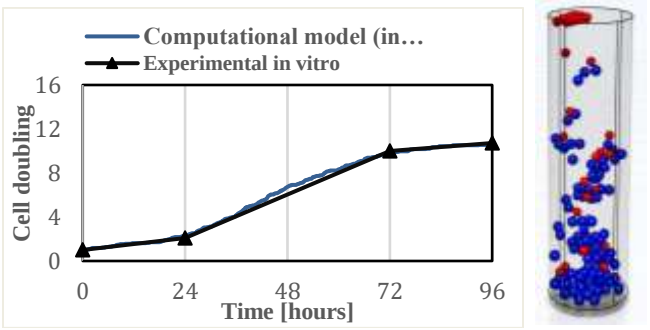

Figure 2. Computational and experimental *in vitro* cell doubling under hydrogel conditions after 96h. Right: ANSYS snapshot at 19 h. (blue: cells; red: hydrogel).